Bio-fabrication:

Experiments and Experiences in Ethics and Sciences

By

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Abstract

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Bio-fabrication: Experiments and Experiences in Ethics and Sciences provides an account of an experiment I undertook in ethics and anthropology as part of the International Open Facility Advancing Biotechnology, the BIOFAB. It offers an analysis of the facility's programmatic attempt to actualize a core claim of the new field of synthetic biology: that living beings can be conceived as collections of interoperable genetic components, constructed through rational design, standardized, and fabricated at scale. It provides a diagnosis of the scientific, vocational, and ethical limits of this endeavor. And demonstrates why, in the end, loyalty to truth and seriousness required an exit from the both the mode and stakes of my undertaking.

My experiment with the BIOFAB constituted a distinctive and final phase of a five-year project to design *Human Practices*, which began as part of the Synthetic Biology Engineering Research Center (SynBERC). Extending ontological and ethical lines of inquiry characteristic of an anthropology of the contemporary, I asked: how are researchers in the BIOFAB bringing things into the world? How are they naming these things, distributing, and modifying them? Equally important, what habits, dispositions, and capacities are being cultivated and managed in order to make such ontological work possible? And, most crucially, what is the price to be paid?

Following intensive participation-observation of the biologists whose task was to put into operation the BIOFAB's strategic vision, the dissertation examines a double-bind at the heart synthetic biology: those who are most capable of taking on the technical challenge of standardizing biological parts are also those least ready to fully commit themselves to such a vision for the future of bioengineering. The ethical and scientific challenge for these biologists was thus how to take a stance toward their work that would simultaneously allow them proceed with a technically difficult experiment, while distancing themselves from the lack of scientific seriousness often attributed to the BIOFAB's undertaking. As the thesis demonstrates, a similar challenge proved equally troublesome for me.

The dissertation concludes that the attempt to incorporate ethics and anthropology as defining elements of synthetic biology reactivates a typically modern problem. Despite efforts to remediate the relations of ethics and science, actual asymmetry in power between biologists and non-biologists encumbers such work. Crucially, the thesis shows that this problem is as characteristic of governance at the highest levels as it is the micro-practices of life in the BIOFAB. In the case of my experiment, such difficulties initially required raising a second-order question: how are asymmetries in power being formed and how might they be unsettled? Ultimately, however, they required an ethics of exit: how can persistent disconnections between power, truth, and ethics be productively refused and, where necessary, left behind?

Parrēsia ***is a human practice and a human risk.***

—Michel Foucault

To Paul Rabinow and Anthony Stavrianakis

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A PROLOGUE TO THE RECENT PAST

The Motion of Inquiry: Prior Determinations

> *I think we have here an injunction that is absolutely important and which corresponds somewhat…to what is found in the first texts, the first Platonic dialogues, concerning philosophy having to be not merely an activity of learning but also disciplined practice.*
>
> —Michel Foucault[1]

From January 2010 to March 2011 I conducted an intensive experiment as the director of Human Practices for a new research endeavor and venue in synthetic biology: the International Open Facility Advancing Biotechnology, or the BIOFAB as it is almost always called.[2] What follows in this thesis is a report on the first six months of that experiment, which were also the first six months of the BIOFAB's operations.

During this period of time the researchers at the BIOFAB addressed a core concern in a sustained fashion. That concern is whether, and to what extent, living systems can be conceived and constructed as collections of interoperable genetic components and whether, and to what extent, those components might be susceptible to scalable fabrication. To put it in terms used by the BIOFAB directors, the problem is the extent to which biological systems are susceptible, or can be made to be susceptible, to rational design. To put it in more philosophic terms, terms borrowed from George Canguilhem, the BIOFAB can be cast as addressing the long-standing problem of the relation of the living being and its milieu.[3] This problem, however, is now being taken up as a matter of design, refinement, and manufacture.

The BIOFAB's undertaking, it bears noting, is not the familiar fare of ontological reductionism, and its question is not whether biology "is really just" an ensemble of parts, as some critics have suggested. The experiment, rather, turns on the question: can living systems be constituted as a design challenge in which instrumentality is the aim, contingency the norm, and imagination the limit? These are my terms, of course, and not theirs.

With regard to my part in the undertaking, during the first six months of the experiment it was agreed that I would be responsible for constituting the elements of an organizational capacity for ethical self-reflection and strategic orientation. As with the biotechnical aspects of the BIOFAB's undertaking, the directors expected that my part of the experiment should be made routine, which is to say, programmatic. What such a programmatic capacity might look like was discussed at length in a series of meetings leading up to the launch of the BIOFAB's work, meetings I will detail in the first chapter. Here it suffices to say that the directors did not really have a clear sense of what such an ethics component would look like, except to stress that it would have a "practical" relation to the BIOFAB's strategic goals.

The core concern of my work, the problem to which I addressed my efforts, and the problem which I will discuss at length in this prologue, thus turned on the question of ethical

capacities. This core concern was inconsistently shared by the BIOFAB's directors and the terms the two co-directors used to describe my possible contribution were never really settled. Early in the programmatic stage of the BIOFAB's operations one director publically described my contribution as "keeping the bioengineers from slipping into nerd rapture." At about the same time, but in a much less public setting, the other director obliquely stated that he only wanted to have me around because "it was useful."

To draw once again from a more philosophic vocabulary, this time borrowing from a much older tradition, the problem as I understood it was how to design and fashion *ethical equipment*—aids for inquiry and practice—that might prove appropriate to the stakes of the BIOFAB's undertaking. How such equipment should be fashioned and how its appropriateness determined actually remain open questions, though I have made a number of initial determinations. Such determinations constitute one of the crucial successes of my experiment.

CONTEMPORARY EQUIPMENT: HUMAN PRACTICES FROM SYNBERC TO THE BIOFAB

The technical work of the BIOFAB is predicated, in part, on a series of prior experimental determinations carried out (principally, though not exclusively) by researchers at UC Berkeley, Stanford, MIT, UCSF, and Harvard—researchers associated with a major National Science Foundation funded engineering research center for synthetic biology, SynBERC.[4] Details of these prior technical and organizational determinations are the subject of the first chapter of this thesis, and will be dealt with there. Here, I provide an account of a different, if related, series of prior experimental determinations. These ethical and scientific determinations provided the point of departure and conceptual repertoire for the Human Practices undertaking at the BIOFAB.

The term *Human Practices* was coined and proposed by Paul Rabinow to specify and differentiate an experiment with synthetic biology he and I have undertaken since 2006.[5] This experiment was designed and elaborated as one of SynBERC's four "foundational research thrusts," with Rabinow as the thrust leader. The term helps specify the ways synthetic biology, as it is currently being practiced, connects problems among and between ethics, security, policy, and organizational development. As a post-genomic brand and nascent scientific endeavor, synthetic biology first began to be funded at a time when the post-9/11 security environment, the globalization of science, and the growing world-wide financial crisis was reshaping and recasting the stakes of the life sciences. Synthetic biologists' diffuse, but provocative, claim that they would make living systems "easy to engineer" (i.e. rational) and make materials and know-how "widely available and open-source" (i.e. post-institutional) presented a specter of danger as well as a dream of prosperity.[6] In this light, institutions like the US National Science Foundation, the UK Biotechnology and Biological Sciences Research Council, and the EU Eurocore Program—though eager to fund synthetic biology in the hope of capitalizing on its promised instrumental benefits—have mandated the inclusion of the human and philosophic sciences to deal with questions of ethics, security, and, frankly, public relations. Human Practices is one response to that mandate.

The term Human Practices was also proposed to help differentiate the experiments with synthetic biology from prior efforts to formulate programs in "science and society" or the "social implications" of science. From the outset of the experiment with SynBERC we stressed the point that neither the term *society* nor *implications* were adequate for framing the stakes of the current undertaking. Since the 1970s bioethicists have been assigned the task of elaborating principles

according to which "good" and "bad" science can be discriminated. Such discrimination was intended to provide an ordering and regulating function, assuring that science would contribute to a healthy society and would guard against pathological implications.[7] It is clear, however, that the post-genomic sciences are not being elaborated in relation to anything like the kind of directed governmental vision that provided the original setting for bioethics and the modern notions of society it took for granted.[8] Moreover, whatever can be said about this heterogeneous assemblage of research programs, synthetic biology is being funded precisely to design living systems as technical responses into environmental, medical, and economic problems.[9] That it will have ramifications in these domains is thus clear and direct and not only merely implied.[10]

Given my prior work in science and religion as well as the ethics of stem cell research, I was aware that elite American bioscientists would be unlikely to take up the difficult and sustained work of cultivating habits and dispositions appropriate to ethical and scientific collaboration.[11] After all, strictly cooperative division of labor between ethics and the life sciences has been a defining characteristic of biotechnical apparatuses for at least two decades, and there is currently little incentive to change these arrangements despite the discursive energies being spent on definitions of "upstream governance." Thus it was against fairly large negative chances of success that we took up the challenge and opportunity provided by SynBERC: viz. the challenge and opportunity think through, design, and (to the limited extent possible) put into practice modes of scientific and ethical practice more appropriate to the post-genomic life sciences. In this light it is hardly surprising that the initial phase of the experiment with Human Practices, which drew to a close during the completion of this thesis, failed to meet our expectations, the expectation of the SynBERC administrators and biologists, and those of the National Science Foundation. The reasons for this are multiple and are discussed at length elsewhere.[12] They concern a peculiar admixture of asymmetries in authority and status between ethics, anthropology, and the biosciences, as well as the trained capacities and incapacities of the biologists and social scientists alike.

That our undertaking ramified in unexpected fashions, however, is hardly surprising and should be expected of any experiment worthy of the name. Thus when the SynBERC Research Director expressed regret that the Human Practices experiment at SynBERC and BIOFAB had not been successful, I vehemently disagreed. By most scientific and philosophical criteria the experiment was resolutely successful. During the course of the Human Practices undertaking first at SynBERC and then the BIOFAB we passed through the difficulties and breakdowns attendant to an uncertain and problematic situation, formulated diagnoses that have stood experimental as well as existential test, and were capable of reconstructing our experiences as a series of determinations for further inquiry. One sympathetic critic responded to our efforts by explaining: "that the experiment would be doomed to failure could have been anticipated, given the established power relations; this was, in the end, an experiment in collaboration for which the ground was not (yet) prepared."[13] Both halves of the explanation are only half right. In a situation where one is working against the grain of established power relations failure of one kind or another is no doubt inevitable; but the failures did not lie with the experiment per se. And the ground for collaboration was certainly not yet sufficiently prepared, but our efforts can be situated in a tradition of experimental undertakings, a tradition which provided us both resources and solace throughout.

A difficulty is that our undertaking has been untimely in the sense of attempting to "mark a critical distance from the present" in a manner that not only establishes "a relation from the

present different from reigning opinion" but that also allows us to "think in a manner that leads to inquiry."[14] Such an attempt, with the disciplines and practices which make it possible, is a challenging task under any circumstances. Attempting to carry out such disciplined practice as part of major undertakings in synthetic biology proved to be a design challenge of the first order. Said differently, our experiment, as untimely, can be judged a success. We engaged an indeterminate and discordant situation, formulated breakdowns as problems susceptible to diagnosis, and proceeded in a fashion which helped determine the situation's critical limitations. In this way it also provided initial indications of how a next experiment might be constructed so as to ameliorate those limitations.

The problem that has animated our efforts concerns a sometimes inchoate, but always insistent, demand articulated by diverse constituencies both national and global that the increase of biotechnological capabilities be pursued in a fashion that does not also entail the intensification of the negative ramifications of such increases.[15]. One response to the demand has been to reimagine and reconfigure the relations among and between the life sciences, human sciences, and philosophy, including religion, in such a way as to facilitate Such reconfiguration—to use technical but accurate terms—requires the design of contemporary *equipment* as well as *venues* to facilitate the fabrication and use of such equipment. The design of such contemporary venues and equipment was the aim and challenge of our undertaking in SynBERC. And, with the lessons learned from SynBERC ready in hand, this aim and challenge defined my efforts within the BIOFAB as well.

Equipment, it bears noting, is a more or less adequate translation of an antique term, *paraskeuē*, a term which can also be translated as *preparation* or *preparedness*.[16] Defined abstractly equipment, "is a set of *truth claims*, *affects*, and *ethical orientations* designed and composed into a practice."[17] Hence, although conceptual in design and formulation, equipment should be pragmatic in use. To the biologists and engineers with whom I have worked the word "equipment" evokes terms like gear or technologies—the tools of their everyday biotechnical work, designed and built for a specified purpose. Such associations are actually partially correct in that *paraskeuē* involve both disciplined work and application of technique. Historically, however, equipment has been a term pertaining to the arts and techniques of ethical practice and spiritual exercise; it has concerned the cultivation of capacities for facing unknown and under-determined futures. In this way it can be said that equipment is not only conceptual in form and pragmatic in use; it is also salvational in purpose: it is designed to be used as an aide and buffer against the negative conditions of an uncertain world. To quote from the early work of what was called the Berkeley Human Practices lab: "Equipment enables practical responses to changing conditions brought about by specific problems and events."[18]

Although the term is unfamiliar, equipment has actually become a familiar part of contemporary biological apparatuses. The most salient examples can be drawn from work in bioethics. A signal achievement of early work in bioethics was precisely the development of practical responses to changing conditions brought about by specific problems and events: the protection of human subjects in research in connection to the Tuskegee affair; bureaucratic norms for patient's rights animated in response to the AIDS epidemic; safety regulations for genetically modified organisms in the UK and elsewhere; and privacy regimes for genomic data in light of the digitization of genetic sequences.[19] In both American and European bioethics those who took up the difficult work of this calibration proceeded with a clear sense that the actual implementation of practices required the adjustment or creation of key facilitating venues:

advisory government councils; institutional review boards; denominational commissions.[20] They also proceeded with an informed, though under-thematized, awareness of a persistent asymmetry in power between the technical and non-technical sciences, asymmetries which often positioned them outside and downstream of the very biotechnical and biomedical capabilities bioethicists sought to remediate.[21]

In recent years the terms of this downstream positioning have begun to shift. Given the changing conditions brought about events that might have otherwise remained unconnected—the formation of the post-9/11 political apparatus, the globalization of information, the theological casting of embryonic stem cell research, the instrumental casting of the post-genomic sciences—a number of scholars have actually been given the resources and institutional occasion to design and experiment with upstream and nominally collaborative undertakings.[22] Such experiments can be figured as one response to a typically modern problem: the mandated inclusion of non-biologists in the formation and regulation of the life sciences reflects Max Weber's insight that the techno-sciences, however instrumentally powerful, cannot tell us how we should live our lives.[23] This mandate, however, entails a double-bind.[24] Although invited to take up a different critical position to the biosciences, non-biologists willing to participate nonetheless expected to confirm and thereby reinforce the first-order and promissory series which animates the life sciences today: technical advance, economic prosperity, and the amelioration of health and security. Hence the persistent expectation on the part of technologists that serious ethical thinking can be reduced to matters of reassurance: communication, community building and public education. Whatever formal equality is being granted to non-biologists within these research enterprises, previous asymmetries in power relations between biologists and non-biologists remain in force.

For those who want to remain closely adjacent to developments in the life sciences, but who are not yet ready to the confirm this first order and promissory series, the question of what ethical equipment is appropriate to the unsettled and turbulent terrain of the contemporary life sciences remains problematic. It remains problematic in the first place because, as the Human Practices group stated elsewhere, "the contemporary is neither a unified epoch nor a culture, but, rather, emergent, heterogeneous, and under-determined, any apposite equipment and venues will need to be variable, flexible, and sensitive to the changes in ethical topology introduced by unfolding events."[25] This means that the most salient ethical questions cannot be known in advance, and that previously stabilized ethical relations and practices, while helpful, are unlikely to be sufficient. It reasonably follows that the design of contemporary ethical equipment will need to be inquiry-based and diagnostic. Such an orientation holds out the promise of making informed determinations about the problematic character of the situation at hand, and therefore also holds the promise of possible reconstruction. The question of appropriate ethical equipment remains problematic in the second place because of the overriding expectation that ethical engagement will principally concern the decisions, actions, and artifacts of the bioscientists. Although the decisions, actions, and artifacts of the bioscientists are certainly matters of import, our experiments and experiences show that a more serious and pressing concerns centers on the challenge of forming or reforming appropriate habits and dispositions. Moreover, and more perhaps importantly, it shows that such formation ultimately entails and requires self-formation. Which is another way of saying that in a situation of blockage and asymmetry ethical work begins with work on ourselves. Such work consists in taking up the question of which capacities are needed in order to better live with and respond to the contradictions characteristic of the modern problem of ethics and sciences that persist in our contemporary situation.

We have given form to this motion from a refusal of the first-order framing of the ethical and scientific stakes of synthetic biology to the question of how to better position ourselves so as to conduct our inquiry. This form consists in the movement between an analysis of the habits, dispositions, and capabilities of the biologists and engineers, and an analysis of our own habits, dispositions, and capacities in our engagements with them. Said differently, the experiment in Human Practices has taken as a first task and obligation an examination of the objects and objectives of biotechnical production in view of the habits, dispositions, and practices which make production possible. It has taken as a second task and obligation an examination of the habits, dispositions, and practices which have made our work possible, and, likewise, which have blocked and encumbered our work. This doubling has clarified that while it is possible to take the work and formation of the biologists and engineers as the object of analysis, it is not yet possible to turn that ethical object into an objective. This doubling has therefore also clarified that it is all the more important to move from object to objective with regard to our own position and capabilities.

The clarification of the terms of the asymmetry between the ability to conduct ethical work on ourselves but not with the biologists can be counted as a principle determination of our experiment in Human Practices with SynBERC. This determination resulted in a foregrounding and emphasis on what might in other situations have been cast as the repertoire of minor vices and virtues: the micro-practices of negligence and care, malice and self-justification, and loyalty and care.[26] Consistent attention to these virtues and vices struck our bioscientific and social scientific colleagues alike as trivial, irritating, and beside the point. Our experiment has shown, however, that these terms, when rendered as concepts for the conduct of inquiry, actually provide a crucial grid for analyzing, and key index for critiquing, the relations of truth production, the exercise of power, and the relative ethical seriousness by way of which research institutions in synthetic biology are actually being constituted and research conducted.

In this light, the experiments both with SynBERC and then with the BIOFAB extend ongoing efforts in *the anthropology of the contemporary*.[27] They can also thereby be connected to a number of closely related practices of critical thought. They can be situated in relation to the themes of what has been called *historical ontology*: how are researchers bringing things into the world (their careers, modes of expertise, institutions, biological objects) and how are they naming, distributing and modifying these things? And they could equally be situated in relation to recent work in the *anthropology of ethics*: what are the actual practices by way of which objects are produced and circulated, what are the formative capacities that have to be established and disciplined in order to make this production and circulation possible, and what stance have researchers taken in relation to the need and demand for such formation? The experiments might also be usefully situated in relation to analytic and critical efforts that Michel Foucault identified as *political spirituality*: what are the modes of reasoning and governance through which one constitutes oneself as an ethical subject of the truth?[28] Foucault's term can actually be misleading as a designation for the type of inquiry and experimentation that has been the focus of my inquiries and experiments. It can be misleading in the first place because although questions of power are certainly in play, these relations of power are not precisely located in the register of politics. In this regard the experiment in Human Practices might simply and more accurately be termed inquiry in *spirituality*.

But the term spirituality is freighted and thus can also be misleading. I introduce it here with an informed awareness that it invites misunderstandings and misgiving on the part of

biologists and non-biologists alike. As the author of the "spirituality" entry in the *Oxford Companion to Christianity* sardonically puts it: "Spirituality is a term much in vogue: it sounds significant, with a touch of mystery, seeming to allow escape from the intellectual quest and wearisome wrestling with mental problems."[29] Moreover, the term raises particular difficulties when evoked in scientific contexts. As Michel Foucault noted, "we recognize a false science by its structure of spirituality,"[30] which is to say that insofar as a particular mode of knowledge production requires work on the self as a requirement of access to the truth, then it cannot be a "real science." And yet, it is one of the key premises of my inquiry that the stakes of synthetic biology lie precisely in the fact that it requires practitioners to form themselves in a particular manner, and that the terms of this formation are fraught. Whether or not synthetic biology is a false science is another question, and one worth posing. It is for this reason that despite possible misgivings, I nonetheless insist the term spirituality is analytically appropriate to the situation in which I have found myself and within which I have undertaken my work. It is appropriate in that it sharpens attention on the experiences, relationships, practices, and institutional norms by way of which scientists (myself included) become capable (or incapable) of speaking the truth as part of an ethical life. Put differently: spirituality is a term that indicates the price to be paid scientifically, ethically, and ontologically for access to the truth.[31] This question of this price-to-be-paid has been of central importance to the work of the Berkeley Human Practices group in SynBERC, and remained so throughout my engagement with the BIOFAB.

Whatever the costs and benefits—and this is the point I would like to underscore—my prior engagement and experiences at SynBERC produced a number of crucial experimental determinations that allowed me to clarify and orient the work with the BIOFAB that constitutes the material of this thesis. Put differently, "the process of inquiry has involved remaining in the midst of things of the world but of transforming them in specific ways so as to give them the kind of form as objects and objectives that is determinate."[32] These determinations arising from work with the Berkeley Human Practices group are scientifically and ethically worthwhile in their own right. They are also worthwhile in that they provided the parameters for delimiting the preliminary designs for further inquiry and experimentation with the BIOFAB.

In the subsections that follow I reproduce three *maxims for inquiry* originally formulated as determinate outcomes of the Human Practices experiment at SynBERC. I introduce them here in order to indicate the motion of my inquiry from one experiment to another. During the programmatic phase of my work at the BIOFAB I began to frame the question of how might these prior determinations had prepared me to conduct further inquiry. To what extent are these determinations, formulated as maxims, useful as equipment for conducting work in a setting which is similar to the setting within which they were originally formulated, but which is nonetheless distinct in salient respects? How might they serve as aids to further work? What is the fashion in which they might be successfully taken up, adapted, and exercised?

DETERMINATION 1. CONDUCT ETHICS AS INQUIRY

"Inquiry begins mid-stream, in a situation, both determinative and under-determined, and moves on (through the process of inquiry itself) to other situations and other problems, themselves both partially stabilized and partially troubled. Thus, it is perfectly appropriate—even rigorous—to begin an investigation with tentative parameters of the situation to be inquired into and tentative understandings of what is at stake."[33]

I have chosen to conduct inquiry into a situation which, by turn of events, was both close at hand and followed directly from my previous experiments. In November of 2009, Drew Endy, a Principle Investigator at SynBERC and professor of bioengineering at Stanford announced that SynBERC had been granted funds to establish a "biofabrication facility" for synthetic biology—a BIOFAB. The BIOFAB would be co-directed by Endy and Berkeley Professor and bioengineer, Adam Arkin, and would function as an associated project of SynBERC. The BIOFAB, on Endy's account, would professionalize the manufacture of "standard biological parts."[34] What such standard parts might consist in, and the extent to which such standardization is even possible are longstanding questions in the short life of synthetic biology.[35] The BIOFAB, as it was proposed, would be the first facility dedicated to answering these questions, and answering them with an eye toward manufacture.

Cast differently, the BIOFAB can be thought of as a proving ground for a double proposition and goal of a select cadre of synthetic biologists: (1) that living systems can be imagined as a collection of interoperable components that can be hierarchically assembled into ever more complex systems, and (2) that bioengineering will never really be as rational and predictable as other engineering practices until and unless such components are specified, refined, and standardized. Understood in this way, two conditions of the BIOFAB's existence warrant foregrounding in my inquiry. First is that the BIOFAB is not actually the first facility dedicated to standardizing parts, even if it is the first professional facility. The undergraduate iGEM (internationally genetically engineered machine) competition and the closely related Registry of Standard Biological Parts, both facilitated by MIT, constitute the most prominent experiment in the production and circulation of biological parts to date. That the iGEM and the Registry have been successful on educational grounds and of more limited quality on engineering grounds is often repeated, though the reality is more complicated than critics appreciate.[36] In any event, iGEM has been the institutional standard-bearer for parts-based synthetic biology. It has not, however, been capable of bearing the weight of the hopes some have placed in this approach to bioengineering. Endy was a co-founder of iGEM; and the competition, with its successes as well as its failures, stands as an immediate backdrop to and justification for the efforts of the BIOFAB.

The second condition that warrants foregrounding is that efforts to produce interoperable parts are only one of multiple design and composition strategies currently being mobilized under the sign of synthetic biology.[37] For the past several years the parts-based approach, with Endy as its principle spokesperson, did provide the manifesto for synthetic biology; it provided a narrative of the stakes and promise for funders and the media alike. This is no longer the case, however. In May of 2010, researchers at the J. Craig Venter institute reported that they had successfully synthesized, assembled, and transplanted the entire genome of a bacterium, effectively producing a phylogenically distinct form of life.[38] JCVI is the most visible of a series of projects underway in synthetic biology to do genome scale engineering, an undertaking that uses design principles and scientific strategies distinct from a parts-based approach.[39] Equally important, in the last two years the use of pathway engineering to produce molecules of interest—biofuels in particular—has also become a headline story in synthetic biology.[40] Pathway engineers, in a fashion somewhat in tension with the BIOFAB's emphasis on standardization, regard their objects as biologically idiosyncratic. As such, standard components from a catalogue strike some of them as being of only limited usefulness. Perhaps most significantly, some within synthetic biology have cast the parts-based approach as "first-wave" work. These have argued that it is time to move on to "second-wave" objects, scales, techniques

and design principles.[41] None of which is incompatible with a parts-based approach, per se. And all of these projects intensify focus on the stakes and prospects of synthetic biology broadly conceived: the hope of rationally designing living systems.

That these conditions represent an outside and possible limit to the BIOFAB's efforts means that they also form an outside and limit to my present inquiry. In late 2009 Endy and I agreed that I would extend and reconfigure my SynBERC experiment in participant observation by joining the BIOFAB as the Director of Human Practices. We also agreed that I would use my work at the BIOFAB as my thesis in anthropology. In this way I indirectly inherited the as yet unmet hopes placed in the standardization of biological parts, as well as the possibility that a parts-based approach is not (at least by some accounts) on the cutting edge in biological engineering.[42] Taken in a different light, however, I was agreeing to participate with and inquire into an ongoing experimental attempt to re-imagine living systems and their susceptibility to design and re-design, with all the possible negative and positive ramifications which might ensue from such an attempt.

Moreover, and perhaps more interestingly, I was agreeing to participate in an attempt to design a venue capable of producing objects that not only don't yet exist, but for which there are no settled specifications. To borrow and inflect the title of an account of another biotechnical enterprise, the BIOFAB is an experiment in creating a venue to make a future.[43] It would have been reasonable to inquire whether or not, or to what extent, the BIOFAB is actually able to realize such futures. My inquiry could have been designed as a narrative about the feasibility of a parts-based approach to designing living systems, and the political and economic relation of such an approach to other prominent projects such as whole-genome engineering. After all, if a parts-based approach to synthetic biology is going to have anything like the impact that its advocates hope, it will need to be made consonant with these other endeavors.

I have chosen to proceed in a different and more limited manner, however. Although my project had a more or less well defined beginning—work at the BIOFAB commenced on January 11, 2010—I have chosen what might, at first glance, be taken to be an artificial end point for the materials presented in this thesis by limiting my report and analysis to the first six months of the BIOFAB's work. As I noted at the outset of this prologue, however, during these six months the BIOFAB directors and team leaders addressed, in a sustained if uneven fashion, the question of what a standard biological part might actually consist in and whether or not the BIOFAB might actually be capable of producing such parts.

In the months since, The BIOFAB team has not resolved these questions. They have, however, contrived a *program* for determining what such capabilities might eventually consist in. It is the formulation of this program that I have chosen to focus on. What I mean specifically by the term "program" will require more careful parsing, and will be dealt with in the next chapter. Here I emphasize that such a program has required ongoing (and unresolved) negotiations of what modes of truth production should be taken to count as serious and worthwhile, and which strategies for governing laboratory conduct will allow for the BIOFAB to meet its stated goals. Put differently, this six month period in the BIOFAB's constitution might be characterized as an experiment in *programming behavior*, to use Michel Foucault's incisive term: "programmings of behavior, these regimes of jurisdiction and veridiction aren't abortive schemas for the creation of a reality. They are fragments of a reality which induce such particular effects in the real as the distinction between true and false implicit in the ways men 'direct,' 'govern' and 'conduct' themselves and others."[44]

By selecting this initial period in the constitution of the BIOFAB and in the constitution of my experiment in ethics, I hope to extend the analytic purchase of what has been called an anthropology of the contemporary.[45] First formulated by Paul Rabinow, the anthropology of the contemporary is a mode of inquiry that is neither modern nor post-modern. Stated abstractly, the anthropology of the contemporary is a mode of inquiry that focuses attention on the unsettling of both old and new elements and the reconfiguration of these elements into new assemblages. Taking "the contemporary" as an object of inquiry requires paying a certain price. In these sometimes brief and unsettled reconfigurations there is no guarantee of lasting significance. Unlike some genealogical approaches, there is not enough historical distance to ensure significance in the name of "general economies of truth and power"; and unlike some modes of ethnographic engagement there is no expectation that significance will arise out of a kind of pure singularity in which the ethnographer enjoys the authority that comes from being a privileged witness.

Whether or not the BIOFAB's program for the invention and production of standard biological parts eventually stabilizes and becomes effective, or remains partially troubled will not be determined for some time. In the meanwhile, however, conducting inquiry into how such a program is being designed and brought into the world gives form to an inventive moment during which a crucial question can be posed: how is truth-telling being practiced, how are lives being conducted, and what is the price to be paid for these scientific, ethical, and—I argue—spiritually consequential undertakings?

DETERMINATION 2. BE RESOLUTELY SECOND-ORDER

"Inquiry works best as a second-order practice. The term second-order denotes a mode of observation-intervention (Betrachtungen) in which the task, to use Niklas Luhmann's cryptic but incisive phrase, is to "observe observers observing." Second-order practices are disruptive in that (at a minimum) they make visible existing habits and dispositions; this visibility often leads to the recognition or demand that such dispositions and habits are insufficient and inadequate on one or another register. It frequently produces responses characterized by irritation, indifference, and the assertion of power to block or silence second-order observations."[46]

Among the policy experts, social scientists, and bioethicists who have actively engaged with synthetic biology there is an overriding concern for questions of risk, safety, and security. [47] The concern is hardly surprising. These topics are often considered the "real" social science concerns, and have been the center of a kind of academic growth industry. And who would disagree? Few deny that synthetic biology, to the extent that it makes biology easier to engineer, introduces new dangerous actions and actors. Indeed, the rise of so-called Do-It-Yourself biology has been a focus of my own research. More to the point in this context, to the extent that the BIOFAB realizes its goals of producing standard interoperable components for the automated construction of living systems, questions of risk, safety, and security can scarcely be ignored.

A question posed in the human practices work at SynBERC, a question which carries forward into my current inquiry, is whether or not these questions of material harm should predominate at the expense of other concerns. There is some question as to whether or not dangers in synthetic biology can actually be assessed as risks, understood in a technical sense. A risk, after all, is a danger that has been given calculable form.[48] Such calculation requires a series of events in relation to which risk assessment can proceed. The hoped-for outcome of such

calculation would consist of quantitative guidelines for the regulation of synthetic biology in such a way as to minimize adverse security events in the contemporary political milieu. Given that, to date, there have been no conspicuous security- or safety-related adverse events connected to synthetic biology, and given that the events of greatest concern are likely to be of low-probability but high consequence in any case, there are genuine questions as to the extent to which existing approaches for assessing risk will produce the kinds of insights that will help reduce the probability of negative outcomes.[49]

For this reason, among others, Human Practices efforts at SynBERC were designed to concentrate on a different, but adjacent, analytic register and a different but connected series of questions. This register and these questions (to repeat what was stated above) privileges an examination of the experiences, relationships, practices, and institutional norms by way of which scientists become capable (or incapable) of speaking the truth as part of an ethical life. We proceeded in this work by taking key terms from the history of philosophy, spirituality, philosophy, ethics and moral theology and employing them as tools for anthropological investigation. The task was to specify and diagnose the ways in which the dynamics of subject-formation play a role in the constitution and ramification of synthetic biology.

We determined that such inquiry is best conducted from the position of the second-order participant-observer, a position which facilitates the work of specifying and characterizing the habits and dispositions of those involved in synthetic biology. This specification, in turn, allows for the identification of those dispositions and habits that are insufficient or inadequate on one or another register. Our work, therefore, also introduced the pressure, sometimes made explicit and sometimes left tacit, to address these insufficiencies and inadequacies. It is not surprising, in this light, that our second-order position has often been met with a strong measure of discomfort and even hostility. I hasten to add that the discomfort and hostility has not just characterized the reactions of the biologists and engineers, but also the other Human Practices participants as well. The critical examination of habits and disposition, after all, has long been a central component of disciplined ethical practice, and the role of discomfort in ethics has a long and tested history.

Such discomfort, I believe, is a crucial aspect of cultivating scientific and ethical practices worthy of the name. This discomfort and the critical reflection that it produces, moreover, make it more rather than less likely that current undertakings will contribute to spiritual practices. Such practices, we could all agree, are themselves crucial aspects of human flourishing and therefore form an integral, if often neglected, part of the scientific life. The term flourishing, to quote an early design-statement for work in human practices, "is a translation of a classical term, *eudaemonia*, and as such a range of other possible words could be used: thriving, the good life, happiness, fulfillment, felicity, abundance and the like. Above all, flourishing should not be confused with technical optimization, as we hold that our capacities are not already known or fixed in advance."[50] Flourishing is not equivalent either to prosperity, technical progress, or even the amelioration of health, wealth, and security—as important as these might be. Rather, flourishing introduces a critical question of how a scientific life, and the life of thought more broadly, should be lived. Further, it introduces the question of whether and how impediments to flourishing might be resisted and overcome, and where such impediments are so endemic as to require exit and reorientation. I have tried to pose these questions in relation to the BIOFAB generally, and synthetic biology in particular, always with an eye toward the question of whether or not the formal work of ethics might be allowed to flourish as an integral part of the overall enterprise.

Remaining resolutely second-order while conducting my work in the BIOFAB has be challenging for many of the same reasons it proved to be difficult at SynBERC—i.e. there is a constant demand to produce first-order deliverables, and the refusal of this demand provokes a range of negative reactions ranging from indifference to hostility. Indeed, within the BIOFAB the second-order position has actually proven more difficult to sustain. The reasons for this are simple. In the first place work within SynBERC was directed by Paul Rabinow, who has accomplished the difficult task of cultivating and refining the capacities for undertaking second-order engagement and for facing the hostilities that it often provokes; this does not make the labor of second-order engagement easy, by any means. It does steel one for the difficulties it will inevitably entail. Within my work at SynBERC I relied on Rabinow's experience and capacities as both bolster and prompt. Although my experiment in the BIOFAB was conducted in close adjacency to ongoing work in SynBERC, the responsibility of remaining second-order was resolutely my own. In the second place the BIOFAB team is simply more closely integrated than the broadly distributed and loose collection of researchers and labs that constitute SynBERC. Unlike SynBERC, the BIOFAB is geographically and scientifically consolidated. During the programmatic phase of work, the BIOFAB consisted of just seven researchers, including the directors, all working in a single location. This concentrated and localized setting facilitated the development of friendly relations and even a sense of mutual concern among many of the junior participants. And although friendship can actually be enriched by second-order observations of habits, dispositions, and activities, such enrichment requires a well-tested trust, which obviously cannot be taken for granted in a situation where careers and reputations are in play. In this sense remaining resolutely second-order was not only scientifically, affectively and humanly difficult, it also required risking negative responses from those for whom I developed a certain affection. My success in remaining second-order was mixed, as will become clear.

I accepted the invitation to participate in the BIOFAB, in part, because of an expressed willingness on the part of both Endy and Arkin to let me proceed in a mode of second-order observation. It is clear in retrospect that neither really had any sense of what such a practice might entail, and were willing to accept my framing of my work as long as a series of clearly defined outcomes could be articulated. Despite this initial willingness and despite the fact that both directors did in fact provide time and space for me to conduct my inquiry and work on my anthropology thesis, there remained an expectation that such observation would eventually fold back into the production of first-order deliverables: guidelines for the licensing and circulation of fabricated biological materials; recapitulations and assessment of the principal criticisms that were likely to be leveled against the BIOFAB; creation of introductory materials on the state-of-play in parts-based synthetic biology to be read by a "more general" audience, and so on. Which is to say that while there was an understanding that I would be conducting anthropological inquiry, even to the point of composing a doctoral thesis, it was taken as a matter of course that such inquiry would ultimately have to have a practical benefit if it were to be accounted worthwhile and credited to me as a contribution to the first order goals of the facility. Given that the directors had learned to include attention to "social implications" as part of their high-level formulation of the facility's goals, the expectation that I would ultimately make directly strategic contribution did not necessarily entail abandoning the critical enterprise I had imagined for myself. In the end, however, it did put me in a position in which the stakes of second order engagement had to be frankly assessed in relation to the compromises to that mode of engagement that would persistently present themselves in the name of maintaining institutional relevance. Which is another way of saying that the possibility of contributing second-order

observations to the practical life of the facility was not ruled out of bounds in an *a priori* fashion. Whether or not there could be a form for the articulation of those observations which simultaneously remained true the core themes of truth, power, and ethics which would be judged worthwhile by the directors or by the facility's auditors was another matter.

Over the long run, second-order observation was increasingly taken to be irrelevant and a distraction by those interested in the establishing the BIOFAB's "productivity" credentials. Said another way, inquiry conducted in a second-order mode, did not in fact produce outcomes that contributed directly to instrumental goals in anything like an explicit and institutionally formal manner. This did not mean, however, that a loyalty to second order work was any less resolutely called for.

DETERMINATION 3. EXERCISE FRANK-SPEECH

"Inquiry and second-order observation, taken together, open a distinctive critical position that anchors and completes this series. Unless the insights produced are put into play in a serious and consequential manner, their ramifications will not be open to scrutiny. And their salutary effects on the practice of thinking will thereby be deflected or distorted. In our experience, and the experience of others, reactions to frank-speech, at least initially, oscillates between the poles of indifference and violence. One must remain alert to the fact that frank speech entails real dangers. Exercising frank speech in consequential situations, however, actually makes one more capable of seeking the truth."[51]

The need for frank-speech as a key element of ethical engagement with the life sciences has rarely been thematized in bioethics, science and technology studies, or the anthropology of science. Equally importantly, the capacity to speak frankly, to speak in a manner that breaks from the performative strictures of simply repeating expert and familiar talking points has been under-developed, under-practiced, and left to wither as part of the pedagogical repertoire of the engaged thinker. Frank-speech, it has been proposed, is recognizable and distinct from other ways of talking about the ethical stakes of the life science by virtues of the kinds of effects it engenders. Whereas ethical discourse about the life sciences is typically enunciated in a such a way that "when an utterance is made the effect which follows is known and ordered in advance, it is codified and this is precisely what constitutes the performative character of the utterance." By contrast, a way of speaking that can be rightly termed "frank-speech" is by characterized by the fact that "whatever the usual familiar and quasi-institutional character of the situation in which it is effectuated, what makes [an utterance frank-speech] is that the introduction, the irruption of the true discourse determines an open situation or rather opens the situation and makes possible effects which are precisely not known."[52] Such irruptions, such unsettling is sadly rare in situations concerned with the ethical and scientific stakes of the contemporary life sciences. Such a lack becomes conspicuous only when we attend to the fact that despite all of the discourse about ethics and the life sciences, it is not at clear that this discourse effectuates outcomes that are not already known in advance. And once made conspicuous, this lack can be taken as a critical failure when it is considered that the question of how to exercise frank-speech was once a central part of disciplined regimes of ethics and truth production.[53]

The exercise of frank-speech has been a defining element in the design of the interventions put forward by the Berkeley Human Practices group and of Rabinow, its PI, in particular. This exercise has usually engendered indifference or irritation; it has also resulted in a kind of professional and vocational brutalization, as I will detail in chapters 4 and 7. Positively,

however, the exercise of frank-speech, consisting of a calculated presentation of our second-order diagnoses, has worked to put our truth-claims into circulation in a fashion that proved consequential in that they were critical of the existing arrangements within SynBERC, they refused the demands for exercises in public relations and reassurance, and were formulated with a rhetoric that did not reduce our analyses to familiar and predominant tropes. In this way, our interventions inevitably disappointed some measures of relevance and worth, though surprisingly for several years they received positive evaluation by some of the National Science Foundation officers responsible for overseeing the Center. In this way, the exercise of frank-speech allowed for the growth of capacities—hence bearing the fruit designed to be the outcome of the practice of ethics. Specifically, it actually made us more capable of seeking the truth and attempting to make it plain in complex and difficult circumstances. It follows that a question I posed at the outset of my experiment with the BIFOAB (in a fashion similar to the other maxims outlined in this prologue) was whether or not exercising frank-speech would be likely to carry the same benefits and dangers for work in the BIOFAB as it had in the previous experiences with SynBERC?

Working schematically, and following specifications provided by Michel Foucault's reading of key antique texts, several elements of the practice of frank-speech warrant highlighting. First and most simply, is that the exercise of frank-speech is perhaps most consequential when undertaken in constituted venues.[54] Traditionally, these venues include democratic spaces in which the problem has been speaking frankly to an assembly of equals as well as venues in which truth was being spoken to a ruling prince or a tyrant. At the beginning of the experiment with SynBERC, Jay Keasling made some effort, however minimal, to fashion the Center as a democratically governed organization. These efforts consisted in a scheduling and hosting series of conference calls with the Center's Principal Investigators. For reasons I will explain in subsequent chapters, the SynBERC PIs were, by and large, uninterested in participating in the governance and scientific life of the Center, except in a kind of indirect fashion. As such, few of them participated actively in the monthly calls. Given this low investment and given the fact that Keasling himself really had no time to run the Center in anything like a careful and concentrated fashion, these modest attempts as some kind of democratic order did not last. Despite articulations of good will and expressions of equality and inclusivity, eventually Keasling formalized what had been happening informally throughout: Keasling, his administrative staff, and a small executive group team made up of select PIs, began to simply make all of the crucial operational decisions autocratically.

The BIOFAB represents yet a different experiment in governing a venue. Formally, it is directed by Arkin and Endy, with Endy as the active scientific director. Informally, and in its day-to-day life, it is governed as a kind of deliberative body consisting of the BIOFAB directors, team leaders, and research staff. This deliberative constitution is in part the result of Endy's openness and Arkin's conviviality. From the outset Endy emphasized that he wanted all of the participants to exercise something like frank-speech—"be honest about what you really think." Endy acknowledged that prior parts-based work in synthetic biology was under-developed and over-stated. Such an acknowledgement could be taken as a premise for free discourse. Perhaps a more salient factor in the creation of this informal democratic and deliberative structure, however, is the fact that Endy and Arkin, like other elite researchers, have too many other commitments and so rely heavily on the senior post-docs for the design of research.

Frank-speech is practiced as a form of public fidelity to the truth; this is a second crucial feature. That is to say, a given speech act does not qualify as frank-speech in view of its outcomes, i.e. its pedagogical effects, its persuasiveness, or its dialogic merit—even where such outcomes are hoped-for and intended. Rather, frank-speech is a matter of publicly making a truth claim one's own. A challenge of frank-speech consists in accepting that knowing the truth is not enough. Rather, frank-speech demands publicly binding oneself to what one knows to be right or good. In the case of human practices, this has meant being willing to risk stating what I think is really going on in terms of the worth, orientation, and significance of the research itself, as well as the habits, dispositions, and capacities of the researchers. Moreover, it has meant stating these things even when such insights are unlikely to lead directly to reform. Put differently, frank-speech means that one must be willing to risk making normative, and not only denunciatory, claims about a given situation, whatever the outcome.

Given that SynBERC and the BIOFAB are scientific institutions there are ample opportunities for participants to "bind themselves to the truth." These opportunities, however, are almost always limited to statements or restatements of claims concerning experimental data and its interpretations. Less frequently do participants take these opportunities as openings for making claims about the worth and direction of the enterprise per se, despite the fact that the hallways are filled with opinions about whose work should be supported and whose should be defunded. The challenge of speaking frankly at the BIOFAB is all the more acute given the nature of the undertaking involved. The BIOFAB has promised to manufacture standard biological parts. Such objects do not yet exist. Indeed; specifications for what such objects might likely consist in do not even exist. This reality produces a difficult situation in which participants must be willing to speak frankly and publicly about human practices, including their own incapacities.

A third feature of frank-speech is that it has traditionally been exercised as a practice of discursive "ascendency."[55] That is to say, frank-speech has been practiced as a means of establishing the authorization to participate as an equal in situations in which access to the exercise of power could not otherwise be assumed or assured. Such a situation certainly applied to human practices. The participation of non-biologists in the development of synthetic biology has been mandated from the outset. This formal inclusion and equality, however, exists in tension with the actual asymmetry in power between the biologists and the non-biologists. In such a situation of asymmetry, the ability to influence the shape and direction of the venue can only be secured discursively. Put another way, frank-speech is matter of trying to influence the conduct of a venue through speech.

The fact that frank-speech concerns an attempt to establish authority indicates a crucial difference between having the juridical right to speak and actually being allowed to speak in such a way as to exercise influence. As I will explain at greater length in chapter 7, in analyses of democratic situations problems of *politics* can be distinguished from problems of *power*. Making use of a distinction in Greek thought between *politeia* (politics understood as concern for constitutional and juridical matters, the framework for the governing of the city and the rights of citizens) and *dunasteia* (a term referring to the actual exercise of power, including its strategies and techniques). As a political problem, taken in light of this distinction, frank-speech can be thought of as a question of rights. Does one have the right to speak the truth frankly in consequential situations as part of those who are formally allowed to govern? As a problem of the exercise of power, however, frank-speech is not a question of rights. Rather, it is a question

of capacity. Among all of those who have the right to speak frankly, how is it that some only actually are able to speak *truthfully* in a way that results in the *effective exercise of power*?[56]

Unsurprisingly, from the outset at the BIOFAB there were clear differences among the directors, team leaders (including me), and technicians in terms of a willingness and capacity to speak frankly. How the question of frank-speech and the exercise of authority are playing out in the BIOFAB, and whether or not human practices can form an integral part of deliberative processes are key questions that I examine in this thesis.

A fourth feature of frank-speech is simply that it entails and constitutes a danger and a risk. Minimally, frank-speech puts into motion ramifications whose outcomes cannot be fully accounted for or contained. More seriously frank-speech brings with it dangers to the speaker herself. These dangers are various. For those who, in an organization, do not share your status, exercising frank-speech entails the danger that they will deride you for what you are saying. For those who are your equals, but who think that the wise and the philosophic should avoid direct participation in power games, they will frequently claim that critical thinkers have no right to be normative. And then there are those who are your equals and who want to govern; these are likely to receive frank-speech as a diversion or a threat. And, given that frank-speech can function as a matter of ascendency, it is indeed a threat. In the case of SynBERC and the BIOFAB it is a threat to the autonomy of techno-scientific expertise.

Given that the BIOFAB is a scientific and not political institution there is little danger that frank-speech will, as it has for countless advisors to princes and tyrants, result in death. The most consequential result would be the modern equivalent of exile—to be fired. Such an eventuality is certainly significant, materially and symbolically. And indeed, Rabinow's continued public insistence that publicly funded research should be evaluated in terms of "flourishing" rather than "prosperity" resulted in his being attacked by members of SynBERC's Industrial Advisory Board (IAB). In behind-the-scenes consultation with the NSF Directorate the IAB helped arrange Rabinow's removal as the director of Human Practices, although he was invited to remain active as a Principle Investigator.

There are actually more serious dangers attendant to exercising frank-speech. In exercising frank-speech one risks binding oneself to claims that might actually prove not to be true. In a scientifically and ethically consequential situation, such as the BIOFAB, there is always the danger that one will speak out of ignorance, malice, wishful thinking, or self-justification, with all the deforming affects that might result. Another more serious danger concerns the fact that speaking the truth to those who do not care to listen has exhausting and demoralizing affects, intensifying an atmosphere of futility. In such a case, the price to be paid for speaking the truth to those who are not in a position to here it may, over time, simply become too high. At that point the question of loyalty and care come into play. What and who is it that one is loyal to, and what and who should one care for. Said differently, loyalty to and care for the ethical and scientific stakes of f inquiry requires taking seriously the possibility that exit and reorientation constitute the appropriate—and even remediative—response to a discordant and indeterminate situation.

I. DISCORDANCIES

CHAPTER 1

BIOFAB: A Program

These programmings of behavior, these regimes of jurisdiction and veridiction aren't abortive schemas for the creation of a reality. They are fragments of a reality which induce such particular effects in the real as the distinction between true and false implicit in the ways men "direct," "govern" and "conduct" themselves and others.

—Michel Foucault[57]

In late 2009, Jay Keasling, the director of the Synthetic Biology Engineering Research Center (SynBERC)[58], with Drew Endy and Adam Arkin, two SynBERC Principal Investigators, requested and were awarded supplemental funds from the U.S. National Science Foundation's Engineering Research Center (ERC) Directorate. These funds were given in order to establish a fabrication facility—a BIOFAB—for synthetic biology. SynBERC was awarded two years of funding for the BIOFAB at a total of $1.2 million.[59] After this initial two years the BIOFAB was expected to either be self-sufficient (through partnerships with industry, grants from other institutions, possible renewal monies, etc.), or to be integrated into SynBERC's operational budget, or to be phased out.

The ERC Directorate was in a position to fund the BIOFAB because of supplementary funds provided through the 2009 American Recovery and Reinvestment Act. Among the official reasons cited for the Act were "job preservation and creation, infrastructure investment, energy efficiency and science."[60] The inclusion of appropriations for "energy efficiency and science" was predicated on the political and economic hopes being placed in the formation of a "bio-economy." To this end, the NSF received an allotment of additional funds. The NSF no doubt thought further investment in synthetic biology prudent. Prominent political and industrial figures, including Steven Chu, the Secretary of Energy and former Lawrence Berkeley Lab colleague and friend of Jay Keasling, were promoting synthetic biology as one key step toward a biologically-based reworking of the political economics of energy. As part of the NSF apportionment the ERC program received several million dollars in supplemental funding to be distributed as supplement to their existing centers, including SynBERC. The directors of the ERC directorate contacted Keasling (no doubt among others) and encouraged him to submit a proposal for additional SynBERC support. The need and possibility of a BIOFAB had been floated for a number of years, especially by Drew Endy, but by others as well. The timing seemed opportune.[61]

1.2 million dollars is no doubt a considerable sum by some standards; in the genomic and post-genomic biotechnical sciences, it is a rather meager amount. These monies are sufficient to allow the BIOFAB to support two or three post-docs, a similar number of technicians, with enough left for operational costs and summer salary for the directors. If SynBERC director Jay Keasling had not arranged for the BIOFAB to receive in-kind laboratory and desk space as well as access to state of the art equipment in the Joint Bio-Energy Institute the undertaking would scarcely have been feasible. To put these modest material conditions into relative perspective it

is useful to keep in mind the funding levels for Keasling's other projects. SynBERC's annual budget is approximately $5 million, and the Joint Bio-Energy Institute (JBEI), a program and facility directed by the Lawrence Berkeley National Labs has an annual budget of approximately $25 million. And these federally funded efforts, although enjoying considerable material support, are surpassed by capital investments currently underway in emerging commercial sectors of synthetic biology. During the writing of this thesis—to offer just one example—Amyris Biotechnologies, a company Keasling founded, raised $85 million dollars in its initial public offering.

From the outset, to put things differently, there has been a remarkable disparity between the meager character of the facility's material conditions of operation and the significance being attached to its biotechnological program. Which is to say that I offer this cursory survey not only to underscore the simple and perhaps obvious point that by the material standards of the contemporary life sciences, the funding and founding of the BIOFAB represents quite a modest undertaking—particularly as base monies for the animation of a distinctive research and production facility. The more significant point only becomes clear when these modest material conditions are seen in the light of the rhetorical and symbolic importance that has been ascribed to the BIOFAB. The BIOFAB has been framed by its organizers, observers, and critics alike as constituting a proving ground for the now 10-year-old claim made by Endy and others that if biotechnology is ever going to realize the long-hoped-for promises of ameliorated health, wealth, and security what is really needed is the know-how to rework biological systems to produce a repository of engineered and standardized components, and a professional-grade production facility in order to produce such components at scale. Actually, to be more precise, the claim is really that the long-hoped-for promise won't be realized until biologists start conducting themselves like "real engineers." It's just that such conduct, and the cultivation of a generation of biologist-engineers who exemplify such conduct, won't really be possible unless and until we have standard biological parts. Such parts lie on the other side of the funding of a fabrication facility for making them.[62]

INITIAL JUSTIFICATIONS

To use the terms proposed to the NSF by Endy, Arkin, and Keasling the importance of fabrication facility for synthetic biology lies in the ability solve a core capacity deficiency in biotechnical engineering: "Current forward engineering capabilities in biological engineering," the directors explained in their proposal, "are vastly inferior relative to existing yet still immature DNA construction and genetic manipulation tools."[63] When recapitulating natural genetic sequences, bioengineers can now successfully synthesize and construct a genome constructed on the order of 8 million base pair genome. By contrast, "today's most advanced engineered genetic systems are typical encoded using less than 20,000 base pairs of designed DNA."[64] As the proposal explains, this represents a greater than 400-fold gap in bioengineers' "ability to design versus write genetic material"—a "bio-integration gap" as the BIOFAB's primary director Drew Endy has regularly referred to it. Bio-technicians are fair hand at recapitulating naturally given sequences, at recapitulating "the actual interconnections of things," as Weber put it.[65] When it comes to the conceptually demanding problems of how to design and compose novel sequences in a functionally successful manner, basic capabilities remain deficient.

The deficiency, is not for lack of proposed "frameworks and methods," the BIOFAB proposal argued. SynBERC itself is organized according to a design framework which deals with scales of complexity in living organism by imagining them through the engineering metaphors of

"parts," "devices," and "chassis." Moreover, the proposal insisted, enough exemplary projects had already been successfully completed by researchers within the directors' labs to formulate the basic strategies needed for successfully animating production. What was lacking then, according to the proposal, was really only sufficient opportunity and infrastructure. The proposal supported this claim by offering comparisons to other more "mature engineering fields," an explanatory and rhetorical strategy common to orienting statements in synthetic biology. Engineers in other fields enjoy the conceptual and infrastructural resources needed to rapidly translate "new foundational frameworks and methods" into "specific applications." Biotechnology, however, "lacks the equivalent of even the simplest machine shop."[66] A biological "design and build" facility—a BIOFAB—could address this lack. The proposal's punch-line was that once a BIOFAB had been made fully operational SynBERC would be able to rapidly design and prototype the genetic constructs needed to support its own projects, "while also producing broadly useful collections of standard biological parts" that would ultimately be made freely available to academic as well as commercial biologists and engineers.[67]

It is not clear whether or not the NSF officers questioned the declarative propositions offered in the proposal; subsequent reports, however, made clear that their principal reasons for funding the facility turned more on the proximate than on the long-range value of such a facility.[68] The opening paragraphs of the proposal acknowledged what had been consistently and strongly stated in each of the SynBERC's annual reviews: that the Center was suffering from a lack of scientific and operational coherence. Arguably, the main cause of this incoherence was the fact that SynBERC's annual funds, though substantial, are ultimately distributed to 18 Principal Investigators at six universities, meaning that no one lab really gets very much direct support and therefore there is very little material motivation to undertake the difficult work of rectifying the problem. The BIOFAB proposal, however, cast the operational incoherence in infrastructural terms. The problem, the proposal stated, is insufficient integration between the Center's "foundational" and "applied work." What this really meant was that the Center's "Testbeds," which were designed in consultation with the NSF to establish an industrial proof-of-principal for synthetic biology, were not being coordinated with the ostensibly foundational work being undertaken in the "parts," "devices" and "chassis" research "Thrusts." The proposal rhetorically took it as a matter of course that "SynBERC Thrust researchers are developing powerful new tools, including innovative first-generation languages and grammars for programming DNA."[69] The problem, however, is that "SynBERC Testbed" can only make use of these "power new tools" through by way of "existing ad hoc materials and methods for assembling and testing their specific engineered genetic systems." Enter the BIOFAB: "the world's first biotechnology design and build facility" to produce professionally engineered, high quality standard biological parts. The BIOFAB might ultimately produce collections of standard biological parts and make them freely available to academic and commercial researchers. But in the near term it will "immediately improve the operations and research pacing within SynBERC." [70]

The point should be stressed that the ERC Directorate had a greater-than-usual stake in SynBERC's success. For a dozen years or so the ERC program has funded centers in the material sciences with a concentration on nanotechnology. SynBERC represents the program's first effort to fund foundational work in the life sciences understood as an engineering enterprise. The ERC director Lynn Preston purportedly spent a considerable measure of political capital getting SynBERC funded. For this reason the Directorate's executives have been especially active in directing and monitoring SynBERC's developments.[71] That monitoring, as I've already noted,

has often been expressed in concern over an apparent disproportion between the coherence of SynBERC's organizational structure and the actual research As a program SynBERC's infrastructure and research plan has a certain organizational coherence: four research "thrusts"—parts, devices, chassis, and human practices—produce materials and standards for several "test-beds." The test-beds, in turn, produce applications of commercial interest to representatives of the biotechnology industry. In this way the thrusts serve as proof-of –principle for the worth of the goal of standardization and the test-beds serve as proof-of-principle for the worth of synthetic biology as a commercially viable undertaking. Functioning together the thrusts and test-beds serve as warrant for the NSF's investment. The Center, in this way, is imagined as a model of co-labor and mutually facilitated productivity.

In practice, things are less rationally orchestrated. Most of the labs pursue research agenda they would otherwise have pursued, with or without SynBERC support and affiliation. This independence is less a function of obstinacy or irresponsibility and more a function of the fact that most of the SynBERC PIs are recognized world-leaders in their respective fields; their labs are well established and well funded. And given that no one lab gets enough funding from SynBERC for the Center to have any real claim on or leverage over research priorities, the agendas of the individual PIs predominate, and SynBERC is left to perform post-hoc demonstrations of coordination. This means that the demand and the task of producing better scientific integration in the name of SynBERC's priorities has fallen largely to the reporting efforts of SynBERC administrative staff. The SynBERC administrators track the development of projects underway in the participating labs in such a way as to make visible points of possible connection. In this way there is a possibility of fostering more direct and active collaborations by helping researchers to recognize shared problems and overlapping projects.

Hence, when Keasling, with Stanford professor Drew Endy and Berkeley professor Adam Arkin responded to the NSF's invitation to apply for supplemental funding, they took this as an opportunity to kill the proverbial two birds with one stone. Endy (and to a lesser extent Arkin) had been pushing for the creation of a biofabrication facility for a number of years.[72] Keasling understood that, whatever its worth beyond SynBERC, a BIOFAB could be proposed and defended as a mechanism by which SynBERC might more effectively address its persistent operational "integration gap"—a mechanism that does not really demand too much more time or adjustment from the SynBERC PIs, who, after all, were brought into the Center as Keasling's scientific equals and university colleagues.

FROM OPERATIONS TO PUBLIC BENEFIT

In this light, and with a contrastive emphasis to the NSF, for the BIOFAB's directors Endy and Arkin the BIOFAB principally worth their time and efforts for its possible long-range contributions. Thus, having noted in the first few paragraphs of their proposal that the BIOFAB would help address problems with SynBERC's operations, the remainder focuses on the ways and reasons why a fabrication facility "will enjoy broad public and commercial support that will help to strengthen and sustain the facility over time."[73] Whatever genetic constructs are used by researchers in the SynBERC testbeds, these same and all other constructs would be made available in a free-to-use to the end of fostering a broader community of synthetic biologists. The proposal promises that within the first year of operation the BIOFAB will "design, construct, and test a collection of 6,000 new BioBrick parts for controlling replication, transcription, RNA processing and degradation, translation, and protein degradation in *E.coli* and *S. cerevisiae*."[74] These aims—the BIOFAB's "C.dog engineering projects"—were framed as "taking the central

dogma of the table as a research question for bioengineering." That these aims are audacious to the point of being conspicuously grand is obvious, how their audacity is also strategic is less obvious, and will need to be examined subsequent chapters. As one BIOFAB team leader would say on multiple occasions, "controlling transcription and translation has basically been the goal of genetics for the last 30 years; and we're expected to achieve this in two years?" A striking feature of the proposal as that these aims were stated as though "taking the central dogma off the table" were only a matter of meeting a series of production milestones. In any event, the key point here is that funding for the BIOFAB may have been justified as operationally important fix for a single institution, but for its directors the fact that it might constitute "the first significant focused investment in the development of open technology platforms underlying and supporting the next generation of biotechnology" was the real point.[75]

Said more plainly, Endy, who has served as the principle directorial force in the daily operations of the BIOFAB, has been resistant to the notion that the BIOFAB should be conceived as a functional unit of SynBERC's organizational structure—a resistance which the NSF has disapprovingly noted.[76] A number of factors contribute to Endy's resistance. Prior to the funding of the BIOAFAB Endy had been vocal at SynBERC meetings about the "opportunity cost" introduced by SynBERC's lack of operational coherence and shared scientific direction. Although he also emphasized SynBERC's worth as a key "convening institution" among leading synthetic biologists, he has been attentive to the ways in which the BIOFAB might become encumbered by the micro-politics of SynBERC's organizational struggles. Endy has also emphasized the fact that the BIOFAB only received funding through SynBERC for two years of operation. Given only a short-term commitment on the part of the NSF, he has stressed that the BIOFAB needs to plan for life beyond the initial period of supplemental funding. Endy is careful to publically acknowledge that SynBERC is providing an incubation function of a kind for the BIOFAB's launch and initial maturation. And he has regularly encouraged BIOFAB staff to cultivate working relations with researchers at JBEI and other institutions whose infrastructure and status are crucial to the BIOFAB's success. He is not willing, however, to direct the BIOFAB's work and or formulate its strategic priorities in a fashion overly determined by SynBERC's short-term operational difficulties.

Endy's resistance to framing the BIOFAB's significance in terms of SynBERC's operational needs signals one minor facet of a more general problem. From the outset of the BIOFAB's work has been marked by a certain measure of indeterminacy. This indeterminacy has technical and operational dimensions to it: how should the BIOFAB go about the work of formulating the experimental aspects of its work, how should it design its operational routines, what are the criteria by way of which it prioritizes its envisioned outcomes such that aims can be met, funding renewed, scope expanded and the like. Such technical and operational indeterminacy is, in part, an artifact of any experimental undertaking. In addition to these technical and operational questions, there has been a persistent indeterminacy at micro-political and ethical levels as well. It has not always been clear who it is that the BIOFAB's work is intended to facilitate, with all the possibilities of rivalries, mixed loyalties, and confused standards of worth that such a lack of clarity might entail. Put differently, if the BIOFAB is not designed to facilitate the work of the SynBERC labs, or at least not uniquely the work of the SynBERC labs, then who? Connected is the question of what kind of scientists or engineers the BIOFAB team members would need to become in order to do their work successfully. The formation of the BIOFAB has entailed the formation of habits, character, and dispositions on the part of those involved. And with all such questions of capacity building and subjectivity come

the matter of what must be left to the side, what is the price to be paid for committing one's life, not only organizationally and scientifically, but also vocationally and spiritually to one endeavor rather than another. It should be noted that as of the writing of this thesis the indeterminacy affected by Endy's view of the BIOFAB's relation to SynBERC has not yet spilled over into discord, although areas of possible discord have begun to show themselves. Such discord, as will become clear, might actually prove worthwhile, scientifically, organizationally, and ethically. Discord, after all, can ultimately serve as a matrix for the production of concord.

It is not surprising that the BIOFAB proposal did not raise these questions, let alone propose strategies to address. The substance of the proposal turns on precedence and vision and less on scientific and organizational specification. The proposal's most detailed section is entitled "Preliminary Results," which describes work conducted by the labs of the three principle investigators have shown promise in analyzing and modeling natural and engineered systems. The section goes on to describe three "recent results that detail the process by which many standard biological parts and devices can be made, characterized, and openly distributed."[77] All the three studies described were undertaken by Endy and his lab. And all three have served as crucial precedents in the effort to establish the BIOFAB's initial program of operation. None of the studies, however, actually do detail "the process by which standard biological parts and devices can be made." Indeed, it is a central premise of this thesis that the BIOFAB's scientific worth as well as its critical limitations lie in precisely in the fact that there is little broad agreement on how to fabricate standard biological parts, nor indeed on what actually constitutes a standard biological part worthy of the name.

In this regard, the proposal is a curious document and served as a herald of a kind of figuration that would prove troublesome to literalize in the details of the facility's operational program. In quite un-problematized terms the proposal promised to animate a production facility for the generation of an object which does not yet exist—standard biological parts capable of controlling genetic expression—but described the generation of such an object as simply a problem of infrastructure and industry.

SYNTHETIC BIOLOGY AS BIO-FABRICATION

Technologies connected to the notion of synthetic biology have increasingly been valued on the presumption of their imminent commercial contributions to the production of biomass-based fuels and industrially important chemicals. Even a cursory look at the press releases of two companies taken to be exemplary of synthetic biology's industrial potential, Craig Venter's Synthetic Genomics, Inc. and Jay Keasling's Amyris Biotechnologies is instructive. Both companies propose that their engineered biological systems provide a platform for the production of molecular precursors useful in the generation of transportation fuels, plastics, cosmetics, detergents, synthetic rubber, and so on. In this respect both companies can be cast as attempting to actualize the promised potential of synthetic biology to solve challenges in renewable energy, the production of inexpensive drugs, and environmental remediation, as well as providing a catalyst for further growth of biotechnology.

Up to 2010, the first year of the BIOFAB's operations, the reputation and reputed worth of synthetic biology was arguably a degree less commercial. Advocates had, of course, underscored the industrial potential of synthetic biology all the way through. But investments of private and government monies in enterprises connected to synthetic biology from late 2009 until late 2010 belie the fact that until only recently synthetic biology was alternately figured as a matter of humanitarian and environmental significance or of bioengineering as the playful

creative development of "biohakers." The two exemplary cases usually offered as warrant for further investment in synthetic biology were the successful engineering of the anti-malarial *artemisinin* by the Keasling group at Berkeley[78] (including researchers at Amyris) and the prominent undergraduate bioengineering competition iGEM[79] (International Genetically Engineered Machines). Both cases, of course, present now-familiar hybridizations of commercial and academic undertakings. *Artemisinin* work was offered not-for-profit; but the same metabolic pathways that Keasling's group engineered to produce the anti-malarial are the basis for the production of precursor molecules for biofuels and other petro-chemical substitutes. And the iGEM competition, though emphasizing and fostering an ethos of openness, sharing, and collaboration, is judged and sponsored by commercial representatives and organizations. By mid-2010, the scale-up of private investment, and emphasis on the prospect of biofuels and bio-economics to position, synthetic biology began to be figured as part of a more worldly valuation game.

Which serves to highlight an important, if obvious, fact about synthetic biology today: the intensification of the instrumental stakes of synthetic biology and the claim that benefits are just around the proverbial corner, has worked to dramatically increase funding and recognition. In late 2009 the Woodrow Wilson Center's "Synthetic Biology Project," estimated that "the U.S. government has spent around $430 million on research related to synthetic biology since 2005."[80] Striking a similar note of growth and potential, a few months later the market analysis firm BCC Research published a report stressing that while "the global market for synthetic biology generated $233.8 million in 2008" we should look forward to an "increase to $2.4 billion in 2013, for a compound annual growth rate (CAGR) of 59.8%."[81] These estimates represent only one kind of measure of the profile of synthetic biology. And more importantly, they are clearly a function of the criteria used to determine what gets to count as synthetic biology and what does not. The key point that I want to draw attention to is that the intensification of the instrumental valuation of synthetic biology has had unsurprising effect of further attracting a heterogeneous range of researchers, institutions, and projects to the brand. Somewhat more surprising and interesting is the fact that many of those who figure their work as synthetic biology in order to take advantage of this new valuation game, find themselves in a position of having to simultaneously frame enough of their work as synthetic biology to get funds and attention, but not so much as to lose scientific credibility with those in positions of power from more established domains of biology and engineering who think that synthetic biology, in the end, is more a question of branding than of scientific substance.

This double game of wanting to capitalize on available resources while wanting to retain a certain scientific distance from the rhetorical excesses of synthetic biology's chief spokespersons increases the salience of a fact that has been true about synthetic biology for a half-dozen years: in practice synthetic biology is heterogeneous assemblage of techniques, technicians, university and non-university institutions, modes of expertise, stylization, use of media, and the like. With increases in funding but not necessarily a parallel increase in scientific credibility, the task of marking out the defining characteristics synthetic biology has become something of a contested and contentious affair. Those interested in clear demarcations usually offer some combination of qualitative criteria (e.g. synthetic biology is a matter of standardization and modularization) coupled to certain historical episodes (e.g. the attempt to design genetic systems on the model of logic gates in electronic circuits), with the coupling taken as a kind of threshold of legitimacy and access. One of the few historians who have spent energies tracking synthetic biology over the last few years proposes that the concepts and

practices currently being attached to the term "synthetic biology" today cohere with proposals articulated in the 1970s, specifically by Sybalksi and Skalka.[82] These proposals emphasized a difference between "describing and analyzing existing genes" and "constructing and evaluating new gene arrangements."[83] This identification of coherence between current and past practices has the merit of dampening present claims to novelty or revolution. But such a comparison tends to foreground the question of whether or not "any of this is new," and backgrounds the question what it is the first-order participants in this contemporary assemblage are actually working to bring into the world and advance as distinctively worthwhile, pressing and important.

Whatever the variation in actual work and projects among laboratories claiming the label, most synthetic biologists would agree that biological engineering is in need of (1) strategies for the rational and standard design of biological systems and (2) programs for the predictive composition of cellular and multi-cellular functions. In 2005 a manifesto-like declaration of principles, policies, and objectives was published in *Scientific American* under the title "Engineering Life: Building a FAB for Biology."[84] The article was written by a collection of biologists and engineers referring to themselves as "the bio fab group." The group was composed of biologists and engineers who have subsequently become some of the leading figures in synthetic biology: David Baker of the University of Washington, George Church of Harvard Medical School, Jim Collins of Boston University, Drew Endy and Joseph Jacobson of the Massachusetts Institute of Technology, Jay Keasling of the University of California, Berkeley, Paul Modrich of Duke University, Christina Smolke then at the California Institute of Technology and Ron Weiss then at Princeton University. The byline describes this group as consisting of "friends, colleagues and sometime collaborators who wrote this article as a group because the diversity of their expertise, and hence of their contributions to the bio fab effort, embodies the interdisciplinary nature of biological engineering."[85]

The rhetorical cast of the article borrows terms and turns of phrase from electronics and circuit-design, and though analogy and metaphor have become commonplace in synthetic biology their use in this article was significant in that it combined such figurative language with an effort to treat infrastructural and technological advances in computer engineering as instruction for work with biological systems. The authors are quite self-conscious about this conceptual strategy, stressing that synthetic biology is not only a question of technological innovation. It is, rather, "a way of thinking about existing biological machines and of constructing new ones, which borrows both language and methodology from engineering." This way of thinking, begins with the decoupling of design and fabrication of biological systems, passes through the development of technologies free laboratory practitioners from undo manual labor and the limitations of resources and time ("much like semiconductor chip lithography) and find actualization in the capacity the ability to imagine biological systems as modularized and functionally specific segments of DNA.[86] "Thinking about existing biological machines and constructing new ones" thus requires the research to learn how to embody a different stance toward in relation to their work, one that disciplines their scientific practices on the model of "silicon engineers."[87]

The article ends with something of a curious turn. Although ostensibly written in the name of the need of a fabrication facility for bioengineering, the conclusion stresses that such a facility is worthwhile not only for the kind of technical capabilities it will provide, but more importantly for the way in which it will support the formulation of a community of practitioners. The article notes that such a community is already beginning to take shape, albeit in a loose and

underdeveloped form. One crucial vector for the tightening of that form is the undergraduate iGEM competition. The competition alone, however, will ultimately be insufficient. Synthetic biology needs a more permanent community of those committed to the principles and practices of engineering—that is, "biologists to think like silicon engineers (and lure more engineers into biology)—particularly when it comes to sharing parts." Biotechnology to date, we are told, "has been characterized by self-contained teams working to develop single-purpose applications, such as one drug compound." Such a diagnosis implies its own solution: to foster an ethos of work, standards, and sharing that will allow many different groups to contribute the same systems and subsystems, working together over space and time. "Our hope," the authors conclude, "is that building a fab for biology will facilitate that progression and help to spur advances as revolutionary as those achieved in the semiconductor industry."

The articles concluding emphasis on the need to foster a certain kind of community, and the place of a bio-fabrication facility in bringing such a community into existence introduces a problem that the article does not take up. In the near-term, what kinds of practitioners and practices will be needed in order to both bring about the technical ability to successfully decouple design and composition and establish functionally reliable norms of standardization and production, but also (and thereby) the cultivation of a community of practitioners who embrace and expand that regime? A fabrication facility, in other words, requires someone to fill a strange, if impermanent, kind of subject position: a bioengineer capable of producing a program for the production of standard biological parts, and producing them in such a way that their circulation will make a new mode of subjectivity (i.e. the mature synthetic biologist) not only possible, but also desirable and maybe even necessary.

STANDARD BIOLOGICAL PARTS

The prospect of establishing a "parts-based" approach to biological engineering has remained a central and prominent (and, often, contested and controversial) feature of efforts in synthetic biology. Indeed, for many including Endy, and to a lesser degree Arkin, such a prospect has become definitive. For almost a decade, Endy has been a prominent spokesperson and organizer for a core set of practitioners who have defined synthetic biology as the effort to conceive and render biological systems as integrated sets of components. Such components should be fashioned, refined, and assembled in a relatively easy and, above all, standardized manner. For these practitioners, terms like *scalability*, *predictability*, *cost* and *utility* are the order of the day. And, as such, the worth of synthetic biology depends on the task and challenge of fabricating standardized parts for biological engineering. Indeed, the question can "we make standardized parts in biological engineering?" has become tantamount to the question "can we make synthetic biology?" The BIOFAB was established to answer this question.

What a biological part actually is, and why such an object may or may not be significant is not as obvious as either proponents or critics might suggest. Despite almost a decade of work, the question "what is a part in biology?" still remains more or less an open and contested question, though various experiments have been tried and progress toward from abstract definition to concrete instantiations has been made. Put more precisely the question really is: what is a *standard* biological part in *synthetic* biology? More precisely still, what *could* a standard biological part *be made to be*? The italics make all the difference, and stand as a challenge to the BIOFAB.

The BIOFAB co-directors Drew Endy and Adam Arkin have been posing these questions, in one form or another, for more than a decade. In 1999 Endy and Arkin submitted a proposal to the Defense Advanced Research Projects Agency (DARPA) to undertake work not unlike the defining aims of the BIOFAB, albeit on a more modest scale. In that proposal, Endy and Arkin argued for the need to fabricate "a set of well-characterized and systematized biological components that can be generically assembled."[88] If biotechnology aspires to have anything like the same capacity for predictable, reliable, and scalable design and construction characteristic of other fields of engineering, such parts, they argued, would be crucial.

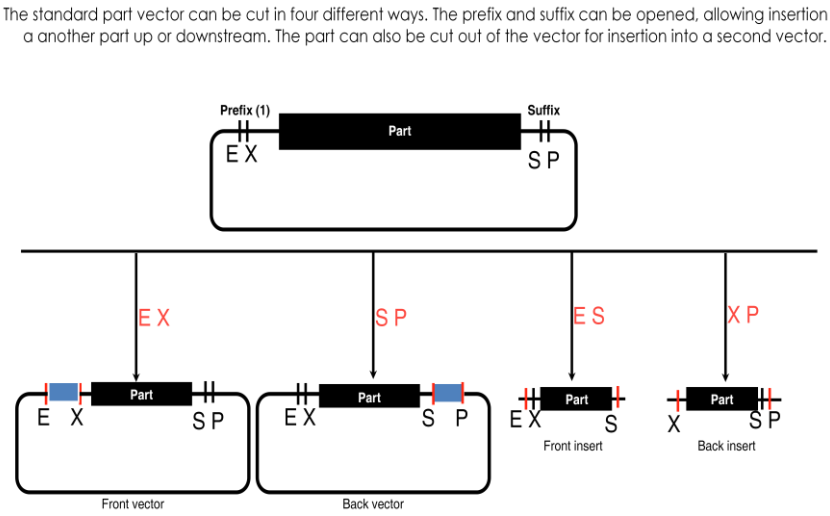
Endy and Arkin relied on analogies to the design of integrated circuits. Unlike designed circuits, "natural biological circuits" have idiosyncratic mechanisms, rates, reactions, and effects. Hence, "rational design of biological systems by humans," they concluded, has "remained restricted to rather small or hit-or-miss efforts and has often relied on the ability to 'select' for biochemical parts that fulfill some criteria."[89] Endy and Arkin were clearly not the only researchers interested in rendering biology in an engineering mode. The biotechnology industry had been attempting to scale and refine the production of "genetic circuits" with designed functions for more than two decades. The various genome sequencing projects of the 1990s had proved to be more a technical than biological achievement.[90] As Sydney Brenner would put it in 2000, the genome projects were only the beginning of the end for genomics. The intensification of high-throughput computing technologies yielded surfeit of data but a paucity of either scientific problems, let alone answers. It is not a surprise, in this light, that the first decade of the 21st century saw a remarkable range of attempts to brand and package the next stage of post-genomics work, brands that could successfully pick up the media mantle, funding, infrastructure, institutional support and instrumental promise of the genome projects.

One response to what comes "after the gene," as Brenner put it, was to imagine ways in which genomic data could be converted not into better biological theory, but into more useful biological technologies and products. And, by the late 90s, a number of researchers who would later come to be prominent figures in synthetic biology had begun to take up their work in this mode.[91] Among these were Tom Knight and Ron Weiss at MIT. From 1999-2001 Knight and Weiss worked on a series of projects to rethink the design and construction of genetic circuits on the model of the basic logic operations used in the design of integrated circuits. Their efforts, like the work of almost everyone else engineering DNA at the time, were slowed by a lack of standard and rationalized techniques for assembling units of DNA. Such a lack, to quote Knight, "forces each DNA assembly reaction to be both an experimental tool for addressing the current research topic, and an experiment in and of itself."[92]

As one means of overcoming the *ad hoc* and tedious character of DNA assembly Knight *et al*. proposed what he called a "BioBricks" assembly standard. In its simplicity the proposal was potentially quite powerful, and turned on the natural capacity of enzymes to cut DNA at highly specific locations in a DNA sequence (restriction sites) using a specific class of restriction enzymes. When a restriction enzyme makes a cut at a restriction site it leaves an "overhang" which can subsequently be made to anneal to a complimentary overhang, effectively suturing the cut. Knight *et al*. ventured that this natural cut-and-paste mechanism could be better leveraged for DNA assembly and thereby for rational design of genetic "devices." He proposed that engineered sequences of interest to be flanked on both the "upstream" and "downstream" ends with specific *double* restriction sites. These paired restriction sites could effectively function as sets of biological parentheses. A would-be engineer could cut the DNA between the parentheses

(either upstream or downstream), and insert a new "part." Moreover, and more importantly, all of this is designed in such a way that the insertion of any new part leaves the outside restriction sites unchanged, making it possible to continue chaining together more BioBricks (Figure 1).

Figure 1: Diagram of Knight *et al.* BioBricks Assembly Standard (sites: E = EcoRI; X XhoI; S = SpeI; P = PstI)[93]



On a basic level, the first BioBricks standard worked as advertised. It did indeed facilitate physical composition in an "idempotent" manner. That is, "each reaction leaves the key structural elements of the component the same" and therefore (in principle) can become part of a "library" of reusable components that can (it is hoped) be compiled into components of ever-increasing physical and functional complexity. The trouble was the BioBricks standard had its limitations, biological as well as political.[94] On the biological level, the main limitation was that although the BioBrick assembly standard provided a simple t solution to the problem of *physical composition* (i.e. getting segments of engineered DNA to physically connect), it did not yet sufficiently account for challenges of *functional composition* (i.e. getting segments of engineered DNA to work together in a predictable manner).[95] Physical boundaries, in other words, do not yet make a functional part. A given sequence of DNA may encode for a function. But it only encodes for the successful performance of that function given a particular set of other relationships. What one would need to know about the behavior of a given BioBrick part *in context*—i.e. how it is characterized—turns out to make all of the difference. None of this, of course, came as a surprise to the Knight lab. One step at a time, as the saying goes.

Eight years following the circulation of Knight *et al.*'s initial report, pressing questions remain. Is a part a self-contained object? Is it a function? Is it a relationship? What do we need to know about the relation between the BioBrick part and the constructs of which it is a portion? And what needs to be specified about the ways in which a part occupies and therefore is partially determined by a biological situation?

Technical challenges aside, the ramifications of Knight *et al.*'s proposal bear noting. Within a few years of his proposal, an initial infrastructure for the cataloguing and sharing BioBricks had been established as the MIT Registry of Standard Biological Parts, and the groundwork had been laid for the generation of BioBrick users through the undergraduate International Genetically Engineered Machine competition, iGEM. Since their inception both the

Registry and participation in the competition have grown by a factor of 100.[96] That said, like most first generation efforts, the critical limitations of this early work have shown themselves. In informal conversations and, increasingly, in publications, practitioners remind each other that the original BioBricks format only works for some kinds of projects and under only limited conditions[97]; that many of the parts in the MIT registry are not sufficiently well characterized to be immediately useful[98]; and that, despite the enthusiasm of the iGEM youth, few projects work as designed.[99]

Lest such limitations be cited as a warrant for stopping course, however, it's also worth remembering that like other first generation efforts, remediatory work is underway. An increasing number of iGEM projects do in fact work as designed.[100] More registry parts are being characterized and integrated into high-level engineering projects.[101] And serious players have proposed new generations of BioBricks standards.[102] A simple lesson learned from these initial efforts is that the notion of fabricating standard biological parts has opened up one possible solution to the trenchant problem of rational design and construction in bioengineering.

Despite the recognized limits, initial efforts to specify and fabricate standard biological parts have helped orient and intensify efforts at making *biology engineerable*. A key strategy throughout has been to ask whether or not, and to what extent, techniques and technologies in other fields of engineering might be useful for engineering biological systems. Hence, the notion of a part. This strategy shows itself in the frequent appeal to analogies among synthetic biologists.[103] Paying attention to how standardized engineering works with screws, computers, integrated circuits, or programming languages, we are told, might take us on the way to figuring out how standardized engineering practices might be established for biology.[104]

A paper published in 2008 by Canton, Labno, and Endy provides an exemplary attempt among the core of first-generation synthetic biologists to formulate strategies for establishing practices of standardization.[105] The paper tackles the problem of standardization by providing a candidate version of a "datasheet" for a device made up of standard biological parts—a sheet of details about the parts that make up their composite device, how they work and don't work under a given set of conditions, what kinds of "inputs" one might need and what kind of "outputs" one might expect. The datasheet, it is proposed, provides the kind of conceptual technology that, if successful, would "enable engineers to rapidly select from a vast list the parts that will meet their design requirements."[106]

Two aspects of the Canton *et al.* paper warrant attention. First, it recapitulates the challenges identified in the Arkin-Endy and Knight proposals and elsewhere.[107] Acknowledging the limits of any strict analogy, Canton *et al.* nevertheless assert that "despite the differences in materials and mechanisms, biological devices may often be defined with functions that are identical to the functions of electrical, mechanical and other types of existing engineered devices…. Consequently, many of the characteristics found on existing device datasheets might also be useful for biological device datasheets." How useful, and useful in what ways remains question. Second, Canton *et al.* introduce a modest degree of definition regarding what a standard biological part might consist in. The authors' write: "We define a standard biological part to be a genetically encoded object that performs a biological function and that has been engineered to meet specified design or performance requirements." The degree of definition lies in their offering specific categories and candidate criteria for "specified requirements" might entail: "first, a definition of the function and interfaces of the device (inputs and outputs);

second, the operating context of the device; third, measured characteristics describing the quantitative behavior of the device."

The authors take seriously that a "genetically encoded object" may not, per se, be a part. Such an encoded object may only be what it is under certain biological conditions. Said differently, they understand that their device is, in some way, a function of the context in which the device is operating. The question, then, is how much can such a device and its constitutive elements be abstracted out of a given context and how much of that context needs to be embodied in the conceptual abstraction which is the datasheet? And which connections and interactions need to be accounted for in something like a datasheet (or a library, or a parts list, or a registry, etc.) in order for a would-be engineer to know what to expect from that part across a range of experimental circumstances?

Such questions press home the point that standardization is matter of selecting which relationships and measurements will be made to count.[108] That is, standards capture a range of relational variables and embody them in a set of measurements, which can be used to anticipate behavior. In this light, the answer to the question of what a standardized part might be turns to a large extent on what one chooses or does not choose to measure. This means that although measurements of "parts" and datasheets of measurements are necessary for achieving standardization, a question remains unanswered: measurements of what? A golden rule of engineering is that measurements are the key to transforming a qualitatively complicated situation into a quantitatively regular and manageable one. It follows that synthetic biology, taken on the analogy of other engineering disciplines, will need to figure out what needs to be measured, in what way, and to what end. Perhaps it goes without saying, but in order for measurements to be significant, they need to be measurements of the things we know we need to know. Not all measurements are equal, as it were.

An analogy, it has been said, is not an identity.[109] The advocates of synthetic biology may want biological engineering to be like other forms of engineering, but presumably the answer to the question of which refinements and which standards are needed for the design of screws or integrated circuits will not be identical to those needed for the design of genetic activity.[110] So, what in biological engineering, taken up with an eye toward the eventual production of standardized parts, needs to be known? And if it proves impossible for the BIOFAB (or anyone else) to give a singular or unequivocal answer to such a broad and imprecise question, this is in no small part because it's also not yet clear what synthetic biologists don't need to know. How one decides to slice this difference between what needs to be measured and what can be safely ignored would seem to make all the difference. A turning point for advocates and critics alike.[111]

THE VOCATIONAL COSTS OF BIOLOGY AS FABRICATION

A basic premise of the BIOFAB is that standard biological parts don't exist, or, rather, they don't yet exist in anything like a satisfactory form. Which is another way of saying that (1) standard biological parts are artifacts; they are made and not simply discovered; that (2) claims about what they might be and why we might care are not (necessarily) also claims about the nature of living systems; and hence, claims about the nature of living systems do not (necessarily) function as warrants for, or rejection of, the notion of standardized biological parts; which (3) makes it all them more problematic that unlike many other engineering disciplines, biology doesn't yet possess shared criteria for what minimal information about a standardized part might be needed. In short, what a standard biological part might (or might not) turn out to

be, and what significance this might (or might not) have for biological engineering, is an open question.

All of this raises two sets of problems. It is my task in what follows to separate out these problems, distinguish them, and show how they are linked. Both problems can be situated in the register of design, understanding design to be a practice oriented toward the work of making or producing. Both can be thought of as formational, and the two have a mutually determinative relation. The first is a question of venue: what does it mean to constitute a BIOFAB? The second can be thought of as *ethical*: what is the price to be paid, scientifically and vocationally, for participating in the work of the BIOFAB? If standard biological parts don't yet exist in a satisfactory form, and if the BIOFAB's existence is justified on the promise of producing such parts, the question is: how is the BIOFAB proceeding with the task of producing a worthwhile organizational form and developing sufficient technical and scientific practices? What are the means by which it is designing its operational portfolio? Crucially, what kinds of truth claims are being taken seriously in this constitutional phase? And how are these truth claims informing the conduct and character of the BIOFAB team leaders and technicians?

A central challenge is that the BIOFAB directors and researchers must buy into the fact that they have been funded to be a professional production facility, with all of the pressures of delivery and credibility that this entails. It is a production facility, more importantly, which has promised to make objects that not only don't yet exist, but for which there are no settled specifications. This means that the BIOFAB team needs to adopt or invent a work mode in which a series of basic research questions will have to be answered, but—and this is crucial—answered only up to a point. That point, presumably, is the stage at which the BIOFAB's collection of engineered objects is sufficiently refined, standardized, and susceptible to predictable and functional composition. Which is to say, that any one experiment only needs to produce just so much data, just so much understanding. Knowing when to stop is, after all, an old artisanal problem. Which kinds of data will prove worthwhile, which problems and analytics will drive their production and characterization, and which forms will be used for articulating and circulating were key programmatic questions.

Technical challenges notwithstanding, constituting a production facility requires work with and on the habits and dispositions of the participating researchers, as much for me as for any of the others involved. In November of 2009, in the process of trying to decide whether or not to participate in the BIOFAB, I asked a junior professor of bioengineering at UC Berkeley and a SynBERC Principal Investigator he thought of the proposed undertaking. This particular researcher conducts work in a parts-based mode and as such has no serious in-principle objections with the BIOFAB's biotechnical agenda. More importantly he is one of the few biologists that had involved themselves in even discussing questions posed by Human Practices. He expressed certain reservations about the prudence of the undertaking. In the first place he was unconvinced that the BIOFAB would be able to produce the parts that researchers really want. He insisted that the most valuable components of designed genetic systems are idiosyncratic and non-obvious. Such parts would likely not be found even in a list of the "thousand most popular." In the second place, and perhaps more crucially, the researcher underscored that even if the BIOFAB could meet the technical challenge of fabricating standardized parts, such an undertaking would be "so boring." Who would undertake the work?

My Berkeley colleague's misgivings point to a key tension implicit in the BIOFAB's work. BIOFAB participants would hold conflicting views concerning what standardized parts

might be and how they might be fashioned as well as what scientific significance should be attached to pursuing work of this sort. He insisted that work on the problem of standardization and of a functionally reliable parts-based is crucial and difficult and could only really be designed and successfully carried out by an adept and biologically astute senior post-doc. At the same time, if the facility stays more or less true to "Endy's proposal" such a post-doc will be spending a significant amount of time and energy simply scaling production, simply making parts. Then again, he suggested, things might not stay true to Endy's plan. Arkin is unlikely to be intellectually satisfied by a purely production oriented undertaking. Work might take unexpected directions. And yet, he concluded, if the BIOFAB really is just a production facility, it is unlikely to lead to the publication of serious scientific papers, whatever scientific stamp Arkin puts on things. As such, the facility will hardly advance a senior post-doc's career. Hence the tension: although animated in the name of production, work would actually only be able to proceed once crucial scientific questions were posed and taken up.

My colleague's hesitations about the worth and limitations of the BIOFAB have proven to be only partially accurate—as he admitted six months in. They have proven inaccurate in that the BIOFAB directors were, in fact, been able to recruit senior post-docs—first Vivek Mutalik, a researcher who had been working Arkin's lab at Berkeley, and, five months later, Guillaume Cambry, a researcher from the Mazel lab at the Pasteur Institute. His misgivings have proven accurate, however, in that these post-docs—team leaders responsible for designing the BIOFAB's actual research and production protocols—have regularly come up against Endy's demand that they justify their proposed protocols less in terms of the scientific merit (which is their tendency) and more in terms of the number and types of parts that they are expecting to produce. Such a demand has often been framed as a trade-off between making things that "just work" and making things that work in a more calculable fashion. What the criteria for "just working" actually entail has itself become an experimental question. My colleague's hesitations were accurate as well in that a core difficulty for Mutalik and Cambray (as well as for others) is what stance to take in relation to their research, how much of their scientific identity to invest in the work of the BIOFAB, and how to formulate a research and production agenda that would satisfy the differing demands and expectations of the two directors.

This difficulty forms the materials for the next two chapters, and here I only introduce the problem. The work of taking up and embodying the demands and expectations of the two directors is both more subtle and more challenging than one might imagine. It is more subtle in that Endy and Arkin are not at odds with each other in the direction of the center. They are, however, quite different in their stylizations of what counts as a good problem, good work, and worthwhile design. These differences are rarely, if ever, spelled out. In the early months of the facility, however, they were a source of irritation and discomfort. They were also, I would argue, generative. They were generative in the first place of indeterminacies, scientific and ethical. They were thereby in the second place partially determinative of the subject positions Mutalik, Cambray and the others involved were made to invent and cultivate. It is this work of invention and cultivation that I think is crucial. This need to hybridize a set of otherwise divergent set of demands and expectations and give them form as a coherent set of scientific practices and thereby as a single and self-consistent mode of scientific subjectivity has characterized the micro-political vector by way of which the BIOFAB's program has been actualized. The extent to which Mutalik and Cambry and the others are able or willing to habituate themselves to this under-specified ethos of production is not yet clear. What is clear is that a dissonance of style

and feel for what counts as good work has become an irritation and a discomfort. Such affect could prove worthwhile depending on how it affects conduct and character.

Part of this irritation and discomfort is a result of the BIOFAB's under-determined relation to its host institutions SynBERC, iGEM, JBEI, and much of the rest of the synthetic biology research community. Particularly in the early going it was not clear what this community would like the BIOFAB to be. Nor was it clear the extent to which the BIOFAB directors would like the needs and interests of this broader community to shape the facility's research and production priorities. Given that the BIOFAB is something of the proving ground for a parts-based approach to biological engineering, these questions remained pressing. Such pressures generated both uncertainty and resolve on the part of the BIOFAB leadership—uncertainty about what work would ultimately be taken seriously, resolve that the BIOFAB is nonetheless the right kind of venue to be creating.

A much more localized, and therefore more direct source of indeterminacy, however, is generated by differences between Endy and Arkin as to how the BIOFAB should proceed. The differences though obvious remained tacit and were rarely thematized in formal setting, though they were frequently discussed informally. Analyzing these differences is crucial to diagnosing how the BIOFAB has approached the problem of making standardized parts. More importantly and more to the point, analyzing these differences is crucial to understanding what kinds of practitioners the members of BIOFAB team were being asked to become, how they were expected to conduct themselves, and the extent to which these modes of conduct would prove adequate to the proposed scientific and ethical stakes of the undertaking.

At the heart of the question "what is a standard biological part?" lies the problem and potential worth of refiguring complexity and context dependence as hierarchies of abstractions (parts, devices, systems, etc.). Endy and Arkin both have a feel for abstraction. This feel—to simplify but not to misrepresent—works in different directions for each. For Endy, an abstraction is an orienting conceptual device that allows for the reduction of complexity in a kind of pragmatic fashion: complexity is black-boxed by seeing how much we can either assume or ignore about how systems work. The BIOFAB has tested a series of promoters and ribosome binding sites, for example, in order to find out whether or not they worked in a fairly predictable way. It turned out that they did. This allowed the BIOFAB to generate a predictive model of how this finite library interacts. For Endy that's good enough. Arkin was also pleased by the results of this simple pilot study. This study, for Arkin, is only worthwhile if it does more than simply train a model to predict combinations from within a given set of genetic elements. He wants it to indicate the physical constants are in these elements that may account for their predictable combination. In this way an abstraction is not only, or even primarily, an orienting device, but is the result of detailed experimentation. Endy's and Arkin's differences concerning what counts as good design and a satisfactory scientific result have not been resolved or even systematically accounted for. So far they have simply been accommodated. Accommodation, it seems to me, can only go so far.

This can be reframed and restated as a kind of summary diagnosis: the situation over the course of its first six months the BIOFAB was characterized by both *indeterminacy* and *discordancy*. Indeterminacy with regard to how the question of what kinds of objects should be made, how they should be analyzed and characterized, and whether or not those objects could be fashioned in such a way as to better determine how to engineer predictable and tunable genetic expression. The rectification of such indeterminacy would require the work of designing,

thinking, and creating the scientific work needed for the eventual determination of the limits of a parts-based approach to the problem of rational design of biological systems. The challenge of giving form to such scientific work, however, is an ethical question: how should the researchers approach their work, how should the carry it forward, what questions would the need to foreground and which would the need to ignore. In short the capabilities needed to animate a program in bio-fabrication require ethical discrimination concerning which practices would prove most worthwhile, and how to align the otherwise un-aligned interfaces created by the heterogeneous range of expectations and stylizations of the two directors and the hanging questions concerning the legitimacy and worth of the BIOFAB's undertaking. The task and challenge was to establish a determinate way forward that might bring about a state of concord with regard to how to take up one's work in a satisfying and worthwhile manner.

For the indeterminacy and discordancy this programmatic period was nonetheless marked by motion and productivity. Mutalik and Cambry designed a series of initial and orienting experiments, some of which have successfully been brought to completion. The team leader for software, Cesar Rodriguez, made headway on the difficult tasks of building computational tools sufficient not only for collecting and presenting the BIOFAB's experimental data, but also for ranking the performance of genetic elements in combination so that users of the BIOFAB's data might be able to design their genetic constructs in a more predictable manner. Joao Guimarães, a graduate student in the Arkin Lab who has been working closely with the BIOFAB developed a first generation set of algorithms, which define a certain modularity among genetic elements involved in tuning the expression of a protein in such a way that performance scores in-combination can be modeled and even predicted in a modestly successful fashion. And the team leader for operations, Lance Martin, established and refined a workflow for the rapid production of "test-rigs" for cloning and testing potential parts collections. And for my part, I produced a first set of BIOFAB Human Practices reports, which both established a work mode for my "deliverables" and began to show the possibilities and limitations created by my position within the overall enterprise.

And yet despite this motion, it should be recognized that things did not go according to plan. This is because the initial proposal for the BIOFAB failed to provide specifics about how work would get done. It consisted rather on a series of justifications for why work should be funded. In place of a plan, the proposal described the work of the BIOFAB as "not an academic research lab" and "not a commercial venture," but rather a production facility. The facility would just make things. And here is where the trouble begins. What to make, how to make it, and how to position oneself in relation to work that will inevitably be difficult but work that one might not ultimately take seriously. Which is another way of saying that it is not surprising that things have not gone to plan, given that things were in need of being invented. And the "things," in this case, included both protocols for the creation of standardized artifacts in a standardized fashion, the specification of design and composition rules reliable enough to warrant a certain amount of credit for scientific seriousness while nonetheless being produced at scale, and, of course, the attitudes and postures and careers of the artificers.

Whatever their scientific and dispositional differences, where Arkin and Endy converge is in a commitment to—my term, not theirs—designing a program for the creation of standardized parts. The term program here has a number of valences. Most broadly, it suggests a "scheme of any intended proceedings; an outline or abstract of something to be done."[112] Less broadly, the term captures something of what Endy and Arkin hope will be achieved with the

C.dog projects—efforts to fabricate collections of parts that can be combined to form reliable mechanisms for regularizing the expression DNA. Less generally still, and taken as a term of greater analytic precision, the term program denotes both a specific kind of object with a specific kind of temporality. As an object, a program indicates the "regimes of jurisdiction and veridiction" (to use Foucault's cryptic but accurate phrase) that are not quite settled as embodied institutions, techniques, or apparatuses, but are nevertheless generative and partially determinative of a certain kind of future. In terms of temporality, a program describes an active relation, a *ratio* in the Latin sense of a reasoned process, between a plan for, and the realization of specific capacities, a relation and quality that characterizes the first six months of the BIOFAB.

My conversations in November 2009 with the Berkeley bioengineer ended with a mutual sense that however scientifically boring the notion of a fabrication facility might be to some investigators, it would be worthwhile to see what actually can be made out of this investment of time, money and effort. My colleague concluded that, minimally, Arkin would find a way to arrange things to address his lab's ongoing work on predicting genetic expression and RNA structures. In the weeks following this conversation I came to think that, observationally, what I wanted from the BIOFAB was precisely to see what it actually turned out to be. Moreover, I wanted to know how this actuality would fare as a proving ground for the 10 year old claims made by Endy and others that what was really needed in bioengineering was a catalogue of professionally engineered and standard components. The BIOFAB team has actually been successful in this regard. It has produced an initial catalogue of parts, those parts are self-consistent, and they have been assigned ranked performance scores determined by their activity in combination with other types of parts in the catalogue. During the period between the proposal for a BIOFAB and the production of an initial set of refined parts, I had assumed, success or failure would depend on the micro-politics of organizational and scientific formation. Whatever the long-term technical successes, the significance of the BIOFAB's program was likely to depend in large measure on the successful formation of the researchers involved—their technical capacities to be sure, but also their ability to reconcile tensions between the demand from Endy that they operate in a production oriented mode, while nonetheless having to sort through the difficult scientific challenges that would need to be confronted.

In sum, this thesis focuses in this six month period on the formulation and fashioning of a biological fabrication venue as a space within which certain kinds of work can be successfully taken up as well as one in which certain kinds of scientific attitudes and postures are both encumbered and required. The challenge then has been to study the convergence and interaction of diverse elements—the immediate background of work on standardized parts, the criticism of this work, and the stakes and investments in synthetic biology. I have also gauged how the media and government attention to synthetic biology has intensified during this six month period. And I have given sustained attention to the varying design styles and scientific commitments of the BIOFAB leaders and how these stylizations have contributed to shaping the milieu within which norms of seriousness and metrics of success were simultaneously unsettled but very much in force. All of which redounds to the ethical and vocational question of what it meant to become a participant in the invention of the BIOFAB's program for the creation of standard biological parts. One of the challenges I faced in attending to these questions as a formal participant in the invention of the BIOFAB was that it was never really accepted by those in power that matters of ontology, micro-politics, and ethics should form the principle materials of my work, despite my

insistence that such variables actually formed the heart of the problem of how one invents a program for synthetic biology.

It follows that I am perfectly aware that I could be focusing on the wrong range of elements, and possibly the wrong problem. The choice of any research project obviously entails paying the price of not studying other things. The critics of parts-based synthetic biology might think that participation in the BIOFAB is both a biotechnical and anthropological waste of time. More charitably, critics might endorse the prospect of a person concerned with questions of ethics as a core participant in these efforts, if only to catalogue how expectations were not and could not be met. In any event, it might (minimally) have been prudent to at least let things play out a bit more. Six months or a year from the end of what I have designated as the programmatic period—let alone two or three years from the end—the possibilities and limitations of a parts-based synthetic biology will have been given a more determinate form. The program will have been put into play, refined, reconstructed, or closed down.

From the perspective of what actually comes to pass with regard to the BIOFAB meeting or not meeting its stated technological goals, it might well be argued that the BIOFAB's initial program was, to quote Foucault, "no more than dreams, utopias, a sort of imaginary production that aren't entitled to substitute for reality." If the aim of the Human Practices experiment was to only to describe the "actual outcomes" and "real limits" of work in parts-based synthetic biology, the efforts of the BIOFAB specifically, I certainly would not be spending the time and effort to try and understand this brief constitutional moment and what I have referred to as its spiritual stakes. But the fact that the "actual outcomes" and "real limits" of the BIOFAB's work are likely to diverge (and indeed have begun to diverge) from the schemas and programs by way of which the BIOFAB directors, funders, and staff scientists imagined possible future outcomes and have worked to determine those outcomes, to quote Foucault again, "doesn't entail that these schemas are therefore utopian, imaginary, etc. One could only think that if one had a very impoverished notion of the real."[113] Minimally, the BIOFAB's efforts at creating a program will establish a core repertoire of practices and strategies for generating truth claims about parts-based biological engineering, as well as for governing the conduct of relationships, partnerships, technologies, techniques and the like. These programs for the creation of biological parts are likely to have determinative affects on the institutional forms, individual careers, and the selection of projects beyond the BIOFAB's current instantiation.

THE QUESTION OF SIGNIFICANCE

I want to recognize at the outset of this thesis that the programs for the creation of standard biological parts may not in fact prove to be significant, and the BIOFAB may be defunded without meeting its core goals as they were stated in the early phases of work. Given the positive reviews and the rising status of both Keasling and Arkin, and the deep commitment on the part of Endy, however, such closure is unlikely. This is the risk entailed in observing and participating in a contemporary and unfolding situation. It is a risk, however, that may be worth taking in that it opens up the possibility of both observing how arrangements of knowledge production, exercise of power, and ethical practices are being settled and unsettled, and, to the limited places where it is possible, participating in the determination of these arrangements.

In this light it is worth quoting the rest of the epigraph included at the beginning of this chapter, in that it draws to a point the challenge and worth of taking a "program" as an object of study. Having stated that programmings of behavior or regimes that induces particular effects,

such as establishing the terms of what gets to count as the distinction between true and false, or the terms of the way in which conduct is governed, Foucault states that the aim is "to grasp these effects as historical events – with what this implies for the question of truth (which is the question of philosophy itself) – this is more or less my theme." It would be more accurate to inflect Foucault's quote and say that the objective is not so much to grasp the effects as "historical events," per se, but as contemporary events—events that are unfolding in the midst of inquiry, and in the midst of which the work of inquiry is situated. This work of grasping contemporary events, I would argue, requires what Paul Rabinow has called "exoticising the familiar." In the case of the BIOFAB, this begins with the question: how, in this more or less familiar space, is the distinction between the true and the false produced? It then opens on to the challenge of determining how the production of true and false claims is made to be determinative for what work is found to be acceptable and worthwhile and what is ultimately left to the side. Additionally, what should be made of the fact as the BIOFAB continued to proceed in a mode of experimental and critical adjustment, modes of truth speaking and the government of conduct were inevitably adjusted? And finally, what am I to do about the fact that, however second-order I hope to be in my analysis, when many of the conceptual tools I have for thinking about the truth claims being made are connected to and are part of those very truth claims? My position, after all, as Endy has publically insisted, is not that of an embedded observer, but rather an integrated participant.

Foucault finishes the passage quoted above by suggesting that those variables which make up a program—truth speaking, power relations, and ethical formation—might be termed *political spirituality*. I introduce it here in order to bring into focus the question of the stakes and worth of everything that I have been talking about so far in this chapter, namely a first set of problems: what it means to constitute the BIOFAB. I have tried to establish that this first set of problems could be distinguished from and connected to a second set, which in the prologue to the recent past I designated with the term *spirituality*: what is the price to be paid, scientifically and ethically, for participating in the work of the BIOFAB? And although term spirituality, as I have already suggested, is likely to introduce misunderstandings and misgivings. It is a term which can simultaneously refer to too much and therefore clarify and specify too little. It is, however, the correct term here and has a useful analytic purchase. The term spirituality designates the experiences, relationships, practices, and institutional norms by way of which scientists (myself included) become capable (or incapable) of speaking the truth as part of an ethical life. Said another way: there is a price to be paid for being able to speak the truth as part of an ethical life, a price that entails forming (or deformation) of one's subjectivity. The question is: what is the price to be paid for those involved in the BIOFAB? And is it a price worth paying? This question, as I hope to show, that particularly applies both to the work of becoming a synthetic biologists and to my experiment in becoming someone capable of participating in such an enterprise.

CHAPTER 2

From Program to Deportment: Affective Ramifications

> *At the beginning of the letter [Seneca] refers quickly to the mental restlessness and irresolution with which we are naturally afflicted. He says: This mental restlessness, this irresolution is basically what we call* stultitia.
>
> —Michel Foucault[114]

The first official meeting of the BIOFAB staff was held on January 11, 2010. The meeting was located in a classroom at the JBEI facility in Emeryville, down a long central hall from the half-dozen assigned BIOFAB cubicles and truncated bench space. The classroom was too large; there were only six of us in a room designed for several dozen. Attending were the co-directors Drew Endy and Adam Arkin, the team leader for biological work, Vivek Mutalik, the operations lead Lance Martin, the team lead for software development Cesar Rodriguez, and me, the lead for Human Practices. The six of us constituted the core BIOFAB staff for the first six months of operation. A bio-informatics analyst and graduate student from Arkin's Berkeley lab, João Guimarães, would join the BIOFAB as a dedicated but unofficial member in February. In June, Endy and Arkin would recruit Guillaume Cambry, a post-doc from the University of Paris, as co-leader of the biology team and hire two junior technicians to support the biology team's efforts.

The meeting was short. Endy provided a brief account of the BIOFAB's mandate and relation to SynBERC. The various team members were asked to introduce themselves. Endy then provided an overview of what he took to be the defining aims, key work priorities and near-term deadlines, and finished by articulating several organizational values. If short, the meeting was significant for what it set in motion. Endy's account of the BIOFAB's mandate was a first articulation for the BIOFAB staff of the future the facility was designed to actualize. The account was similar to other formulations most of us had heard Endy deliver about the future of synthetic biology in other settings; and it was an account that would be inflected and adjusted as work proceeded. The formulation was distinctive in this setting, however, in that it introduced the tacit and unsettling expectation that each of us would come to embody that future and to make it possible for others to embody it as well.

The introductions, constituted a first attempt for each of us in relation to one another and our shared endeavor, to stylize our prior work as prolegomena to the current undertaking. And it was a first attempt for each of us to attempt a public statement of the stance or posture we were expecting to take up in relation to the kind of facility and future that Endy had presented. These statements were, of course, more or less fictive. All of us to one degree or another were involving ourselves in the BIOFAB because it presented a step forward professionally, though we did not say so. We were joining the BIOFAB in part because of the status of the project, the project directors, and the elite institutional setting. None of us were indifferent to the biological and engineering stakes of the undertaking. And several of us said something consonant with the

kind of biotechnical, ameliorated, and prosperous future that Endy had figured for us. Mutalik said something about the kinds of problems that energized his scientific interests; and Arkin, in addition to a kind of humanitarian statement about the worth of bioengineering, offered several biographical anecdotes that gave insight into his appetite for new experimental problems. I pointed out that none of us (including myself) had really said anything about the scientific virtue of curiosity and whether or not the BIOFAB was likely to be the kind of setting in which such curiosity might flourish. I also wondered aloud what the vocational stakes of our shared undertaking might or might not be.

These self-stylizations are worth calling out in that they have proven to be crucial vectors in the development of the BIOFAB, establishing organizational priorities and norms of what would be taken as good conduct. The future that Endy articulated, and which he would adjust and rearticulate in public statements as well as in the micro-politics of daily expectations, was not actually a future all of us took seriously. It was to that extent a future not all of us were comfortable identifying with or working to bring into being.

The discomfort had several sources. One source of discomfort was the apparent asymmetry between the experimental difficulty and scientific seriousness of the kinds of biotechnical outcomes Endy's proposed future tacitly entailed and Endy's apparent impatience with what he has often cast as the overly nuanced modes of work characteristic of most biological projects. For almost a decade Endy has vigorously insisted that biologists need to learn how to be better engineers, and never the other way around. The senior participants in the BIOFAB were trained as biologists. Another source of discomfort was that the future Endy imagined for the BIOFAB and thereby for synthetic biology was stated in declarative terms. It left no room to question whether or not that future was more or less likely, more or less feasible. And there was certainly not question of whether or not it was more or less desirable. The question was only how to bring it about. This declarative mode was unsettling insofar as the imagined future for synthetic biology not only *included* the work of the BIOFAB but was framed as *dependent* on the work of the BIOFAB. And each of us was not only positioned as a character in Endy's narrative, each of us was positioned as crucial to that future's eventual actualization. We were expected to design and bring into being the technologies, techniques, practices, and relations adequate to the realization of that future. That is to say, the design of Endy's future would largely fall to us. To the extent that the participants in the BIOFAB did not accept as worthwhile the future described by Endy, or doubted that Endy's approach was not biologically or socially feasible, an affect of unease was inevitable. Such unease would, at times, turn into irritation. And irritation would eventually become a low grade though pervasive uncertainty.

STYLIZING THE FUTURE

Endy has been a prominent spokesperson in the short-life of synthetic biology. A principal reason for this prominence is that Endy has provided the most coherent and, in multiple settings, the most compelling series of manifestos for synthetic biology. He has been a central figure in efforts to imagine the future of synthetic biology as one in which the engineering of biology becomes increasingly a matter of child's-play in the double sense of a practice which is relatively easy as well as fun.[115] This imagined future is compelling for its persuasiveness to non-specialists and its usefulness to specialists. In his vision biological complexity and the ad hoc nature of experiments in designing DNA can be managed through the creation of standardized components, facilities for the decoupling of design from fabrication, and the use of hierarchies of conceptual abstractions (e.g. "parts," "devices," "systems" to black-box (or at least background)

and thereby manage questions of complexity.[116] Endy has provocatively proposed that a key criterion of success in synthetic biology will be ignorance of how biology works.[117] We will know we have developed sufficiently powerful capacities for bioengineering when all designers of new biological systems need to know is how to use databases of characterized components, computer aided design technologies for selecting and configuring those components, and access either to at-home synthesis technologies to "print" their designs or low-cost high-speed fabs to which designs can be submitted and constructs returned.

In addition to his work articulating a possible future for synthetic biology, Endy has expended tremendous energy and time speaking, networking, and facilitating key projects and organizations on behalf of synthetic biology. Several examples could be cited. He provided the articulation of the core vision ("making biology easier to engineer") and organizational imaginary for SynBERC (parts-devices-chassis).[118] He was a founding co-director and co-developer of an ensemble of organizations dedicated to making circulating and advancing the BioBrick approach.[119] And Endy was centrally involved in the animation of both the iGEM (International Genetically Engineered Machines) Competition and the MIT Parts Registry, two of the defining venues in synthetic biology.[120]

Most relevantly, Endy has spent tremendous time and energy positioning himself as the principal advocate for the future of synthetic biology, a future that centers on the fabrication of biological parts as the key to unlocking the promised goods of biological engineering. Without Endy's persistent "pitch" over the course of a number of years the BIOFAB simply would likely not have been funded. That said, the BIOFAB was only actually funded when Keasling leveraged his status as a leading figure in biofuels development to get the deal done. Which is, of course, another way of saying that Endy's ability to provide a compelling vision of synthetic biology's has been crucial; it has not yet, however, proven to be scientifically sufficient.

Assembling a Manifesto

Endy is able to frame a vision for synthetic biology that is colloquially articulated, evocative, and, for many, persuasive. It is deceptively spontaneous and eager in tone. Deceptive here should not be read as deceitful; Endy is nothing if not earnest in his presentations on synthetic biology—before congress, a classroom, colleagues. Deceptively spontaneous characterizes Endy's style. He is a practiced rhetorician. The enthusiastic and plain spoken presentations, which are captivating in their mood of forthrightness, are not simply extemporaneous expressions of someone captured by enthusiasm. Endy has developed a feel for the way in which a down-to-earth style and forward-looking statements of imagined possibility affect an audience. A striking feature of discussions with Endy is how quickly he takes up an architectonic posture toward new ideas. When an idea interests him, he becomes restless, moves to a whiteboard, and begins sketching out how the idea might be ordered, framed, and presented. Crucially, Endy has not only developed a feel for how to frame a vision for synthetic biology, he has cultivated the performative capabilities to make such a vision persuasive.

Endy has been formulating manifestos for synthetic biology for a least a half dozen years. The manifesto gets readjusted from time to time: Endy has a feel for the changing expectations and tastes of his audience. Several topical elements have remained consistent, however, and these, in one form or another, have had a shaping effect on Endy's expectations for the BIOFAB. The first element is standardization. In both his publications and public talks Endy has made sweeping claims about the significance of standardization for the realization of the modern world.[121] He offers a range of examples: "Railroad gauges, screw threads, internet addresses,

'rebar' for reinforcing concrete, gasoline formulations, units of measure, and so on." He proposes further examples from biology to show that the life sciences, up to a point, are also properly modern: "standards of varying utility now exist for DNA sequence data and genetic features, microarray data, protein crystallographic data, enzyme nomenclature, systems biology models and restriction endonuclease activities."[122]

Bioengineering is an exception, and to that extent out of time. Bioengineering "has yet to develop formal, widely used standards for most classes of basic biological functions (for example, promoter activity), experimental measurements (for example, protein concentrations) and system operation (for example, genetic background, media, growth rate, environmental conditions, and so on)."[123] Bioengineering's most significant failure, as Endy casts it, is actually not a lack of standards for manipulating biological substrates (i.e. standards for parts development). Rather, its most significant failure is that it has not yet developed sufficient "social standards" for conducting work across space and time: processes for open standards development, appropriate licensing arrangements for sharing materials, digital protocols for sharing data, and so on. In order to illustrate this point, in his talks Endy frequently shows an image of a Roman viaduct, noting that without standards for how to cut and assemble stones, these structures could not have been built and maintained across generations.

The second consistent element of Endy's manifesto has been the notion of decoupling the design and construction of synthetic biological systems.[124] Endy tells the story of his first years at MIT and the courses in synthetic biology he designed with Tom Knight, Randy Rettberg and others. In these courses the instructors proceeded by implementing operational and conceptual strategies borrowed from, and basic to, the successful development of integrated circuits. A key to this success was the development of facilities that could manufacture designs made by individuals or groups who might otherwise not have the time or resources to fabricate their worn integrated circuits. In this way, technicians could spend their energies producing designs rather than carrying out the labor of construction. "Very-large scale integrated (VLSI) electronics," Endy has explained on several occasions, "only became practical once rules were worked out to enable the separation of chip design from chip fabrication." The notion of decoupling thus introduces a possible division of labor in bioengineering where designers and technicians play the roles of architects and builders. Effective decoupling would, of course, imply and requires advances in standardization. If designers cannot conceptualize systems without having to instantiate them to see if they work as expected, they cannot yet move to a mode and scale of work in which others provide fabrication. Hence an implied two-fold challenge for a BIOFAB, fostering rules as well as facilities for fabrication.

A third element of Endy's manifesto concerns the strategic use of abstraction hierarchies.[125] Endy's work at MIT, with the iGEM Competition, and then with SynBERC was marked by an insistent framing of synthetic biology as a task of generating biological *parts*, that could be combined into *devices*, that could be built onto *chassis* in order to form functionally complex *systems*. This specification had a double affect: it facilitated a means of managing complexity and it provided the schema for a division of labor. In 2005 Endy wrote that the key to abstraction hierarchies is that they allow individuals working at one level of complexity to effectively ignore details at other levels while still being able to interface their work with efforts underway on those other levels. During the programmatic phase of the development of the BIOFAB Endy's emphasis on abstraction hierarchies began to shift to an emphasis on "whole genome engineering" and "whole genome programming." (The circumstances of this shift will

be discussed in chapter 5.) Combining these two he has framed the efforts at the BIOFAB as an undertaking to create standard Expression Operating Units, or EOUs that one day might be composable into Expression Operating Systems, or EOSs.

Figurative Determinations

The formative characteristic of Endy's manifesto for synthetic biology, what shapes its motions and sets its ramifications, is the fashion in which he takes up prior developments in engineering, figures them as the future of synthetic biology, and thereby positions that future as determinative of present needs and actions. Endy begins with analogy to highlight an ostensibly shared characteristic of two objects. Endy compares the development of voltage standards to the possibility of establishing standards for determining the number of polymerase molecules that pass through a given segment of DNA per second; he compares the development of strategies for economizing the production of integrated circuits with the possible strategies for regularizing the design of metabolic pathways; he compares the relation of genetic expression and genome-scale cellular activity with computer programming and the functioning of computer operating systems.

The crucial subtly about this comparison is that synthetic biology does not yet exist in anything like a stable form. The use of analogy to make claims about its defining characteristics can only really be an exercise in specifying candidate features of a future one is expecting, desiring, or attempting to actualize. In this way there is a kind of transference that takes place in Endy's use of analogical materials. Rather than introducing them as cases or instances for making a comparison, he frames them as examples of general characteristics that are (or rather, that he thinks ought to be) defining for synthetic biology. Put differently, a rhetorical shift from analogy to metaphor takes place. Where analogy is a figure of speech involving comparison, a metaphor is a figure of speech involving the transfer of a description from one object or action to another in a fashion that suggests such figurative transfer is by some measure literally applicable. Figuring synthetic biology in this fashion involves the simple but crucial move from statements like "synthesis technologies today are like the printing press," to statements like "our main challenge today is to learn how to write DNA.

Hence, synthetic biology is not just analogous to prior efforts in engineering. The defining features of those efforts are also descriptive of synthetic biology. And, again, since the forms and venues for synthetic biology have yet to be settled, these defining features can only be cast in the future tense. This future tense, however, is presented declaratively as self-evidently desirable and on the way to actualization: it is that future to which one is compelled to be oriented. The metaphoric definition of synthetic biology is put forward as a vision of a future that needs to be made determinative of the present. This discursive reversal of the priority of the future over the present, this proposed reversal of cause and effect in which the possible near future becomes defining for present actions, constitutes a third figure of speech alongside analogy and metaphor: metalepsis.[126]

Metalepsis is a mode of speaking in which the metaphoric is used to reconfigure a relationship of priority between the future and the present. By way of analogy to instances such as the formulation of voltage standards, the construction of complex integrated circuits, or the programming of computer operating systems, Endy imagines a future for synthetic biology and states it as a set of defining parameters for work undertaken today. This figuration has been treated by some as visionary, or at least as a vision that mobilizes enthusiasm. It has been criticized as salesmanship or merely the rebranding of existing biotechnical efforts. Its ramifications, whatever the polemics, have become complicated and consequential. As Endy's

figuration of synthetic biology has been formulated as recommendations, connected to sources of funding, and eventually instantiated in institutional settings, attempts have been made to recapitulate the metaleptic as the organizational and managerial. The figurative future has been literalized and imposed as an ordering imperative on the present. And this attempt at literalization characterizes the programmatic outlay for the BIOFAB.

Scientifically, Endy's figurative vision for synthetic biology has been criticized as naïve about the actual challenges of biological complexity.[127] Indeed, in many of his presentations, to non-specialists and specialists alike, Endy has suggested that if we just had the right kinds of refined and standardized components, units of material could simply be compiled into genome scale "operating systems" for living cells.[128] These presentations have lacked technical detail about how such refinement and standardization might actually be achieved, and have equally lacked a detailed defense of the suggestion that genome-scale operations within a cell can be composed in an additive fashion by way of modularized genetic elements.[129]

Endy's response to these criticisms has been both vehement and strategically evasive. To those who say that biology is too complex, he responds that the relative constraints of complexity and the limits of modularization is an open question, which means we have to try.[130] To those who say biological organisms do not really have "parts," he insists that he is not trying to understand what nature is, but how it can be reworked.[131] To those who say this is about branding, he repeats the prior modes of biological engineering have never been rigorously standardized and so these efforts are, by dint of scale, organization, opportunity, unlike previous efforts.[132] Presumably his responses do not satisfy critiques of the feasibility and worth of synthetic biology and criticisms of him as its advocate.[133] However, he carries himself as though he does not really care, at least not unless these criticisms actually encumber his efforts. He advocates overcoming uncertainty through disciplined effort. It may be, he'll confess, that biological substrates per se will not support everything he'd like to do; but the primary blockage is that there is not yet a critical mass of individuals trained as engineers. Such a dedicated team working in a standardized fashion, and who deport themselves with a something-is-better-than-nothing stance toward the engineering of biological systems would ultimately be able to do it. What he actually means by "trained as engineers," "standardized fashion," and a disposition that favors the less-than-perfect, is not always clear. His restlessness for a future characterized by bioengineers of a certain type, and his brusque and even impatient insistence on that future's priority, however under-defined, has nonetheless been a dominant factor in the BIOFAB's development.

MAKING ENGINEERS: THE FIGURE OF RATIONALIZED PRACTICE

In meetings at the BIOFAB, particularly in the early going, Endy almost never speaks in the conditional about the future outcomes of the BIOFAB's efforts. He has occasionally acknowledge that the extent to which the BIOFAB will achieve its aims in the near term remains to be seen, and the extent to which biological substrates are susceptible to rational design and control remains to be seen. Rarer still he will describe the work of the BIOFAB as experimental, though resolutely not hypothesis driven. Experimental here refers less to the question of whether or not something like "the ability to program DNA at the genome scale is technically feasible," and more a recognition that no one else has really tried to animate a BIOFAB in anything like the same way it is now being attempted. In this sense, questions of organization, routine, protocol, and priorities need to be decided and adjusted as work advances. Endy speaks with vigorous insistence about the BIOFAB creating thousands of new standard biological parts, and that it will

do so in a way that facilitates functionally calculable composition of biological components at scale. And in his interactions with the BIOFAB he does not question the worth of the stated objectives, only that it cannot yet be taken for granted that other biotechnical practitioners will understand and thereby appreciate what the BIOFAB is trying to achieve. In short, the only questions would seem to be methodological and rhetorical: how will the BIOFAB go about meeting its goals and which framings of those methods and goals will prove to be persuasive as credible and worthwhile.

To be more precise, to the extent that Endy directly addresses methodological and rhetorical questions it is because his diagnosis is that the principle blockages to realizing the imagined future for the BIOFAB and thereby synthetic biology are subjectivational and therefore also jurisdictional. Making biology more engineerable is a matter of making biologists more like engineers—formative work that requires institutional support and resources adequate to securing the space and time to overcome what Endy takes to be the learned incapacities of trained biologists.

Biotechnical Warrants

Endy emphasizes neither possible scientific or technical limitations to the BIOFAB's undertaking. The task at hand is an engineering problem, and one for which there is now sufficient biotechnical precedence to warrant the BIOFAB proceeding apace. From the first meeting and over the course of the first several months Endy made regular references to several prior efforts in synthetic biology as initial warrants and strategic guides. The first, discussed in the previous chapter, was the study led by Barry Canton on the "Refinement and standardization of parts and devices."[134] Endy encouraged the BIOFAB team to read the Canton article as an exemplary outcome of his lab's efforts at MIT. It is exemplary in that it captures work in synthetic biology at multiple scales and across several labs and recapitulates this work as a design-ready artifact: a datasheet. In this way, the paper stands as a kind of proto-deliverable for the BIOFAB. In addition, Endy directed the BIOFAB team to Arkin's published review of to Canton *et al.* [135] Arkin's review, though critical, proposed a series of key refinements and next steps. In addition to these two, Endy would also cite as bioscientific warrant a study by another of his MIT students, Jason Kelley. Kelley *et al.* proposed a first-generation "reference object" embedded in designed genetic circuits to be used in conducting relative measurements.[136] The Kelley study, in Endy's view, stands as precedence for the possibility of conducting and sharing measurement of part function across operational contexts. More important, it was a crucial demonstration that standards for measurement of parts established for one lab might prove comparable and therefore worthwhile for others.

Endy asked the BIOFAB team to review these studies as successful first attempts to actualize key elements of a parts-based vision for biological engineering. They served to both justify and orient the work of the BIOFAB. And, at least early on, Endy expected that the BIOFAB team could proceed by simply taking up and refining the work presented in these papers. In relation to Canton *et al.*, it would continue the work of making and refining parts so as to produce datasheets; in relation to the Arkin publication it would combine an emphasis on refinement with more sophisticated management of biological context; in relation to Kelly *et al*., the BIOFAB would create a suite of reference objects to allow for relative measurements of the parts that the BIOFAB would be making and distributing. In sum, these studies were introduced as proleptic instantiations of the future Endy wanted for the BIOFAB. That future, as Endy has regularly and provocatively put it, will have been realized when "the central dogma has been

taken off the table as a research question for biological engineers." The "central dogma," of course, entails the foundational mechanisms for the genetic expression of proteins. The subtext is that the biotechnical warrant for the BIOFAB's work runs not only to the production of parts, but for the resolution of the key factors in the engineering of DNA.

More important to Endy than these previous studies was the iGEM competition. During the first eight weeks of operation he made regular reference to iGEM as both warrant and indication of possibility. As warrant, iGEM was characterized by a number of features that Endy would appeal to as constitutional elements for the BIOFAB's program. Principal among these was the central pedagogical proposition that in order to become better *bio*-engineers, student competitors need to first understand what it meant to be better *engineers*. Would-be synthetic biologists need to develop and leverage standardized practices—standard protocols, standard materials, standard construction methods, etc. They need to learn to black-box and thereby mange complexities and uncertainties to the extent possible and feasible. They need to learn how to implement the operational and conceptual strategies borrowed from, and basic to, the successful development of integrated circuits such as decoupling design and construction. And they need to use, refine, and resubmit modular parts housed in a common registry.

The appeal of such an approach is testified to in the tremendous growth of iGEM and the MIT Registry.[137] In 2005, for example, the field of participants expanded from five to 13 teams, and from one to four countries. By 2010, more than 150 teams participated, representing over 1700 participants, from countries around the world. No less striking is the growth in parts contributed to the registry. From the few dozen parts contributed in 2004 when the Registry was first being established, there are now over 12,000; of these, the registry managers have over 5,000 physical samples, which they are able to distribute to participating iGEM teams. Endy not only regularly made reference to iGEM as the largest single producer of standardized parts in the world, but on several other occasions he has rehearsed the fact that though the best synthesis work conducted in the best-funded and advanced labs results in the production of genomes consisting of hundreds of thousands of base pairs, the MIT parts registry has shipped out hundreds of thousands of BioBrick parts.

On one level, this vision of scale and proliferation is evocative. It can be interpreted as a testimony to both technical and social feasibility of standardization. To this extent it is not altogether surprising that the BIOFAB, proposed as a production facility for "thousands of new BioBricks parts," would somehow be integrally connected to the same vision for the future of synthetic biology which continues to inform the iGEM competition. On another level, however, claiming iGEM as a precedent for the BIOFAB's might be construed as scientifically limiting and thereby as a limitation on the BIOFAB's seriousness and credibility. iGEM, despite its significance as an educational experiment and as a driver for the expansion of synthetic biology, has been criticized as lacking sufficient quality and consistency. Just days after the first meeting of the BIOFAB, for example, the journal *Nature* published a plain spoken article entitled: "Five Hard Truths for Synthetic Biology."[138] Of these five hard truths three were directed at the parts-based approach to synthetic biology generally, and iGEM specifically: that standard biological parts are actually not well defined and poorly characterized; that such parts can't reliably be assembled into consistently functional circuits; and that even where characterized, parts are usually incompatible and therefore inoperable across biological and laboratory contexts.

All the senior organizers involved in iGEM acknowledge that engineering biology is rarely straightforward and almost never predictable, even with the help of reusable parts and a

registry. Moreover, the parts in the MIT registry were made, characterized, and registered by other undergraduates, many of whom are also trying out synthetic biology for the first time. As such it is hardly surprising that many parts would not yet be sufficiently characterized, and their performance across different contexts would produce unexpected results. More to the point, these criticisms of iGEM's relative lack of quality and sophistication are sometimes circulated by senior researchers in synthetic biology as evidence for the limitations of a parts-based approach—or at least the limitations of a parts-based approach that appears to strip away the difficult scientific questions of biological complexity and context-dependence. Hence, the extent to which BIOFAB identifies with iGEM and takes iGEM as the precedence for its work can be counted as a measure of the extent to which it might be opening itself up to the criticisms which have been leveled at the BioBricks program in general, the iGEM competition in particular.

Endy is certainly not ignorant of these criticisms and their possible implications for the BIOFAB's scientific reputation and institutional credibility, but it is precisely in view of these criticism that Endy cites iGEM not only as warrant but as occasion and indication of possibility. In the first meetings with the BIOFAB team Endy raised these criticisms of iGEM and a parts-based approach to bioengineering. Acknowledging the limits of prior work, Endy nonetheless insisted that the criticisms are usually "politically" and not "scientifically" motivated. It is not clear exactly what Endy meant by the term political in this context. He did not seem to mean that the criticisms arise from bad motives (though this might be the case). The term rather seemed to serve as a contrast term to *experimental effort*. A characteristic of the criticisms of the BioBricks agenda, Endy stressed, is that they are usually advanced as arguments for shutting down and not for rectifying or improving research.

Subjectivational Indications

At the first BIOFAB group meeting Endy underscored that the limitation of iGEM and the MIT registry has not been their vision for modularization, standardization, and sharing. The limitation, rather, is that these efforts have never been facilitated by a professionally run "parts factory." Endy stressed the notion of professionalization. No one should be surprised that the MIT registry of parts would be inconsistently designed, constructed, and tested; it was created by teams of undergraduates working under conditions of limited time and resources. The BIOFAB can remedy this situation. It can make parts that are well characterized; it can make the parts that teams really need; it can produce best-available standards for measurement and construction; it can make parts that function in a calculable fashion when composed.

To this end, Endy underscored, professionalization must become a core value for everyone at the BIOFAB, a metric by way of which work at the BIOFAB should be conducted and the quality of its products judged. Professionalization meant most simply paying a technical team to focus on and get work done in a regularized fashion that other labs often treated as peripheral or ad hoc. In this way it also meant being able to take up a certain stance toward one's work in which the capacity to get things done could be contrasted to a kind of self-indulgent (and hence unprofessional) impulse to know more than was needed. The standard of need in this case was not altogether clear, but it certainly turned on images of scaled production. The notion of professionalization carried both methodological and rhetorical imperatives for the BIOFAB team. The demand was that we proceed by stating what was going to be made, frame it as a product, and proceed as hastily as feasible toward completion and circulation.

In this light, professionalization entailed a certain price to be paid. Endy expected that the members of the BIOFAB team would cultivate a disposition toward synthetic biology cast in the

terms of his manifesto and mediated by an emphasis on production. Minimally, and concretely, this meant developing the managerial habits of articulating weekly efforts in terms of outputs justified in view of target deliverables. More seriously, it meant being willing to adopt a posture toward one's work in which a feel and desire for scientific seriousness would become tempered in favor of motion, circulation, and accessibility. In all cases it meant being willing to face the impatience with which Endy was likely to receive presentations of work done and plans for work yet to be completed. Endy exhibited a constant restlessness for a more homologous relation between his sense of what the practice of synthetic biology was supposed to consist in and how the members of the BIOFAB comported themselves and articulated their work. Philosopher George Canguilhem wrote that the machine can be distinguished from the organism insofar as the "rules of a rational accounting are rigorously verified. The whole is strictly the sum of its parts. The effect is dependent on the order of causes. In addition, a machine displays a clear functional rigidity, a rigidity made increasingly pronounced by the practice of standardization."[139] If Canguilhem's definition can be taken as an approximation of Endy's hopes for the eventual form and function of biological pats, it can be first taken as a statement of a kind of dispositional stance that one would need to adopt in order to produce such parts. The problem was, given the experimental nature of the objects to be invented, it was on yet clear what such a disposition of increased rational calculation might actually consist in.

A number of analyses of synthetic biology written from the philosophy and social studies of science have made much *epistemologically* of the stated aim of proceeding under a Fermeyian sign: "We don't understand something until we make it."[140] Not enough has been made *ethically* of this same claim. What is crucial to understand about Endy's push and impatience about the biotechnical future is not only that it entails a certain theory of knowledge. Endy is more interested in what it is that is actually being made than in the question of which theories of knowledge may or may not allow work to proceed. What is more crucial to him is that a synthetic approach entails and requires a certain form of scientific life. Given that such a form has only been traced in the most general terms, what this actually means is that when the BIFOAB staff present their plans and their work, they were typically met by Endy with resistance and instructions for readjustment. Whether or not a dynamic of self-presentation and critical rebuff ultimately proves sufficient to making standard biological parts remains to be seen. Equally important, whether or not such a dynamic could produce a stable and coherent form of scientific life, one that could be recognized as worthwhile by the BIOFAB team and therefore one that could be actively pursued, has remained a crucial question at the heart of the BIOFAB's undertaking.

It would be an oversimplification to say that Endy was proposing a strategy in which an intensification of habits and focus, and the scaling of fabrication alone would suffice to make incremental progress toward the long-range qualitative goals of establishing the know-how needed to rationally design genetic systems and scales of significant complexity. It would not, however, be a fundamental misconstrual of the expectations articulated in the early weeks of the BIOFAB's programmatic development. Endy takes it as a principle task as the director of the BIOFAB to instill and enforce a vigilant focus on the practical outcomes of work. Practical, in this case, is calibrated only to the generation of biological parts for an imagined user community. And although Endy is perfectly aware that such parts and their refinement will require facing any number of biological unknowns, he resists the suggestion that these unknowns can be affectively addressed by way of anything other than the attempt to make biological parts. In moments of discursive short-hand Endy will repeat familiar tropes of "no more endless discussion" and "let's

just get to work." Or, more curtly, he will interrupt discussions demanding, "Why are we talking about this?" Or "Why are you working on this?" Or "I don't understand what you're saying."

Stephen Shapin has called attention to a diagnostic mistake made by many in the social studies of industrial science. Shapin points out that a number of prominent studies have assumed that university researchers are hesitant to work in industrial settings, and that the source of their hesitation is the desire to work on "fundamental" rather than "applied" questions. [141] The claim is that university researchers do not want to expose their scientific work to the instrumental demands of commercial life. Citing the trade-organization writings of research managers working in industrial settings, Shapin shows that how far off the mark these sociological and historical assessments can be. Industrial research managers complain to their professional peers that the challenge with working with formerly academic researchers is *not* that they have to be forced to adjust their work to the excessively-pragmatic demands of industrial life. Rather, the research managers tell their peers, they actually have to devise methods that keep university researchers intellectually engaged with foundational questions and actively involved in scholarly communities. Quoting a director from Eastman Kodak, Shapin writes: just because of the accumulating temporal distance from the pure research experience of university training, "there is almost invariably a tendency [for any research worker] to move in the direction form fundamental to applied work. The practical problem pointed to here was not the strong and persistent socialization into academic values presumed by academic sociologists but its opposite—the mater-of-fact willingness of researchers to *abandon* such putatively distinct values."[142]

Shapin's insights notwithstanding, this motion from the fundamental to the applied has not held true in the case of the BIOFAB—at least it did not during the BIOFAB's programmatic phase. Several months into the endeavor, Endy said with a note of exhaustion: "it still takes a tremendous amount of work on my part to synchronize our work." Endy's statement was not a reference to the work being done, i.e. the coordination of the various operational components so as to achieve collaborative outcomes. Rather, he meant he still had to work to get the researchers to think about their work as calibrated to the quantitative production of parts. Of course the BIOFAB, unlike industrial research, is not oriented toward the creation of applications. In this sense the distinction between fundamental and applied research, which is so often used to figure a distinction between university and industrial science, is not particularly useful rhetorically or analytically. A different pair of terms that returned from time to time in Endy's direction of the facility was: *practical* and *not-useful*, terms meant to be consistent with the goal of producing, measuring, assessing, and circulating parts. The blockage, the de-synchronization to use Endy's language, has not been the result of the team's failing to understand that Endy wants to cultivate an ethos of product-oriented outcomes. It is, rather, the result of complications in determining what such an ethos would actually entail, and whether or not the scientific price to be paid for such product-orientation might be too high. To the extent that the BIOFAB team has been clear about what such what that ethos might entail, they have not yet found a comfortable way to inhabit the modes and dispositions which Endy would judge sufficient.

AFFECT: UNEASE, IRRITATION, IRRESOULTION

In the early weeks of establishing the BIOFAB's initial protocols and work plans, Endy not only needed to make the case that the construction of standard biological parts turned on the cultivation of professional standards of productivity. He also and more importantly needed to make the case that such an approach was actually scientifically feasible, professionally credible,

and vocationally worthwhile. Such efforts were not altogether successful, in that Endy's account of the worth and possibilities of synthetic biology and his assertions concerning the place of the BIOFAB in that story had not yet been (and would not altogether be) internalized by the senior post-docs on the BIOFAB team. One outward sign of this lack of internalization is that the post-docs, though comfortable discussing data related to the BIOFAB's experimental efforts, once such data was available, were not comfortable presenting and framing that data in terms consistent with Endy's overall narrative about the BIOFAB's enterprise. Such hesitation is no doubt partially dispositional. On the biology team's side of things neither Vivek Mutalik nor Guillaume Cambray are comfortable with an American biotechnological entrepreneurialism, and the tendency to be declarative about the salvational inevitability of scientific pursuits. Moreover neither has been given sufficient opportunity or pressure to become comfortable with a manifesto and prospective-oriented style of scientific self-presentation. More importantly, Endy's figurative mode of establishing the parameters for the BIOFAB's strategic goals has generated as much discomfort as it has biotechnical output.

This is not to suggest that the BIOFAB team has actively resisted Endy's vision or agenda, but that they did not yet find it satisfactorily scientific. Endy's emphasis on the need to produce professional datasheets for well-characterized parts was basically taken as self-evident. The need for software to support and drive such part production was accepted as well. The emphasis on BioBricks, on iGEM, and on reference objects as prior precedent, however, generated a measure of unease. A critical fact about the BIOFAB's development is that the team has come to expect Endy's product-oriented rectifications of their presentations without becoming comfortable with his product-oriented reframing and valuation of their work. To paraphrase John Dewey: for the staff biologists, the question of the worth of the BIOFAB's undertaking, could not be answered by argument—at least not argument on Endy's part.[143] Rather, what was needed was an experimental method and organized effort that would demonstrate to them that the catalogues of components they were producing had a plausible relation to the future of bioengineering and Endy was stylizing it. Such a state of affairs is hardly unusual in the contemporary sciences. After all, as Dewey put it almost a hundred years ago, the reasons for conducting experimental work "are not abstract or recondite. They are found in the confusion, uncertainty and conflict that mark the modern world." The experiment that needed to be conducted at the BIOFAB concerned the techniques and protocols needed for creating standardized parts. In this way, the BIOFAB might also be able to experiment with the modes of professionalization which Endy was advocating. Success on the former might have produced sufficient familiarity and thereby confidence in the latter.

Unease

A marked feature of working for the BIOFAB was the discomfort of finding one's work and therefore one's scientific place in the world being implicated in Endy's narrative about the future. To be made a character in someone else's future can be troubling.[144] It is troubling in that Endy's figuration of synthetic biology incorporates the meaning of the present into the imagined future. Articulated it with the forceful assurance, this incorporation has the practical effect of both determining what work gets to count as worthwhile or legitimate, but which future one finds oneself obliged to help bring into being. Add to the projective force of Endy's account of the future of synthetic biology the fact that he is the principle director of the organization and the implications become clear: by agreeing to work at the BIOFAB, the members of the BIOFAB team were actually putting themselves in a position in which they would either need to accept their role and comport themselves as part of a certain narrative about the future and as part of a

managerial effort to bring that narrative to actualization, or else develop strategies of resistance, compromise, or exit. Whether and how to respond to Endy's narrative about the future work were questions that created significant unease.

For Mutalik, and in a different way for Cambray (and for me in a yet different register and with different stakes), the troubling affects of Endy's push to imagine the details of the BIOFAB's program on the basis of a declared future were felt twice over. First, as just indicated, was simply the discomfort of being made part of someone else's narrative while occupying a position of minority status. Second, and more crucially, was the fact that Mutalik and Cambray both felt a certain skepticism about the future for bioengineering that Endy envisioned, or at least about the possibility of realizing it in anything like them boot-strapping and product oriented mode that seemed likely to be the mode as things moved forward. To be more specific, Mutalik was not persuaded that prior efforts such as the development of work with BioBricks, the iGEM competition, or the work undertaken by Endy's students at MIT were scientifically adequate to the biologically complicated reality of tensions between the integrated and context-dependent character of living systems and the stated goals of modularization, regularization of functional composition, and prediction and control of gene expression. The catch-phrase of "taking the central dogma off the table" was tantamount to solving the core challenges of the genetic sciences; Mutalik did not think that the BIOFAB—nor anyone else for that matter—was ready to meet such a goal or even really to envision a plan for how one might eventually meet it.

Mutalik had been working in a proximate relation to synthetic biology; his prior research in molecular and cell biology was focused on transcriptional regulation. At the time that the BIOFAB was funded he was directing a project engineering elements of genetic expression as a post-doc in Arkin's Berkeley lab. Prior to this he had worked for as a senior researcher in Carol Gross' lab at UCSF, where he specialized in strategies for predicting the strength of targeted regions of DNA activity.[145] Crucially, though experienced with biological problems of direct relevance to work at the BIOFAB, Mutalik had little professional or vocational investment in carrying forward a vision for the future of synthetic biology, per se. He had agreed to take on the role as the scientific lead for the BIOFAB partially because it simply offered an opportunity to work more closely with Arkin on an interesting problem. And though that problem involved the production of biological parts, Mutalik understood the key aim of the enterprise to center more directly on reworking the mechanics of genetic expression in such a way that the expression of specified proteins might be engineered at predictable levels. Mutalik, in this respect, approached work at the BIOFAB as an opportunity to contribute to a scientifically substantive matter.

It bears acknowledging that Mutalik, like others on the team, had also taken on the position at the BIOFAB for the simple reason that I represented a step up in professional status. As a senior post-doc in Arkin's and Gross' labs Mutalik had enjoyed a certain freedom. He was ready to move beyond the familiar post-doc work of only designing his own research projects and overseeing student rounds, and to take up the work of developing a more programmatic agenda. The BIOFAB offered a greater degree of supervisory responsibility and responsibility for shared research undertakings. Mutalik was, for all intents and purposes, hired to fill the role of the BIOFAB's research director—particularly before Cambray arrived to join him in these responsibilities. He was not actually given the title and authority of the official research director, however, despite being the research director in practice. Arkin and Endy, after all, were often only on site Monday mornings and Friday afternoons. This asymmetry between the expectation that Mutalik would scope out the core research agenda and his official status would eventually

prove to be one source of irritation. It would prove to be a source of irritation precisely at those points where Mutalik tried to deal with his unease about Endy's vision and approach by asserting a different and more biologically rigorous set of questions and protocols. And although these protocols in some adjusted from would eventually become the primary substance of Mutalik's work and the work of his team, they were almost always initially received and critiqued by Endy as falling outside the spirit and mandate of the BIOFAB's product-oriented goals.

Irritation

At the outset Mutalik was unsure how best to assert himself in response to Endy's brusque and occasionally dismissive style. At the end of the first meeting, Mutalik was asked to produce an initial set of questions and an initial project scope for the first phase deliverables. He was asked to complete these by the end of the first week, and then, over the course of the subsequent few weeks, to produce the basic experimental bases according to which ongoing work could proceed. How to go about that work was not made clear and Mutalik did not know how much freedom to exercise in animating the operational program. There were indications, as I've already noted. These were obfuscated, however, by what appeared to be the not-yet-consonant goals of (1) large scale production of "standardized parts" and (2) the refinement of those parts in such a way that their function in combination allowed for progress toward the predictive control of genetic expression. Another indication for how to proceed, of course, was suggested by Endy's outline and emphasis on professionalization. That Mutalik (with the other members of the BIOFAB) would be expected to deport himself in a manner consistent with the PI's vision for the outcomes of the project is not usual. The problem lay in figuring out precisely what this deportment meant, and what the price to be paid might be in terms of reforming his experimental habits and sense of scientific rigor.

The deliverables section of the original BIOFAB proposal, estimated that the infrastructure needed for producing the ~6,000 new BioBricks parts would be well in hand by the end of the first six months, with the library of parts completed at the 18 month mark. The proposal gave less focused attention to, but indicated throughout, that this library of parts would be designed in such a way as to facilitate the "scaleable rational engineering of the central dogma in *E. coli* and *S. cerevisiae.*" The task and challenge, then, was not only to produce libraries of parts, per se. The challenge, "more specifically," was to "design, build, and test a collection of engineered genetic components that control DNA replication, constitutive RNA production, RNA processing and degradation, translation initiation, and protein degradation." What was meant by "control" in the context of the proposal was not specified. But whatever this term was taken to mean, and however incremental progress was to be accounted, it was clear that the BIOFAB would be not just a production facility. It would be a production facility for the fabrication of components of a certain quality. That quality, in turn, would be measured by a certain capacity. And that capacity, as Endy would put it: was to build collections of parts whose functional reliability would allow for the "programming of DNA." Speaking in more exact terms, Arkin put it this way: the aim of the BIOFAB is to produce components that interoperate in such as way "that in a given genomic and environmental context that predictively expresses two proteins at defined mean and variances (relative or absolute)."

Mutalik proposed to begin by designing a basic genetic architecture for genetic expression within which the BIOFAB's collections of parts could be made, tested, and characterized. In conversations with Arkin, Mutalik determined that a consistent architecture was the most important first step for undertaking a controlled attempt to regularize the context of

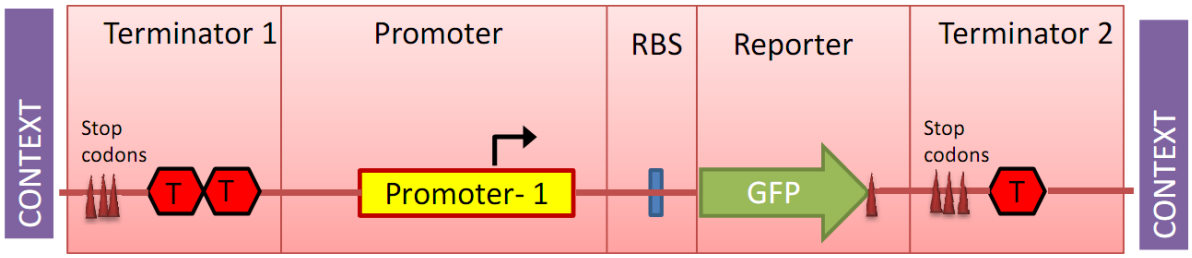
interactions that might affect the mechanisms upon which the expression of a protein relies. In this way the BIOFAB's attempts to develop a scoring system for the functional activity of any one element within this "genetic expression cassette" could be connected to a stabilized genetic environment. That is to say, a regularized architecture would allow the BIOFAB to say: element X of the genetic expression machinery seems to be stronger than element Y *within the following genetic environment*. Such an architecture would anticipate and counter one of the chief biological criticisms of previous work with BioBricks—that insufficient attention was paid to the ways in which the activity of elements in genetic expression is partially a function of contextual variables.

Mutalik conceived of his architecture as a linear set of interchangeable components, thought to be necessary for the expression of a single protein, and whose relations to one another have been specified and therefore can be defined, modularized, functionally re-composed, tested and fine-tuned. As a design strategy Mutalik proposed defining the physical boundaries of his cassette by left and right "insulators," intended to serve both as junction points for constructing assemblies of multiple units (hence, which function on a logic of assembly like BioBricks), and as buffers for regularizing (though not blocking) interactions with other elements of genetic context. In this way the cassette might be made to function as a standard rig for the measurement, characterization, and refinement of libraries of parts, as well as a platform for scaling complexity in functional composition (see diagram 2).

Equally important, by specifying the elements of a single cassette, Mutalik could also begin to propose an experimental strategy and production schedule. Each element of the cassette could be conceived as a deliverable to be refined, multiplied, and characterized against the other elements. The relations between the elements, their direct physical junctions, as well as the secondary structures they were likely to form by interacting with each other could likewise be specified and conceived as projects and deliverables. In this way Mutalik provided a template by way of which he could begin to multiply the incremental steps by way of which each element could be designed, constructed, tested against the other elements, measured, and if found worthwhile, multiplied and varied.

Endy seemed to appreciate Mutalik's attention to the details of genetic context, but he was eager to find a way of rendering his proposed work as part of the story he would be telling about what the BIOFAB was doing and what it would deliver. To this end, and drawing on an analogy to computer programming, Endy proposed referring to this standard architecture as an *Expression Operating Unit* or EOU. The term EOU suggests an identity between the expression of a single protein as the basic unit in the overall operation of genomic activity and a single algorithm as the basic unit of code in the activity of an operating system. The EOU thus represents a kind of "middle-out" strategy for working on the problem of standardization. It is middle out in that a given EOU could be composed of multiple standardized genetic parts (BioBricks or otherwise), and a given EOU will be designed to be modular and inter-operable with other EOUs so as to form what might be called an *Expression Operating System*. This terminology would prove crucial in the lead up to the BIOFAB's first review, which took place just a few weeks into operations.

Figure 2: Diagram of Expression Operating Unit v.1.0



Though appreciative, Endy was also impatient. He was eager to push forward and begin making libraries of parts—consistent with a "proven" architecture or otherwise. He reiterated the suggestion that "something is better than nothing" and encouraged the technical team to simply start making biological components, measuring them, testing them, and developing some scoring system by way of which their activities could be ranked and datasheets made available. One exchange in particular stands out. Mutalik was explaining the elements of his design, attempting to show why a systematic and incremental construction of the "rig" would provide a reliable context for measurement. Endy interrupted Mutalik, told him he did not understand what he was saying, didn't know why he was focusing so much energy and attention on details such as the structure of the insulator elements. Endy announced that the BIOFAB could not afford to have "philosophic discussions." He wanted Mutalik to move quickly to the question of which class of part he was going to make first ("promoters, terminators, ribosome binding sites?"). And how he would propose to scale production so that the BIOFAB experimental team could meet its goal of making hundreds of each of these parts, perhaps ordering them into "decades" of performance strength.

Mutalik comports himself in a manner that might be cast as gentlemanly. He is cordial. He asks questions. And he listens. He also is confident enough in his scientific skills and experimental capabilities to feel sure that the innovative elements of his designs were in fact quite important and worthy of consideration. Moreover, he was attuned to the range of basic biological questions that would need to be addressed, if not answered, on the way to "scalable production"—at least scalable production of an improved library of components. In this light, he did not know what response to Endy's disruptive insistence on productivity was either appropriate or likely to be effective. Mutalik expressed feeling both slighted and irritated. He was clearly angered by the sense that Endy was not taking the time to listen carefully and therefore not respecting the fact that he had something important to say. At the same time he was willing to take Endy at his word when Endy insisted that he did not really understand what Mutalik was saying. Mutalik took seriously that miscommunication might actually be the real problem, and thought seriously about how to adjust his style of presentation and how to be more careful in his use of language. He also took seriously that this was also more than a matter of miscommunication and also a tension between the kinds of questions Mutalik thought needed to be answered, and the kinds of outcomes that Endy was demanding.

To Endy's request for a more carefully articulated work plan for scaling production, Mutalik spent two weeks scoping experimental protocols in excruciating detail, ordered on the basis of the architecture he had proposed. His work plans included minutiae pertaining to how each class of designated component would be designed, ordered, checked, cloned, measured and

characterized. Not really understanding what Endy or Arkin expected in terms of designs and plans, and being understandably unsure about the relation between the expectation that he would generate libraries of parts, but that these libraries would provide the basis for understanding the rules of functional composition and predictive design, Mutalik exhausted himself in an expanding scope of detail.

Endy was not satisfied. And even Arkin expressed a certain disappointment. The dissatisfaction and disappointment had nothing to do with the amount of time and energy Mutalik had spent developing his plan. The negative response, rather, centered on how he presented the plan. Mutalik had only made his way through a few of his dozen or so PowerPoint slides when Endy interrupted him and asked him to express himself in terms of products and deliverables. When Mutalik insisted that this is where he was going Arkin interrupted, trying to re-script Mutalik's slides in a fashion that would satisfy Endy's demand. Arkin proposed using the logic of reverse engineering. What are the rigs that need to be built in order to generate and test desired parts? He moved to the whiteboard in the room and began to detail what such test and production rigs might consist in. Getting clear about these, he proposed, would then allow Mutalik to go back to the question of hierarchies of responsibility, Gantt charts for designing and ordering oligos, procedures for cloning and measurement, and so on.

The response to Mutalik's presentation is worth noting for two reasons. First of all, it begins to show the tensions between a metaleptic style of conceiving scientific futures in which the imagined future is made to be a determinate of the present, and a style that is oriented to thorough planning. It is not at all clear that any plans could have been composed that were adequate to the kind of deliverables that define the BIOFAB's agenda. The BIOFAB's goals, after all, are experimental. And any attempt try to lay out a production plan for reaching those goals is bound to only underscore the fact that there are no straight lines in experimental practice. Second, and no less pertinent, the response exemplified the discordance in the situation generated by the difference between the declarations of engineerability and the realities of experimental immaturity, between the norms about what constitutes the appropriate comportment of a synthetic biologist and the trained dispositions of a molecular geneticist such as Mutalik.

In a moment of irritation, after a meeting in which he again felt blocked and unable to explain himself, Mutalik threw up his hands and complained that the goals of the "C.dog project" were nothing short of the proposed aims of genetic engineering for the past 30 years. What had molecular biologists been hoping to accomplish for the last decades other than the controlled expression of specific proteins under specific conditions? "I am supposed to deliver plans for libraries of biological parts which will make such control possible?"All the same, in the first weeks of operation Mutalik was expected to take the lead on selecting a class of parts which would constitute the first BIOFAB collection, designing the genetic architecture within which those parts would be tested and characterized, and developing the work plan that would move the BIOFAB toward its goal of producing thousands of functionally composable standard biological parts. Mutalik's sense that he was being asked to produce something of a roadmap for the resolution of the core problem that had perplexed geneticists for a generation produced an acute discomfort, as one might imagine. As Mutalik put it to me one afternoon: "I'm supposed to do what other senior researchers not been able to accomplish in decades of work?"

Irresolution

Some on the BIOFAB team took the promised outcomes of synthetic biology more or less for granted, and accepted the proposition that a fabrication facility was vital to realizing those outcomes. Several participants had come to the BIOFAB having previously worked in Endy's lab at Stanford and had elected to leave Endy's lab and join the BIOFAB in large part out of a sense that such program was particularly exciting, particularly cutting edge. As one participant put it, he had been working for a biofuels company when he had heard Endy interviewed on the radio about the near-term possibilities of synthetic biology. He had been inspired enough by the interview and by the prospects for synthetic biology as Endy had spelled them out, that he contacted Endy, arranged a place in his lab, quit his job, and moved to Palo Alto to become a technician in the Endy lab.

Others were less sanguine about the revolutionary potential of either synthetic biology or the BIOFAB. And yet because the BIOFAB was an undertaking sponsored by Adam Arkin, it was thought to hold the prospect of at least being technologically sophisticated. And because it was directly connected to Jay Keasling's facility, and so was bound to have a certain profile. Endy's attempts in the early going to cast the work of the BIOFAB as the professionalization of previous efforts with BioBricks, nonetheless left Mutalik and others uneasy about what they had actually gotten themselves involved in. These allusions to past efforts as a kind of warrant and precedence for the BIOFAB seemed to lack sufficient scientifically serious. And here is where a tension entered in. The effort to design and manufacture collections of parts that were characterized in such a way that their use might make the design and construction of new systems more predictable was indeed a scientifically serious and difficult proposition. That this could be done by simply "making thousands of new BioBricks parts" wasn't.

In this light, it is hardly surprising that Endy's "something-is-better-than-nothing" framing of the BIOFAB's work would not only contribute to an environment of unease about the scientific stakes and worth of the undertaking, but that it might eventually produce irritation among those who would need to adjust their habits and expectations if they were to take up Endy's programmatic ambitions in a sustained manner. From the outset Endy was committed to the notion that sophistication and subtlety in unpacking the molecular nuances of genetic expression needed to be bracketed in favor of an intensification of production and manipulation. Such production and manipulation, facilitated by the right technologies, would allow for the generation of libraries of genetic objects at scale. Once such scaled production was underway two possibilities could be opened up. The first is that the generation of a quantitatively significant reservoir of materials would not only provide a catalogue of characterized elements for others to use, it would also provide the datasets needed to identify those places where refinements were likely to increase the consistency of part-performance across contexts. The second, connected to the first, is that scaled production of a professionalized sort would create a situation in which the lessons learned from other domains of engineering—particularly the standardization of materials, the use of abstraction hierarchy, and the refinement of norms for measurement and sharing—might begin to become normal for bioengineering. Said differently, the possibility of qualitative improvements in prediction and control lay less in the register of biological feasibility and more in the possibility of routinization and incrementalization of production. Scientific seriousness of a more familiar sort was less important.

In this regard Endy prioritized flexible and regularly adjusted manifestos as a means of orienting work. The challenge for those doing the work was how to live into, live with, and

contribute to the actualization of those manifestos.[146] A key step, in his view, was a willingness on the part of biologists capable of high-level experimentation to take up a more pragmatic and object-oriented posture to their work. Such a bearing would require being willing to pay the price of conforming to the authorized and authorizing standards of other scientific disciplines—be it molecular biology, chemistry, genetics, or even other domains of engineering. Norms of success and seriousness in these disciplines are no doubt far from settled or even clear, they may not even be contradictory to those of synthetic biology as practiced in other setting. The point that Endy pushed was that these other disciplines and their norms of practice constitute part of the problem. The terms of credibility for work in the BIOFAB would need to be cast in terms of a certain view of the future, an ability to demonstrate strict commitment to product generation, and thereby a reworked relation to one's own work. As Endy told the lead biologists on at least one occasion: "stop worrying about publications."

The extent to which the BIOFAB team members were affected by the unease and irritations that characterized the early going was revealed in t heir uncertainty about how to deport themselves. The challenge was to find a means of positioning themselves in relation to their work in such a way that Endy's demand for a certain kind of professionalization could be more or less taken up, but taken up in a manner that did not really require them to reform their sense of what counts as scientifically worthwhile. Such a situation ultimately became marked by irresolution—a restlessness with regard to the question of whether or not the BIOFAB was the right place to be pursuing their scientific work and scientific careers.

In this regard I was affected by the situation in a fashion not unlike the other team leaders. In the lead up to the BIOFAB, Endy and I met several times to discuss the role Human Practices might play in the BIOFAB. Over the course of several meetings I made it clear to Endy that I wanted to do work of the second-order sort that characterized the work of the Berkeley Human Practices group up to that point. I suggested that the BIOFAB offered the opportunity to experiment with the practical effects of such inquiry and analysis in that it would allow me to take up a closer position to the organization and practice of research as it unfolded. I proposed to Endy that I work on a series of problems which had been identified by the Berkeley Human Practices group. Two of which seemed most pertinent. First, the proposal for the BIOFAB had indicated a biotechnical goal of fabricating biological artifacts that were functional across a range of culture conditions. Playing on the notion of culture, taken in an anthropological sense, I proposed examining how it is that the work of the BIOFAB was likely to interface with and ramify across other programmatic efforts being animated under the sign of synthetic biology.[147] Second, the proposal for the BIOFAB had indicated that it would make its work "freely and openly available." The problem of the open distribution of material, data, and know-how had been foregrounded as part of the Human Practices agenda from the outset. In the fall of 2009 the Berkeley Human Practices group had conducted an extensive review of the uses and failures of the notion of "dual-use" as to frame an effective response to these aspects of synthetic biology. I proposed to Endy that I take up the question of how the BIOFAB might pose and strategically take up the questions of biosecurity and preparedness connected to the circulation of its work, but in a fashion that deliberately moves beyond the figure of dual-use. These two questions, I proposed, would provide a research portfolio that was scientifically and ethically serious, and held the promise of being directly connected to the BIOFAB's operations.

Endy countered by suggesting that a key reason for having me participate as part of the BIOFAB (he would later publically state "Bennett is not embedded in the BIOFAB he is part of

the BIOFAB) is that it allowed for "human practices in practice." It was not clear exactly what this implied about his view of the work I had been conducting as part of the SynBERC human practices thrust, other than the under-defined proposition human practices needed to be "useful for operational decisions." Endy suggested, in a friendly manner, that the significance of my proposed research agenda would be lost on most technicians. That even he, whose everyday life is saturated with synthetic biology in its extra-technical dimensions was not altogether clear about the full implications of what I was proposing. In this light, I recommended that I proceed on lines more consistent with what he hoped would be the ethos and orientation of the BIOFAB. He suggested I address my work to a series of topics that, although familiar to most longstanding participants in synthetic biology, would be both new and foundational to recent participants, particularly the new hires at the BIOFAB. These included surveys of parts-based bioengineering, of the iGEM competition, of the openness and sharing in biotechnology, of the differences between evolutionary and parts-based strategies, among others. The BIOFAB, after all, was set to make biological parts that were basic and pedestrian on some level, and not for that reason unimportant. He further suggested that I take up a kind of product-oriented mindset toward my human practices participation. To this end, he thought I should address one topic a month for six months, producing a short introductory report. After six months we would reassess the worth of proceeding in this manner, and, perhaps shift to a more inquiry oriented phase of work. I agreed to this plan.

By the end of January I had finished a first draft of the first of these reports. The title and theme was "What is a part?"[148] The report provided a brief overview of the key challenges the BIOFAB was likely to face in animating its program, taking this up in biological, conceptual, and ethical terms. This first draft was distinctive in that in it I tried to include materials from interviews with Endy and Arkin, from select synthetic biology publications, as well as materials from the philosophical and anthropological resources that had proven crucial in the prior work of the Berkeley Human Practices group. The draft tried to do too much. Indeed, much later, after several more drafts, much refinement, and much cutting, a frequent response from those who read it was that they did not really know what kind of an audience it had been written for. In any event, it was clear from the first draft that the report was unlikely to satisfy either the first-order expectations of the BIOFAB directors, Endy in particular, or my human practices colleagues. Eventually, much of the philosophic material was removed, although it tacitly provided conceptual structure. And the shortened report was given additional biotechnical credit through the addition of more technical material and more technical references. The final version was certainly closer to an essay in the philosophy of science than it was a kind of technical white paper of the sort that Endy had imagined.

It was clear to me that the resulting product was neither as anthropologically nor ethically serious as I would have preferred. It was also not clear to me how to adjust its degree of scholarly and critical seriousness while still producing a document that would satisfy my contractual obligations and my growing collegial sentiments toward the other members of the BIOFAB—as well as my earnest desire to take forward this experiment with thinking and writing as an integrated member of a biotechnical research team. There were three strong reactions to the report. The first was an attack by Endy's former colleagues at MIT who accused me of writing the history of part-based bioengineering as if their work was an afterthought. The second was praise from a number of biotechnicians who had publically positioned themselves as critics of the BIOFAB. The third was from colleagues in the human sciences who had been anticipating something both more sophisticated and more attentive to the critical stakes of the

enterprise. Most troubling for me was the third group. This report was the first piece of work they had read from Human Practices that had only my name on it.

In this regard the affects of unease, irritation, and irresolution that characterized the situation at the BIOFAB in its early going structured my experience as well. Like Mutalik, I experienced the discomfort of not knowing whether or not a willingness proceed with work that was likely to be received as less sophisticated, work justified in the name of productivity and accessibility was worth the price to be paid in terms of the uncertain position it put me in with colleagues in ethics, philosophy, and anthropology. That said, whatever affective consonance I experienced with the BIOFAB technicians it bears noting that my position was not equivalent to theirs. Despite Endy's insistence that "Bennett is not embedded," it was clearly understood from the outset of my participation with the BIOFAB that I would be writing an anthropological thesis on my experiences. In this sense my participation in the work of the BIOFAB was more tenuous and less professionally and vocationally risky than the participation of the other senior members of the team. It was more tenuous in that it was likely to be more difficult to adjust my work to the operational goals of the facility. And it was less risky in that any failure on the part of the BIOFAB to meet its technical goals was unlikely to constitute any professional or vocational blockages. There were certainly other dangers to which I was exposed in choosing to work as an integrated member of the team, and these will be discussed in later chapters. Here it is enough to say that the promise of an anthropological outside to my work meant that whatever irresolution and restlessness I may have felt was less poignant or frustrating than it might have been to the other members.

IRRESOLUTION: FROM UNCERTAINTY TO INDETERMINACY

In his book *The Scientific Life* historian of science Steven Shapin, surveying a number of theorists of "late modernity" states an affinity with their "attention to the accelerating institutional, intellectual, and moral *uncertainties* of the present and recent past." Such typically modern uncertainties, he proposes, "reach their highest pitch in many of the scenes in which new scientific knowledges and new technological artifacts are made." The proposition scarcely needs to be defended. The idea that late modernity is marked by "intense and accelerating *normative uncertainties*"—that is, uncertainties not only about what *can* but also what *should* be done—has become something of a commonplace. Less evident is Shapin's further claim: that within scientific and technological settings such uncertainties have an integral relation to what he calls "the personal dimensions of institutional actors."[149]

Shapin follows in a tradition of thinkers attentive to the place of virtue, familiarity, and charisma in the modern world. The subtitle of his book *A Moral History of a Late Modern Vocation* is an invocation of Max Weber's analyses of science and modernity. And his introduction states his intention to follow lines of inquiry opened up by Rabinow's anthropological investigations. Casting these in historical perspective, Shapin attends to the vocational registers in which "the radical uncertainties mark the venues from which technoscientific futures emerge" are given form and direction by way of the quotidian management of those uncertainties" through the personal, the familiar, and the charismatic.[150] Shapin strives to show how it is that in the midst of institutional settings in which expectations of rationalized order and procedural efficiency are a norm of organizational life, research directors faced with the myriad quotidian uncertainties of experimental practice must embody the kinds of virtues and capacities that allow them to simultaneously order and protect a space of activities less susceptible to such routinization. Quoting from theorist Stephen Turner, Shapin casts this

state of affairs as a kind of "age of charisma" for the industrial sciences, an age which belies many scholarly accounts of the character of outcomes-driven techno-scientific undertakings. Whatever Weber imagined when first introducing themes of virtue, charisma, and vocation in an analysis of the modern sciences it seems unlikely, Shapin suggests by way of Turner, that he would have imagined a future in which biological research would be animated by "the personal force of publically acclaimed charismatic personalities."[151]

A crucial feature of the BIOFAB's undertaking has been the ways in which uncertainties about production, performance, and vocation have been connected to and partially formed by what Shapin refers to as the personal virtues of the research directors. Virtue terms such as charisma, familiarity, and trust are keys to understanding the BIOBAB's program, as are the deficient forms of these virtues. Additionally, and in relation to uncertainty and virtue, are three variables to which Shapin gives relatively less attention. The first is what can be referred as the modes of veridiction—truth-telling—that have often constituted the form of the virtues under consideration. *Mode* here should be stressed. Second is the range of affects produced in relation to this truth-telling. Crucial, of course, are the dynamics of authority and credibility, whose role in forming situations of truth-telling have been well studied. Less care has been paid to the affective variables that also play a determining role and the problem of what posture one embodies, the deportment one determines is appropriate and tries to establish and take up, in relation to truth-telling as one response. These dynamics of authority, affect, and the problem of deportment have a determinative effect on the actual conduct of work and the subject positions which make such conduct actual. To this extent these dynamics and connections—uncertainties, virtue, vice, truth-telling, affect, subjectivity—put into question precisely the vocational stakes of which the subtitle of Shapin's book remind us.

Though Shapin's project provides a useful topical summation, his analysis does not, in fact, cohere with the developments as they unfolded in the early programmatic phase of the BIOFAB. Shapin's historical account takes among its primary aims demonstrating that in situations of uncertainty about the future the charisma of research directors moves things forward by establishing an ethos of relative certainty and trust. At the BIOFAB the *uncertainly* at play is less about the unknown character of the future and more an affective response to the scientific and subjectivational *discordance* generated by the unsettled relation between Endy's metaleptic figuration of synthetic biology and an adequate literalization of this figuration in the quotidian demands of planning and experimentation. Moreover, this unsettled relation is characterized by the fact that "the personal force" of Endy's "publically acclaimed charismatic personality" generates as much irresolution as it does trust.

Indeterminacy and Irresolution

Endy does not position himself as the kind of scientific expert whose experience, genius, or force of vision might be adequate to moving a situation of uncertainty to a situation of certainty. He has, however, taken up a position relative to the future of synthetic biology which is unapologetically certain about the feasibility and eventual actualization of a parts-based approach to biological engineering. The analyst might characterize this performance of certainty as sociologically naïve. And such a characterization no doubt has merit. Endy does not know what the future outcomes of the BIOFAB will actually entail, any more than anyone else involved in experimental practice. The early efforts at the BIOFAB have been characterized by the familiar uncertainties produced by the attempt to configure of a constrained research enterprise, to align experimental systems with unfamiliar domains of biological activity, and the

difficulties bound up in synchronizing milestone-driven research and the actual production of scientific knowledge are all familiar. Which is another way of acknowledging that, of course, the analytics of uncertainty, with all this entails in terms of the ever receding horizon of promised certainties, could be taken up as a means of characterizing the work of the BIOFAB.

Such an analytic, however, leaves something out, something which Endy's style and stance of certainty helps brings to analytic focus. The initial months the BIOFAB's operations have been marked not so much by *uncertainty* as by *indeterminacy*. Indeterminacy, as the word obviously suggests, concerns greater and lesser degrees of determination. The operational question at the BIOFAB in the initial period of the formulation of its program was not primarily how to move from a state of uncertainty to a state of certainty. Rather, it was how to move from a lesser to a greater degree of determination in an unsettled situation. Endy's strategic aims for the BIOFAB, however much these were periodically adjustments in Endy's manifestos, were almost always asserted in declarative and certain tones. And he exercised a persistent impatience with regard to those places and times in which the work of the BIOFAB seemed to be directed toward anything other than these conclusive goals. His style contributed to the generation of a situation in which the challenge was to design modes of practice within which the team could begin to find a determinate way toward those goals. This work of moving from lesser to greater determination was encumbered in at least two ways. It was encumbered by the question of whether or not Endy's assertions about the future outcomes of the BIOFAB's work were actually warranted. And it was encumbered by the difficulties produced by the stylistic differences between Endy's charisma and Arkin's veridictional mode.

Indeterminacy, as stated in the last chapter, concerns the work of knowing, thinking, and especially of creating.[152] Such work, in the case of the initial development of the BIOFAB, certainly required a scientific form for its eventual determination (and therefore an appropriately designed scientific situation). It is one thing, after all, to commit to an enterprise of producing standardized parts; it is another to know what a first-generation of such parts might look like. Although the problem of establishing a BIOFAB was characterized by well-recognized *scientific* indeterminacies such as the question "what is a part," it was also and more importantly characterized by less well-recognized *ethical* indeterminacies. The experimental question was not whether or not biological substrates can be refashioned in such a way as to open up the possibility of greater predictability in design of living systems. The question, rather, was how can the future of biological practice be *made* to be like the vision of parts-based engineering that Endy and others had advocated for several years, and for which the BIOFAB has received its funding. A question such as "what is a part" is only interesting to Endy insofar as it helps get work underway. Endy, like others, has confidence in the relation between the work of making and the incremental movement toward a determination of the capacity to make things in a more determinately controlled fashion. Whether or not such an experiment in capacity-building-through-making will ultimately be recursive enough to rectify the conceptual and pragmatic shortcomings and blockages it will inevitably encounter still remains to be seen. All of these terms—indeterminacy, productive experimentation, recursive rectification, and the like—are not Endy's terms. His are terms of production and certainty. And these terms, his terms, assertively declared in the initial months of BIOFAB operations, contributed to a situation of indeterminacy about the form and future of the BIOFAB, and its participants.

CHAPTER 3

Ontological Proliferations: Subjectivational Ramifications

Where is the living being? We see individuals, but these are objects; we see gestures, but these are displacements; centers, but these are environments; machinists, but these are machines.

—George Canguilhem[153]

The inaugural meeting on Monday January 11 began a rhythm of bi-weekly BIOFAB team meetings. Monday mornings the team would meet for what were initially referred to by Arkin as "hanger missions"; Friday afternoons, correspondingly, the team would meet for "hanger briefings." The objective of these regular meetings was to establish a structure of orientation, accountability, and regularization.

Both Endy's and Arkin's primary labs were off-site. Arkin's lab was only a few miles away on the UC Berkeley campus, but his appointments as the Director of the Physical Biosciences Division at the Lawrence Berkeley National Laboratory, PI and Co-Director, Virtual Institute of Microbial Stress and Survival, and Director of Bioinformatics at the Joint BioEnergy Institute meant that his availability for the BIOFAB was limited to scheduled meetings. Endy, for his part, was less organizationally bound to other projects and administrative appointments; he had arranged his schedule to be present at the BIOFAB several days a week. This meant, however, commuting the hour from his home and lab in Palo Alto, at Stanford, with all the potential for disruptions and rescheduling that such an arrangement inevitably entailed. Moreover, Endy, like others prominent in the world of biotechnology traveled incessantly. And although he took care to prioritize his time on site at the BIOFAB and eventually began to trim back his off-site obligations, such regular travel nonetheless meant that the Monday and Friday meetings were the times when the team could count on direct interaction with the directors, and were thus all the more crucial during the programmatic phase of operation.

Over the first two months of operation the meetings themselves became a kind of site and object of experimentation. The plan at the outset was for each meeting to consist of short presentations by each of the team members (PowerPoint slides expected, of course). These presentations were initially prepared according to a multi-part formulation of the organizational structure of the facility's work. Eventually, all of the BIOFAB's activities would be conceived on the basis of convergent problems and the aim of producing a targeted set of capacities. These capacities were framed in terms of the primary goals of the C. dog project, framed as a product to be released as a series of incrementally improved versions (C.dog v1, C.dog v2, etc.). At the outset, however, each of us conceived of our work as constituting something like divisions of a broad organizational undertaking. As such, the Monday morning task of presenting the scope of our work for the week was complicated by the obligation to explain how these activities fit into a larger organizational picture. Given that the larger scientific picture had not yet been sufficiently determined, this proved to be a cumbersome exercise. In a parallel fashion, at the Friday

afternoon meetings, each of the team members were expected to provide a report on how their division of the BIOFAB's work had proceeded that week—a task, again, consisting of enumerating the specifics of the week's activities, but with an eye toward organizational progress and coordination.

FROM DECLARATION TO VERIFICATION

The dynamics of the meetings were consistent. Endy was restless to get work underway and pressed for the immediate initiation and scaling of production. He regularly checked presenters, demanding they explain the relevance of the matter at hand in terms of strategic priorities and abruptly terminating conversations that seemed divergent. The provocation "I don't understand why we are talking about this" was emblematic of Endy's demand that things "staying on track." What it meant to "stay on track," in the early going, was not always clear to technicians and post-docs. Hence the tensions of a double impatience: impatience when the team did not seem to "get" the BIOFAB's mission or priorities; impatience when such a perceived failure informed the weekly activities.

Prior to coming to BIOAB Rodriguez and Martin had worked in Endy's lab at Stanford, and were familiar with his brusque and somewhat impatient manner in the meetings. Such familiarity, unsurprisingly, did not mean that they were not at times frustrated or embarrassed by Endy's critical interventions. It did, however, mean that they trusted that the director's mood and mode were not to be taken personally. Others were not familiar with Endy's style, and they were confused and occasionally frustrated by these interruptions. As such, these interruptions produced confusion and occasional frustration, as I explained in the previous chapter. Over the course of the first two months a number of us were working hard to close out previous projects and research commitments. This meant that we had insufficient time to undertake the painstaking task and challenge helping to develop the operational scope and the work priorities for the BIOFAB's experimental team. Given this situation, Endy's disruptions and demands for clarification could be particularly discomfiting.

On the occasion of a particularly terse exchange, Mutalik expressed frustration at not being able to "communicate more effectively" with Endy. No doubt communication was a contributing factor to the slippage and friction. But equally important were differences in style and disposition. Mutalik, though often frank-spoken, carries himself with a cultivated politeness and patience. Endy's insistence that Mutalik adjust to a product-centered approach to his work, and his impatience when such adjustments did not seem to be forthcoming, produced initial discord. After one attempt at Mutalik clarifying his experimental approach Endy responded, "I get it, you're a geneticist!" What such an assessment entailed is not clear; however, it was clear that being a geneticist was not, in Endy's view, the same thing as being a synthetic biologist. If the experience of judgment was uncomfortable, it nonetheless produced a certain motion. Motion would eventually contribute to experimental progress and progress to the production of data. Data would become something of an arbiter and buffer for the dynamics of the meetings.

I rehearse Endy's style and disposition here in chapter 3 in order to introduce a contrast that it struck with the style, disposition and mood of the co-director Adam Arkin. Arkin, like Endy, can be charismatic. His charisma is of a different sort and is directed to a different audience. The persuasive force of Endy's vision for synthetic biology seems to be felt most strongly by non-biologists looking to move into bioengineering from adjacent domains, by funders and regulators looking for strategies for better leveraging the long-standing instrumental hopes of biotechnology, and media representatives interested in a narrative about the future

possibilities of biological manipulations. Arkin's audience more often consists of scientific colleagues and engaged students. Arkin is a master of the scientific disquisition. He is capable of detailed and systematic assessments of a wide range of biotechnical and computational topics, and holds his audiences' attention with forceful scientific authority. When discoursing on a topic about which he has a particular interest or about which he particularly cares—problems with measuring RNA in cells, strategies for interfacing computational capabilities and quantitative presentations of data, or the physical limits of synchronization within designed circuitry—Arkin exhibits a capacity for pedagogical synthesis of an extraordinary quality, despite sometimes talking at inaudible speeds. Arkin's obvious pleasure in thinking through how problems are framed, details arrayed, and protocols carried out generates engaged energy and even enthusiasm for those listening who care about the same topics, at least it has for those on the BIOFAB team.

The affective force of Arkin's intelligence and masterly treatment of both scientific materials and experimental design is not only a product of spontaneity and earnestness. In a fashion not dissimilar to Endy's, his style and capabilities are also cultivated and long-practiced. Formally, Arkin was trained as a chemist. Materially, he has focused his work on the evolution and dynamics of biochemical networks. Crucially, he made his way through college at Carlton, graduate school at MIT, and a post-doc at Stanford by fostering a capacity for computational design and a feel for modeling. His formal training, his work in modeling and his efforts to bridge computational and experimental work in biology combine to position Arkin as a unique figure. Early in his career, Arkin, not satisfied with virtual models, and in lieu of finding biologists technically adept to conduct wet-lab experiments as a counter-part to his work in modeling, Arkin shifted his focus to bioengineering. Arkin has the disciplinary resources of mathematics, bio-physics, chemistry, the computational sciences and biology ready at hand and is capable of shifting scale and focus from the concrete demands of laboratory protocols to the intellectual topography of systems theory—a kind of single embodiment of the trans-disciplinary demands of synthetic biology. To this extent, Arkin's professional course has followed and given form to broader trajectories in biology over the last two decades. He gives the impression of having experienced an accidental administrative rise through elite scientific institutions, while otherwise making his way by dint of a feel for engineering systems. Arkin tells a story of hacking phone systems as an undergraduate. His etiology of the vocationally bound experimentalist resonates with his mood and disposition, even as it strikes a dissonant note with his institutional status.

In the days following the first BIOFAB meeting, Arkin, by email, began to specify some of the practical details the team would need to consider and address. These details included many of the basic decisions the team would need to make in order to get operations underway, whatever experimental portfolio was given shape: what bacterial host would the BIOFAB use for its initial experiments? What would be the first vectors and insert locations in those vectors? As the BIOFAB began to imagine the genetic constructs it might build, what functional components would be included and what would the first set of those components look like? What assembly methods would be used? And what measurement techniques would be introduced as standard practice for characterization work? Such attention to specifics had the effect of making the qualitatively broad objectives of the C.dog project seem less visionary and more practicable, concrete, and susceptible to incremental scientific actualization.

More importantly, and in addition to these rather basic operational details, were Arkin's Friday afternoon "scientific sermons," as the BIOFAB team jokingly referred to them. For

several weeks in the first month of operation Endy needed to miss several of the Friday meetings. On several of these occasions Arkin held forth on themes and questions central to the experimental undertaking at hand. The effect of these discourses was to instill the BIOFAB team with confidence in Arkin's scientific credibility and with trust in his ability to direct the facility's research. If, in the first few weeks, Endy frequently performed a combination of declarative assurance about the outcomes of the BIOFAB's work and frustrated impatience with the team's inability to reflect that same tone and orientation, Arkin often performed a kind of scientific expansiveness and biotechnical sophistication. His end-of-week discourses were remarkable because they were simultaneously thematic and detail-oriented. Crucially, Arkin connected these detailed themes to the key biological challenges the C.dog project would need to confront. These disquisitions again had invigorating and reassuring effects. And despite the fact that, upon reflection, they actually served to demonstrate and underscore the difficulty of the challenges and somewhat limited possibilities of success they nonetheless generated both curiosity and an enthusiasm for the undertaking. Additionally, they exhibited a level of scientific seriousness which had the effect of persuading everyone involved that they too must be scientifically serious and the project at hand scientifically worthwhile.

VERIFICATION AND THE PROBLEM OF CONTEXT

From the outset, Arkin has returned in a consistent fashion to three interconnected problems. The first concerns audience. Who should the BIOFAB take as the primary, or at least initial, recipients for its work? In discussing the incremental milestones for the C.dog project Endy has suggested that the minimal requirement is that the experimental team needs "to deliver something that others can use." On multiple occasions over the course of the first few months, Arkin posed the question: who are these others? Arkin proposed that one candidate "user community" might be participants in the CAGEN (Critical Assessment for Genetically Engineered Networks) competition. CAGEN is sponsored by the National Academy of Sciences, hosted by Caltech, and styled in the tradition of other high-technology competitions such as the DARPA Grand Challenge. The CAGEN competition, Arkin explained to the BIOFAB team, was being developed as a kind of iGEM for advanced engineers. Each year the competition hosts would specify the mean and variance of the expression of a specified protein in a specified host organism. They would then challenge participants to design genetic systems capable of producing that protein at those specified levels. Unlike iGEM, the designers of the CAGEN competition would take it for granted that participants would be well equipped with expert know-how, high-level technologies, and sufficient funding. What would it mean for the BIOFAB to produce standardized parts, characterization protocols, analyses, models, etc., if its target user was a participant in the CAGEN competition rather than the iGEM competition? In brief, if the BIOFAB does not specify who it's actually making biological parts for, then it cannot really anticipate what it is a prospective user is actually going to want to do. If it doesn't know what users are going to do, then, as in any design situation, it won't have clear specifications for what users will ultimately need or for knowing whether or not it has met those needs.

Hence a second and more technically specific problem: how should the BIOFAB measure what the objects it makes and what kinds of "scoring" will be considered useful, credible, and worthwhile? A principal warrant for much of the work being conducted in synthetic biology is precisely that unlike other engineering disciplines bioengineering lacks even the most basic shared standards for refining and regularizing the objects and protocols needed for design and composition. The problem of standard measurements is basic to this unsettled situation. How

should the activity and performance of designed systems be measured in such a way that others can understand, appreciate, and reproduce the designed system with those same measurements? And in the case of the BIOFAB, should the measurements and protocols be as highly exacting as possible and hence the production of libraries of parts relatively slow and only reproducible by other experts with access to the same techniques and technologies? Or should they be as high-throughput and easy to replicate by less experienced and well-equipped practitioners as possible? Should the measurements of components in a system be indirect, through the use of "reporter genes" such as optic readings of green florescent proteins? Or should it be relatively more direct such as biochemical assays of the exact amount of RNA being generated in a given design?

And thus the third problem. The questions of audience and measurement standards are difficult to settle in such a way as to achieve a sufficient measure of generalization (i.e. broadly useful standards). This is due in significant part because of a core scientific question at the heart of the BIOFAB's operations, namely that biological systems are extremely difficult to engineer in a consistent and regularized fashion. They are yet again more difficult to engineer in a fashion that allows for predictive design through the use of disaggregated and standardized components. These difficulties (and thus how best to address them) can be framed in any number of ways. One of which may simply be that biological systems are not susceptible to such bottom-up and generalized design strategies.[154] For Arkin, the chief and enduring problem, the principal biological challenge that the BIOFAB will need to face is the problem of *context dependence*. That is to say, the behavior of a given element of within a biological organism is in significant part a function of where it is located in the cell's genetic architecture, which host cell it is in, and what environmental conditions hold at any given moment. Moreover, given that the organisms in question are artifacts of biotechnical manipulation, their status and activity is also dependent on the operational context of the experiment—how materials are handled, what media it is treated with, what kinds of activities are selected for, and so on. The question of how the BIOFAB should go about addressing the problem of context dependence turns in part on its strategies for standardization and thus on the imagined community of users.

Arkin's disquisitions on the range of challenges connected to development of the C.dog projects, frequently to these three: users, measurements, and context. To the extent that these problems were taken up and addressed in an operationally coherent manner, and therefore made real for the BIOFAB's work, Arkin's disquisitions were at once serendipitous yet strategically beneficial. They were serendipitous in the simple sense that Arkin did not plan or schedule these expansive interventions; as often as not they consisted in Arkin holding forth on problems that had been occupying him in his work beyond the specific aims of the BIOFAB. In this way they were also strategically beneficial, whatever the prompt for these discourses, they provided an opportunity for the BIOFAB team to benefit from the energy generated from Arkin's own scientific curiosity and appetite for problem solving.

As sources of orientation for the BIOFAB team in their efforts to orient and animate the first phase their work, Arkin's impromptu lectures struck a contrast to the team's interactions with Endy both in terms of Arkin's style mode. Endy's style of presentation in the BIOFAB meetings can be characterized as declarative and strongly future-oriented. Arkin's can be characterized as pedagogic and provocative. By pedagogic I mean that beginning with a key topic, Arkin would proceed by way of testing the limits of the BIOFAB team's understanding of that topic. Posing a series of questions Arkin would begin to demonstrate that the team didn't actually understand the experimental subtleties of the problem at hand. Often Arkin would test

the team with questions in order to show that, in fact, a given problem (e.g. an assessment of relevant differences between two strains of *E.coli* for a given operation) did not yet have sufficiently satisfactory answers, and so needed to be approached through careful attention to experimental design and procedures. This pedagogic mode in which he would test the limits of the team's understanding of a given question, would in this way give over to a more provocative style. Arkin would begin to multiply and array the depth and dimensions of a problem: simultaneously showing how these multiple elements might eventually be susceptible to calculable regularities and patterns, but that those regularities and pattern were not yet in hand.

In this regard Arkin's mode of scientific truth-speaking can also be contrasted to Endy's. Where Endy's mode combined declarations about future outcomes with appeal to the prior work with BioBricks as a kind of warrant and orientation, Arkin's mode was decidedly *verificational*. Verification denotes a specific and delimited mode of reasoning, and Arkin would only treat as serious those truth claims which can be verified through the reduction of particulars to calculable regularities or patterns. The challenge of establishing possible rules for the calculable engineering of genetic expression was animated precisely by this dynamic. Could enough data be generated, organized, analyzed and modeled such that patterns of regularity could either be identified or engineered? Arkin was clear that such a possibility was likely to turn on establishing probabilities that could be managed within an acceptable range. Such probabilities, however limited in scope, would nonetheless constitute a significant biotechnical advance with regard to the forward engineering of genetic expression.

A distinctive characteristic of Arkin's verificational mode of reasoning and speaking the truth is an incessant movement—a kind of unsettled openness. This movement and openness is produced through the attempt to verify truth claims, on the one hand, through facts, and on the other hand through generalization or theory.[155] This incessant movement marked Arkin's discourses concerning primary technical and biological problems facing the BIOFAB. He would proceed by naming a problem, such as: how does one determine the parameters needed to predict gene expression? In a detailed fashion Arkin would then demonstrate that despite the fact that we know the equations, the processes of measurement and the range of available technologies, in combination with the variability of micro-biological and laboratory conditions make these parameters extremely difficult to specify in a stable and consistent fashion. In this way Arkin would detail the technical specifics at hand, align these specifics with generalized features of a problem, and show the BIOFAB team how progress might be made—but also that such progress itself was bound to be limited. It is hardly surprising that Arkin's pedagogical style, demanding verification, proved to be as much a complicating factor as a resolution of the simple question "what should we do and how should we conduct ourselves in doing it?"

The first of Arkin's pedagogic disquisitions, offered at the first Friday meeting, proved to be crucial to the BIOFAB's initial orientation. It focused specifically on the question of context-dependence in biological systems and the art of experimental design in view of accounting for as well as leveraging such context-dependence. Endy, having led us through a briefing of work on operations, software development, and human practices, closed the meeting and rushed out to take a scheduled call. It was late afternoon on a Friday and no-one seemed in no hurry to break things up, least of all Arkin who was expressing the energy and excitement generated by a planned project finally being underway. In light of my first human practices task, which was to compose a report on the question "what is a part?", I took the opportunity to ask Arkin if he could clarify the relevance for the BIOFAB of a criticism of parts-based biological engineering:

namely the claim that biology is simply too complex to be rendered susceptible to a part-based mode of design and composition. In framing my question I pointed out that in a published response to Canton *et al.*'s paper "Refinement and standardization of synthetic biological parts and devices"—one of the papers that Endy had cited as a precedence for the BIOFAB's work—Arkin seemed in fact to offer just this kind of critical evaluation.

In the abstract to Canton *et al.*, the authors rehearsed what has become a familiar diagnostic gesture: "The ability to quickly and reliably engineer many-component systems from libraries of standard interchangeable parts is one hallmark of modern technologies." To this claim they added a self-critical if equally familiar[156] caveat: "Whether the apparent complexity of living systems will permit biological engineers to develop similar capabilities is a pressing research question." The caveat is a curious strategic maneuver in that one of the premises of parts-based work in synthetic biology is that however biological systems "really work," the aim and the challenge is to refactor those systems so as to make them work differently. I asked Arkin to explain to us the double move he makes in light of to Canton *et al.*'s caveat. The double move consists of a kind of critical intensification. Arkin—who accepts what the authors have stated to be the case—namely that biological systems might be too complex to be rendered as standard interchangeable parts, then elaborated examples of things that might go experimentally awry. These examples, drawn from Canton *et al.*'s own work, show how Canton *et al.* might not really be taking complexity seriously enough. The second part of the double move (and hence my question) is that Arkin frames this critical intensification as an attempt not only to show the limits of Canton *et al.*'s undertaking, but also to support a more carefully considered and therefore presumably more feasible program for parts-based work.[157]

Arkin paused before responding to my question. The problem, he suggested, might not actually be complexity. "Complexity," he insisted, tended to be a kind of hand-waving term like "robustness"—a term which, although quantitatively meaningful in other domains engineering, was basically under-specified and overused in biology. "What does complexity actually refer to in terms of the challenge of making standardized parts?" he asked. Is it number of components needed to make a meaningful genetic circuit? Is it the sheer number of interconnections within a given cell or multi-cellular environment? Is it the multiplicity of states that characterize or determine those interactions? Is it the nonlinear and stochastic physics of these states and interconnections? All of these variables certainly would seem to undergird the criticism that "the overwhelming complexity of living systems will prevent biological engineers from fully achieving" the same capacity for control and standardization that has been achieved in other fields.[158] But, Arkin insisted, most of the time we don't know if this is what critics of parts-based bioengineering are referring to when they cite complexity.

In view of such rhetorical under-specification, Arkin proposed that the challenge faced by synthetic biology and by the BIOFAB specifically might be better framed in different terms. Reference to "the sheer complexity of living systems" tends to imply a multiplicative problem wherein there are too many interconnections doing too many different things. The challenge, rather, may be to take better account of the ways in which living systems and their constitutive elements find ways of managing these interconnections such that some of them are more rather than less significant at any one time. The fact of these strategies and the difficult biological question of how they work—or the technical question of how they can be leveraged—are captured better by the notion of *context dependence* than *complexity*. In this light, and as an orienting first step, Arkin proposed that the experimental designs for the BIOFAB would need to

proceed by conceptually and experimentally connecting three related problems: the problem of *host context*, *genetic context*, and *environmental context*.

The BIOFAB team would need to select an organism to serve as the host for conducting its first generation of experiments. Given the BIOFAB's aim of producing generally useful specifications and materials for standardization and interoperability, the selection of host is obviously crucial. "Which bacterium will be the most relevant or worthwhile for demonstrating our capacities and the worth of our work?" Sketching an image of a phylogenic tree on the whiteboard, Arkin asked: given that there is an estimated 10^{33} microbial cells on earth, which one should the team choose? One of the familiar and tested model organisms? *E. coli*? Yeast? If *E.coli* or yeast, which strain?

Expanding his image of the phylogenic tree, Arkin began to multiply a series of questions: we will want our constructs to work in one host but want to know if they will work in related hosts? And do we know what kinds of genetic relatedness matter for synthetic biology? The bacteria on one branch of the tree might be very similar to another one right next to it. But perhaps they evolve at very different rates? Or perhaps one is more "promiscuous" with its DNA than another? From one host organism to another the sets of genes are quite different. From case to case, how will those differences matter? At what point do mutations become problematic? On even the finest branches of the tree, where variation is most slight, we still find myriad little differences. "Will these differences matter? Sometimes."[159]

The biological question is: which organism will prove to be the most appropriate test environment for a given engineered construct? But should the host strain be selected on the basis of optimal performance alone? Or should might it be selected on the basis of who else is using that same strain? Researchers at the Joint Bio-Energy Institute, for example, employ an engineered strain of *E. coli* useful for the development of the metabolic engineering that they focus on. This customized *E. coli* might be worthwhile for engineering the isoprenoid pathways for the production of biofuel molecules. But is it worthwhile as a general "chassis" for the production of elements that we hope will eventually work in multiple host contexts? Researchers downstairs from the BIOFAB in Amyris Biotechnologies like many other commercial metabolic engineers use *C. cervaisiae*, yeast, for industrial scale production. Does the BIOFAB want to establish credibility with industry as a primary objective? If so, perhaps it would be worthwhile to produce a library of elements suited to *C. cervaisiae* rather than *E. coli*.

The question of how designed DNA constructs can be made to function in a given cell type—even a cell type as thoroughly studied as *E. coli*—is not obvious. Moreover, it is a question that cannot be satisfactorily answered in advance of experimentation work. The range of possibilities, under different experimental circumstances might be narrowed by appeal to the design specifications of the object one ultimately wants to make (e.g. are you making an isoprenoid pathway that produces artimisin or biofuels; are you trying to program the cell's ability to produce a certain protein at a certain level in order to harvest molecules or in order to form a certain kind of cellular population). In the case of the BIOFAB, however, the point is to design a technology platform that will work for and across an under-defined range of projects. The question is thus actually more difficult than which strain will most effectively support the activities of a given construct or set of constructs. The question is how designed DNA might act across and between various cell types, even across and between closely related strains of a single type. Presumably, if the BIOFAB is after standardization, some level of predictability of performance across various hosts will be crucial.[160]

"Let's say we've chosen our strain." Drawing the ectoderm of an oblong shaped cell next to his phylogenic tree, Arkin asked, "how will our engineered construct interact with and be determined by the DNA in the cell? Once a targeted sequence of DNA has been refined or designed, it has to be inserted into the cell's genetic context. Where in the ordering of a cell's DNA should it be placed? Does it matter? Usually." Should it be inserted directly into the chromosomal DNA of a given cell? If so, where in that chromosome should it be placed?[161] Upstream or downstream of which other genes? Or perhaps the designed construct should be inserted into the extra-chromosomal DNA in the cell. Such plasmid insertions would be much easier to affect, but should the facility choose a plasmid that makes a high number of copies within a cell (and therefore lots of copies of the designed construct) or a plasmid with a more precisely controlled number?[162] The architecture of these relations and their junctions are likely to produce interactions and recombinations; which of these will prove useful and which disabling? How should these be designed, tracked, assessed, characterized, and accounted for?

Once a genetic construct has been designed, inserted at a specific site in a specified plasmid, and that plasmid inserted into a characterized host cell, a range of variables will need to be considered. What medium will should the cell be given? What kind of container will the media and host cells be placed in? How should the cells be measured? How should measurement instruments be calibrated to assure consistency? The problem of genetic context, in other words, is intensified by the fact that cells live in an environment, however controlled the experimental conditions. This environment—other cells, nutrients, structures, temperature, signals, pressures, and so on—have formative affects on the host cells and the performance of the designed construct. And indeed, within the relatively managed space of laboratory technologies and protocols, questions of environmental context are actually intensified through efforts to direct, select, and stabilize the functions and states of living organism within a designed milieu. The problem of environmental context, with all it entails in terms of operational context, is perhaps the most variable and difficult part of the undertaking.

Given such complexity, the question is not whether standardization is possible, i.e. whether or not biology can be made easier to engineer. Rather, the question is a matter of scope and degree. A challenge then is to design *projects* which are points of entry into this broader *problem* as a means of opening up new points of view and thereby expanding *capacities*. To this end, Arkin proposed substituting the problem of biological complexity for the problem of context-dependence. That substitution, he suggested, would allow the BIOFAB to foreground an experimental question that while broad, would also seem to be susceptible to specification and experimental intervention. The question is: if evolved biological systems have developed strategies for re-using a finite set of motifs and elements to produce multiple forms and functions across a variety of contexts, to what extent can engineers either leverage or redesign these naturally given strategies or produce their own strategies? Such a question can be taken seriously to the extent that we understand the evolved mechanics of genetic expression as warrant and justification for the effort.

Biological systems, after all, are composed of a finite number of motifs that function in a kind of modular and combinatorial fashion, modules and functions that are "shared, tuned and rewired across and within organisms to create new behaviors." Evolutionary biology, taken up in this way, can be characterized as exhibiting modularity-in-context. Moreover, it is the case that living organisms have evolved a number of strategies (some spatial, some temporal, some topographic) to ensure that, despite the overwhelming number of *possible interactions* within

even a given cell or between a cell and its environment, only a smaller subset of *actual interactions* are relevant at any one time. This distinction between the possible and actual interactions would seem to be crucial to the calibration and success of the BIOFAB's program. No less so is the question of the extent and limits of the BIFOAB's ability to rework the terms of this distinction. The problem in answering this question, however, is that although existing mechanisms may allow living organisms to manage complexity and context dependence, these same evolved strategies themselves are also characterized by a kind of contextual fine-tuning.[163] Whether or not such contextual fine-tuning can be made a part of a strategy for the rational design of living systems did not really seem to be in question. How to go about the work, however, was an open and difficult proposition.

REFACTORING CONTEXT DEPENDENCE: THE LIVING BEING & ITS MILIEU

It is worth introducing a clarification at this point: the distinction I introduced to summarize Arkin's assessment of context dependence, the distinction between possible and actual interactions and the question of the relevance of this distinction for the work of the BIOFAB, constitutes a reframing of what Arkin actually said. I point this out because the distinction and the reframing served, at the time, as a way of recasting the BIOFAB's research agenda and initial programmatic efforts in terms that I found engaging and conceptually worthwhile. In a fashion similar to others on the experimental team, I was uneasy about the scientific merit of Endy's production-oriented vision for the BIOFAB and of my role in working to realize that vision. As I explained in the previous chapter, the uneasiness turned, in part, on the question of whether or not I had gotten myself involved in a scientific program worthy of the name, or if the BIOFAB was simply going to be a facility for the recapitulation (albeit at scale and with a certain additional rigor) of previous work with BioBricks. The question was not whether or not such re-capitulatory work was worthwhile, per se. The availability of well-characterized libraries of parts will very likely prove a useful resource. The question rather, to put it honestly, was whether or not a product-oriented mode would prove analytically engaging and ethically serious.

Arkin's emphasis on context dependence, and my reframing of that emphasis as a question of possible and actual interconnections, engaged my scientific curiosity and thereby energized my intellectual engagement with the BIOFAB's endeavor. Indeed, his impromptu lecture catalyzed enthusiasm for everyone in the room, including me. For my part, as explained in the prologue, the BIOFAB presented a worthwhile opportunity for carrying forward the Human Practices experiment on multiple counts. Not least was the fact that as the first facility strictly dedicated to the production of standard biological parts, the BIOFAB constituted a sort of proving ground for the proposition and hopes of a parts-based and open-source synthetic biology. Additionally, the intensification of interest in and support for social scientific engagement with synthetic biology had been predicated exactly on worries connected to this proposition and the dangers it ostensibly entailed. Hence, the opportunity to participate in a sustained an integrated fashion with the micro-practices of everyday life in this facility was more than justifiable. What Arkin's emphasis on the problem of context-dependence added was the activation of a scientific and philosophic curiosity, which had begun to wane. My report-writing responsibilities, contractually agreed to, were at risk of becoming transcriptions of the directors' basic statements about the BIOFAB's operational priorities. Several times over the course of the weeks following these exchanges with Arkin my Human Practices colleagues pointed out to me that I was

repeating, rehearsing, and extending my reframing of Arkin's explanation of context-dependence in rather impassioned tones.

My enthusiasm turned on possible connections I was beginning to revisit between parts-based synthetic biology and the writings of philosopher and historian George Canguilhem. It seemed to me that the problem of context dependence and the goals of modularization might constitute a possible re-problematization of the long-standing problem of "The Living Being and Its Milieu"—to cite the title of Canguilhem's important essay.[164] That problem, at once conceptual and experimental, concerns the relation between the individual organism and its environment, how that relationship should best be understood, and the ways in which that relation may be opened up or constrained by biology taken up in an experimental mode. I held that that the problem and program of parts-based bioengineering could be fruitfully reconceived using Canguilhem's terms and analytic framing. Those terms and framing became a point of orientation for my work and engagement, including the formulation of my first deliverable, the report "What is a Part?"

In his essay Canguilhem poses a question concerning the dynamics of mutual determination: what are the ways in which scientists, since the early 19th century, have conceived of living organisms as being determined by or determinative of their environments?[165] Canguilhem proposes that prior efforts to think through the question could be arrayed in relation to two analytic and experimental poles. At the one pole is a cluster of conceptualizations that are characterized by *mechanistic* understandings of the relation of the organism and its milieu, understandings in which the organism is basically a function of its relation to the milieu. At the other are characterizations that can be called *genetic* understandings of that relation, understandings of the organism as having a genetic endowment that basically resists the milieu in its constitution and expression. Between these poles one finds a more limited set of conceptualizations that can properly be called *biological*, a limited set in which the dynamics of mutual determination are both more subtle and more uncertain.

The Milieu as Mechanistic

Canguilhem explains that the notion of the milieu, if not the term, has been crucial to scientific apprehensions of the form, function, and experience of living organisms for at least two centuries. The notion of the milieu had previously been developed as a partial solution to explanatory problems in physics and mechanics on the one side, and anthropo-geography on another.[166] The question in relation to these previous developments was whether and how the notion of milieu might be different for biology.

Canguilhem proposes that the first theorists to pursue this biological question in a sustained fashion inherited the concept of the milieu from 18th century French mechanics, Newton had introduced the notion of the *ether* (and hence the concept of the milieu) in order to solve the problem of how to account for action at a distance. Ether, Newton proposed, could be understood as the medium of action. Hence a milieu in this case is first of all a space between two bodies, but not only a just a space. Rather, as a fluid, ether "penetrates all these bodies"; they are constituted by it. The active principle is the milieu. Moreover, because the milieu, the ether, could be defined strictly in terms of physical properties, relations among various phenomena, including organic phenomena, relationship that served to constitute those phenomena was strictly mechanical.[167]

The problem for 19th century sociologists, geographers, and biologists, was whether or not such a mechanical notion was really sufficient.[168] Was it possible to comprehend "the ensemble of actions that act on living beings" without presuming that the actions of a living being could be satisfactorily explained by an account of the physical properties of that ensemble? Comte is the first to frame this biological question in mathematical terms: how should we determine the function of the interaction between the organism and the milieu? And if the function is indeed produced by an ensemble of variables, the task of scientific thinking is to determine the function *by* those variables and determine the significance of each variable *by* the function. And what are the variables for which the milieu is a function? Those that can be studied empirically, which is to say those that can be understood in terms of physical and chemical invariables. The answer to the question of the living being and its milieu was that "the quality of an organism [can in fact be] reduced to an ensemble of quantities." The milieu designates "an indefinitely extendable line or lace, at once continuous and homogenous, and with neither definite shape nor privileged position."[169]

In Darwin, the field of elements and movements again consists only of those things that are susceptible to empirical study. These elements and movements, however, are no longer under-lying physical or chemical actions and reactions. Rather, the elements and movements consist of living beings in relation to one another. Canguilhem explains by analogy: with Darwin the milieu constitutes a judgment of each living organism; if one passes that judgment, one temporarily becomes part of the jury, awaiting judgment again someday. If not, one is judged unfit the mechanisms of the milieu, one's relations to other living beings carries out the sentence of elimination from the vital order. In either case the individual organism is again a function of the milieu.

Canguilhem summarizes the mechanistic position in this way: once the organism is conceived in relation to a milieu in which its apparent individuality is "endlessly negated by exteriority," then the milieu becomes "a pure system of relations without supports." The milieu is primordial: "the milieu thus comes to be invested with all power over individuals; its power dominates and even abolishes that of heredity and genetic constitution…the organism gives itself nothing it does not, in reality, already receive." [170] Organisms, whatever their apparent integrity, always refer back to the milieu as the source and explanation of their being.

The Milieu as Genetic

The clear outside to the notion of the mechanical determination of the individual organism by the milieu is, of course, the formulation and rise of the science of genetics. With the work of Bateson, Morgan, Muller, and others the determinism of the milieu began to be displaced in favor of the hereditary integrity of the organism through the germ-plasm. "In creating the science of genetics, they came to maintain that the acquisition by the living being of its form and, hence, its function depends, in a given milieu, on its own hereditary potential and that the milieu's action on the phenotype leaves the genotype intact." Put differently, with the work of Morgan and Muller and their collaborators the direct formation of the living being by a physic-chemical milieu, a formation that would conceptually conform to older notions of a mechanical and determining fluid or an encompassing and determining world, began to be replaced by emphasis on the genetic "autonomy of the living in relation to the milieu." These researchers certainly understood that the physico-chemical milieu played a crucial role in the actualization of form and function, and designed experiments to produce selectable mutations accordingly. But in these cases, the milieu was never really a factor in determining the integrity

of the living being. Rather, it was only a factor in modification, selection, or elimination and not the production of new forms.

With the intensification of molecular genetics in the second half of the 20th century and especially the development of recombinant DNA, with all of the techniques and technologies that have facilitated its expansion and instrumentalization, the earlier genetic supposition of the integrity of the individual organism against the milieu has gone out of sharp focus. Nonetheless, the notion that the genetic material is the active principle in the formation and therefore function of the living organism remains central. The notion of the milieu as a zone of actualization has certainly been brought nearer to the foreground, relatively speaking. One could take as an example the creation of technologies which allow genetic engineers to test colonies of cells against the selective conditions of cellular cytoplasm and the experimental conditions (e.g. oxygen levels, population density, carbon sources, temperature, etc.). Such technologies underscore an appreciation for the dependence of the expression and successful functioning of a given genetic construct on its environment.

The Milieu as Biological

The mechanistic notion of the milieu in which the individual organism is simply a function of the relations and elements in the environment, and the genetic notion in which a living being's form and function can remain indifferent to the constitutive pressures of an environment, begin to show their explanatory limits in the geographical sciences. By the late 19th and early 20th centuries, Canguilhem notes, these sciences have begun to take "complexes" as their principle object and concern: "complexes of elements whose actions mutually limit each other and in which the effects of causes become causes in turn, modifying the causes that give rise to them."[171] Familiar of such complexes included the cycle of temperature and wind generation and the exchanges between plants and their environments. The principle that causes can become and be treated as supervening causes began to reconfigure the conception of milieus in relation to living beings as well. Such reconfiguration had as a principle feature and conceptual advance the requirement that organic actions could not simply be treated as physico-chemical reactions to a provoking environment. Rather, the organism itself needed to be understood as essential to the play of organic movements. Such a shift in conceptualization thus required a different order of confirmation: the organism would have to be considered as a being "on which not everything can be imposed, but its existence as organism consists in its proposing itself to things on the basis of certain orientations that are proper to it."[172] Or, to put in Canguilhem's terms: "the animal does not react as a sum of distinct molecular reactions to a stimulant that can be divided into units of excitation. Instead, the animal reacts as a whole to total objects, and its reactions are regulators for the needs that govern them."[173]

This conceptual shift introduces the possibility of a properly *biological* and not just genetic or mechanical mode of explanation. A biological mode of explanation requires taking seriously a kind of interplay between the organism and the environment within which dynamics of scale and temporality require a scientific flexibility and willingness to adjust what one is choosing to emphasize at various moments and under various conditions. As Canguilhem puts it: "one must understand that the relationship between the organism and the environment is the same as that between the parts and the whole of the organism. The individuality of the living does not stop at its ectodermic borders any more than it begins at the cell. The biological relationship between the being and the milieu is a functional relationship, and thereby a mobile one; its terms successively exchange roles."[174]

Such notions, Canguilhem explains, actually recall and reactivate formulations first proposed by Larmark. Unlike the mechanical views of physics and anthropo-geography, Lamarck insisted the action of the milieu on the organism is not a "direct action by the exterior milieu on the living." The action, rather, is indirect and passes through the intermediary of need.[175] The term *need* here is crucial, and helps clarify the connection between Canguilhem's framing of the problem of the milieu and the BIOFAB's consideration of the problem of context-dependence. "Need," Canguilhem explains, is of course a subject term. It therefore might seem out of place and out of bounds in an account of material causes and effects. But considered from the point of view of the living organism, a given ensemble of influencing circumstances dominate and determine the experience and fate of an organism only insofar as the organism responds. It is in this sense that, from the organism's side of things, of all the possible effects a milieu might have, only some are actually significant. The intermediary term that explains that selective interface is need. If the influencing circumstances meet the organism's needs, the organism will survive and maybe even thrive. When circumstances change, however, the organism's needs must change as well. Such a conception would seem to have important implications for the notion and possibility of a biological part.

"This I not to contest," Canguilhem adds, that the exchanges between a living organism and the milieu "happens through reflexes whose mechanism is physico-chemical." The *biological* question, however, is precisely: what are we to make of the fact that out of "the abundance of the physical milieu, which produces a theoretically unlimited number of excitations," the living being only responds to some and not others? And therefore what do we do with the fact that the living being therefore plays an active role in constituting both the time and space of its milieu? And what then do we do about the fact that insofar as the milieu has a determinative effect on the living being, that determinative effect can be cast as one indirect form of self-constitution? Put differently: what should we do, conceptually and experimentally about the fact that the relation at hand is not between a living being and the milieu, but more precisely between the living being and *its* milieu.

It is obvious that the differences between and among mechanistic, genetic, and biological modes of conceiving and approaching the relation of a living organisms and its milieu entail crucial consequences for the formulation and design of research. It seemed to me that Arkin's disquisition on context dependence was a way of activating the question of the extent to which a program for the production of standard biological parts needs to be properly *biological* or whether, and to what extent, it can be made increasingly more *mechanical* or *genetic* or some combination of those two. The former, of course, would require putting the parts-based agenda in abeyance; rather than focusing on modularization and additive design, attention would need to be attuned to those places where fields of interactions make biological objects specific and stable. And the latter, by contrast, would intensify and simplify a parts-based agenda. Genetic understandings, taken in the sense discussed by Canguilhem, entail conceptions of living beings and their milieu which are ultimately more stable, calculable, and hence (to the extent that they that they hold) easier to predict and control than properly biological conceptions.

Beyond possible uses in rethinking experimental designs for the technical team (possibilities that were remote, despite my enthusiasm and attempts to make these conceptual reframing part of the discussion), Canguilhem's historical-philosophical analysis of the living being and its milieu provided concepts and conceptualizations that contributed to greater curiosity and care. It also in this way brought me into a closer and more attentive adjacency to

the experimental dimension of the biotechnical stakes of the BIOFAB's work, an adjacency from which the question of the significance of the BIOFAB's undertaking might be productively addressed. One of the great philosophers of science in the 20th century, George Canguilhem, took up the question of how the individual life is formed and ordered in relation to its environment, with all the political and ethical resonances it entails, within the register of biology. Any warranted means by which the elements of the BIOFAB's program can be assembled with a broader biotechnical problematization of living beings and analyzed by way of Canguilhem's concepts would seem to be all to the BIOFAB's good. Not only might the work of producing such connections prove to be a worthwhile exercise for those undertaking the daily work of the BIOFAB's program—the central task over the course of the initial months—it might also help specify a series of conceptual and pragmatic stakes whose form and ramifications for rethinking the limits of engineering living organisms and their contexts could be carefully charted as the facility's work progressed.

Canguilhem's conceptualizations indicate topics and questions in relation to which the work of the C.dog project might be specified and thereby connected to a historically, disciplinarily, and ethically richer set of problems. Such connections might allow for the C.dog project and the problem of context dependence to be *re-factored*. The term re-factored, common to mathematics and programming, indicates both analytic and remediative tasks. Analytically, the verb "to factor" means to resolve a complex quantity into individual factors. Similarly "to factorize" means to break up an ensemble into discrete elements: "The principal use of factoring, is to shorten the work, and simplify the results of algebraic operations." This work of rendering things in a discrete form, shortening the work, and simplifying the operations facilitates and opens up the work of remediation—of changing media and of thereby making things better. So, for example, in computer programming, *re*-factoring means to take a complex compilation of code, break it into constitutive units, and reassemble it in simpler and more functionally manageable form. The question that I began to formulate in response to Arkin's disquisition on context-dependence is whether or not Canguilhem's insights into the problem of the living being and its milieu might provide a few clear concepts which could be used to re-conceive the work of the BIOFAB and the relation of the BIOFAB team members to that work in a fashion that might be judged an improvement. In this sense, Canguilhem's concepts could provide me an aid to practice, and possibly for others within the BIOFAB as well.

PROPER & PRIVELEGED MILIEU

Reflecting on the notion of need as an intermediary between the living organism and the milieu, Canguilhem suggests that a centered being is capable of having a relation to *its* milieu, stated in the possessive. Insofar as a living being plays an active role in its self-constitution, determining when certain environmental elements are significant and when they are not, it can be said to have a *proper* milieu. "It is characteristic of the living," Canguilhem surmises, "that it makes its milieu for itself, that it composes its milieu." This proper relation between a living being and its milieu is neither static nor limited. A proper milieu does not suggest that a living being can only be at home in its "native land." A simple lesson from evolutionary dynamics, after all, is that a change in environmental conditions causes mutations, and that those organisms which successfully adapt are able to maintain a healthy relation to their milieu. The changed milieu remains proper. Drawing a contrast between Lamark and Darwin on this point, Canguilhem points out that the idea of a selective environment being a hostile environment is not quite right. The milieu only becomes pathological when it is no longer proper to the living being,

when the living being can no longer adjust its needs to its environment. The notion of a proper milieu is thus one in which the living being can "enter into a debate" with its environment, to quote Canguilhem's metaphorical phrase.

Returning to Arkin's disquisition on context-dependence, it could be said that the notion of a proper milieu highlights precisely what is so difficult about establishing a standardized experimental situation. If a living being can have a proper milieu in the sense just described, it can also have what might be cautiously termed an improper milieu—a milieu in which it is over-determined by its environment. Such over-determination is precisely what is going on in the experimental situation being constituted at the BIOFAB. Canguilhem again: "To study a living being in experimentally constructed conditions is to make a milieu for it, to impose a milieu on it." Such an imposition is not a problem per se. It might be a problem for those who are interested in observing the "nature" of the living being. But such observation is far from being on the agenda at the BIOFAB. The question at the BIOFAB, by contrast, is whether or not biological artifacts can be made to act in a programmable, predictable and regulatable fashion. The difficulties of an experimental situation, and what this implies in terms of the constant threat of pathology on the part of the organisms involved, thus weigh heavily. If a living organism is partially determinative of its relation to its environment and therefore of its form and function, and if this is because out of all of the conditions it might face it "picks out" only those that are relevant, what are we to do about an experimental situation in which a series of stimuli are isolated and reduced? Such a reduction might be strategically favorable as part of an effort to control the number of variables in play, but it creates a situation which has little "sensibility" for a living being. "An animal in an experimental situation is in an abnormal situation, a situation it does not need according to its own norms; it has not chosen this situation, which is imposed on it."[176]

Such experimental restrictions and impositions, Canguilhem proposes can be thought of as a "privileged milieu." It is privileged in the sense that it favors certain behaviors (cast, in this case, in terms of "performance") over others. "Privileged does not simply mean objectively simpler—an organism, after all, finds it simpler to do what it privileges. It has its own vital norms." [177] It is privileged in that it constitutes a situation in which the milieu makes more demands of the organism than it allows of the organism to make of it. Such asymmetry in the relation between a milieu and an organism is, biologically speaking, one that risks slipping from health into pathology.

FROM BIOLOGY TO ETHICS

The initial experimental challenge and operational task in the BIOFAB was to create a two-part trajectory. Moving in one direction the task was to establish a series of operational protocols that assured the BIOFAB could specify and control as many contextual conditions as possible—genetic, host, environmental. Moving in another direction the task was to begin to make and characterize a range of functionally specified genetic elements so as to test the extent to which their performance varied (or, more usefully failed to vary) across contextual permutations. In the weeks following Arkin's emphasis on the problem of context dependence, I became increasingly attentive to the extent that context dependence, having been foregrounded, would figure in the design of wet-lab experiments. I was interested in the question of the extent to which individualized genetic function would need to be characterized not only in view of a given context, nor only in terms of the sequences that constitute the kind of immanent character of those individualized functions, but also in terms of the mutually adjusted relation between

those two. In other words, I was interested in the extent to which the interplay and mutually determinative relation of biological elements to their milieu could be constituted, refined, and eventually designed. The measure of that extent, it seemed to me, would require some attention to the ways in which biological elements were being "commanded by a milieu" as well as the ways in which functions characteristic of an element in its proper milieu could be retained and leveraged under experimental conditions. The challenge, after all, was not only to design standardized parts. The challenge was also design parts whose functions in combination would be anticipated in a calculable fashion.

All of which indicated two registers within which the stakes of the BIOFAB's undertaking could be taken up. The first was, properly speaking, ontological. The ontological register pertained to the challenges associated with what was being made, biotechnically, and how it was being characterized and refined. In an ontological register, the challenge of leveraging the features of a biological entity characteristic of its activity within a proper milieu precisely by way of placing it within the regularized setting of a privileged milieu seemed absolutely central. Arkin took such a challenge to be feasible, if undertaken with the proper verificationalist attention to detail. We know that evolution has a combinatorial logic to it—there are only finite number of biological motifs and moves. This combinatorial logic, however, is such that the function and significance of any one part of a system depends, to a greater or lesser extent, on its relation to other contextual variables. Whether or not those contextual variables are of a similar combinatorial ilk, and therefore whether or not a sufficient number of contextual parameters can be "brought on board" and accounted for in the design of a standardized part is another question altogether.

A second register within which the stakes of the BIOFAB's undertaking can be taken up, which in the early months of the BIOFAB's operation were actually more crucial and pertinent than these ontological questions. If the distinction between a proper and privileged milieu indicates an ontological problem of how to engineer standardized biological elements, it also indicates an ethical problem: how to constitute the BIOFAB as an experimental facility in which certain kinds of subject positions would also need to be invented (i.e. the BIOFAB as privileged milieu), with all such a need implies in terms of adjustment, formation, resistance, and possible adoption (i.e. the possibility of the BIOFAB becoming a proper milieu). After all, to return to where this chapter began, Arkin's disquisition on context dependence proved crucial not only because he provided specific details that might be directly helpful to the BIOFAB's experimental work. In fact, as I will note again in the concluding section of this chapter, it was actually not yet directly helpful operationally and scientifically. It was crucial, rather, because it provided enthusiasm, energy, and a sense of scientific seriousness. Which is another way of saying that what was in question during that disquisition were not only the biological substrates that were the substantive topic of Arkin's discourse; also in question was the capability of those in the room listening to Arkin to face up to the verificationalist challenge, and to comport themselves in such a manner that the biological and operational subtleties being brought to articulation would prove consequential—especially for the researcher's sense of what it meant to conduct their work successfully.

Moreover—and this is the crucial point—that question of capability was not simply a matter of technical skills (although obviously such skills cannot be taken for granted.) It was also the question of whether or not those of us on the BIOFAB team would be willing and able to become the kinds of researchers, or scientists, or engineers, who are capable of persisting under

the conditions of the kind of milieu that Arkin and Endy hoped to constitute as the BIOFAB. To what extent could the BIOFAB be a milieu that commanded and thus required a certain set of actions and to what extent could the team member involved both come to embody and contribute to those privileged actions? A proper milieu for those of us involved?

TRUTH-TELLING, AFFECT, SUBJECTIVATION

Eduard Claparede writes: "What distinguishes the animal is the fact that it is a *center* in relation to ambient forces that are, in relation to it, no more than stimulants or signals; a center, that is to say, a system with internal regulation, whose reactions are determined by an internal cause: a momentary need."[178] To this extent, the milieu on which the organism depends is structured and organized by the organism itself. "It is for this reason that, within what appears to man as a single milieu, various living beings carve out their specific and singular milieus in incomparable ways. Moreover, as a living being, man does not escape from the general law of living beings."[179] And hence a problem on two scales, moving in two directions. One the one scale was the problem of constituting biological parts in such a way that they could be made to function consistently, or at least predictably, across changes in the environment; a question of whether or not the "part" could be made to "structure and organize" its milieu. On another scale was the problem of creating a scientific environment in which the researchers at the BIOFAB could flourish, while managing to conduct their work in a fashion determined by the specifications of the experimental conditions, i.e. the need to fabricate biological parts.

Whatever else can be said about it, the BIOFAB is a privileged milieu which is requiring a recalibration of what counts as proper on the part of those involved. The BIOFAB—whether structured by Endy's product-oriented insistence or Arkin's attention to the details of experimental design—is a facility unlike the previous facilities in which those responsible for programmatic design were educated and habituated. Such a difference obviously entails a certain excitement. It also, however, entails a certain departure from other milieus within which their capacities and vocational dispositions had been cultivated. Moreover, from its outset it was unlikely to be constituted as a milieu in relation to which "various beings carve out their specific and singular milieus in incomparable ways." If we follow Canguilhem in affirming that the "the world proper to man," is a world in which, "the field of his pragmatic experience, the field in which his actions, oriented and regulated by the values immanent to his tendencies," and therefore that "the environment to which he is supposed to react is originally centered on him and by him," then it is seems worthwhile to ask: what is the extent to which those whose task was to carry out the work of the BIOFAB actually had a hand in "picking-out quality bearing objects and situating them in relation to each other and to themselves." Which, of course, a way of asking whether or not the BIOFAB might become a proper milieu.

The members of the BIOFAB team are participating in the design of an experiment milieu in which the demand is that they formulate a program for the production of standard biological parts. The members of the team obviously do not live their entire lives in this space, nor are they likely to work at this facility for more than a couple of years. The BIOFAB nonetheless constitutes a milieu which is demanding a difference. Participants are being asked to invent and take up subject positions calibrated to the needs of the milieu and not to their proper needs. The BIOFAB should be considered a privileged and not yet a proper milieu. The term "not yet" is crucial. Because it indicates the question of whether or not, or the extent to which, each of those involved will find a way to embody the scientific and organizational virtues that

are being asked of them in the name of the undertaking. This is a problem and a difficulty made all the more acute by the fact that the subject position that each member of the BIOFAB was being asked to invent and take up consisted of multiple and under-determined elements. One of the multiplying factors in this situation is the difference between Endy and Arkin. This difference, so I am clear, is not a fundamental disagreement about what the BIOFAB should be doing, per se. Rather, it is a difference in style and mode, a difference which produces quite divergent affects. In some respect each scientist on the BIOFAB team needed to decide the extent to which they will be willing to develop themselves on the image of Endy's vision for things, or of Arkin's feel for verificationalist reasoning. The problem, quite simply was this: how to give one embodiment to the disjunctive stylizations of synthetic biology and modes of experimental practice presented and performed by Endy and Arkin, stylizations and modes presented as both exemplary and necessary to fulfilling the aims of the facility.

It bears noting that although Arkin's verificational mode was inspiring it was not yet scientifically salutary: it introduced a sense of the possible, but at the level of programmatic design was neither directive nor systematic. In retrospect it is clear that the details Arkin enumerated did consist of critical design elements and lessons learned that should have been incorporated; and indirectly they were insofar as they had cautionary effects. More directly, his intense deconstruction of the problems at hand affected the team as something like a Socratic exercise. The point of the disquisition was not that Arkin necessarily had the answers. Rather, the point was to demonstrate to the team that they did not have the answers yet either—either to the scientific questions or to the question of how an experiment might be more sufficiently designed. The difference in the case of Arkin's examination is that the BIOFAB team, unlike Socrates' interlocutors, already knew that it didn't know. The team (though this was not necessarily clear to at the time) was less in need of appreciating the critical limitations of design and context dependence and more in need of direct instructions.

Although Arkin enumerated specific details that would need to be considered, it was not at all clear where the limits of such an enumeration actually lay. How many variables about context would need to be taken on board in order to effectively design a program for producing standardized parts, with all such a program would hopefully entail in terms of improving prediction in genetic expression? It was clear from tone and thrust of Arkin's examination that the answer was finite. Context-dependence could, Arkin seemed to be suggesting, be managed—at least up to a point and within a certain range. The question, of course, was: what is that point and what is that range? This question would seem to be amenable not only to experimental determination, but even possibly to experimental resolution. And this is the difficulty and the self-perpetuating power of reasoning in a verificationalist mode. It is a mode, after all, which involves incessant movement between an attempt to move from multiplied arrays of particulars to calculable and thus general regularities. In other situations such a mode has produced powerful technologies predicated on the calculation of probabilities. It's limitation in the case of the BIOFAB, however, is that it does not provide criteria for knowing when enough detail is known to begin the work of converting data into technology. To be fair, Arkin's elaborations have almost always included detailed experimental steps that should be attended to and taken. The fact that these details were almost always embedded in a broad array of other specifications tends to give them the rhetorical cast of being demonstrations rather than instructions. What is demonstrated is that there is something else yet to be done. And even after a year of operation it is rare for the BIOFAB experimental team to receive Arkin's disquisitions as directives to be followed in anything like the detailed fashion that they are elaborated.

In light of Canguilhem's distinctions among a mechanical, a genetic, and a biological mode of scientific engagement, the question which needed to be asked was not the one contained in Endy's provocative claim that the BIOFAB was about becoming better engineers and not better biologists. That provocation had become familiar in synthetic biology and has been used by Endy and others to brand and distinguish the importance of their vision for bioengineering. The distinction could not be ignored because it provided the terms in which Endy could insist that the team care more for manufacturing than for understanding. In view of Canguilhem's conceptual distinction between the living being and its milieu and between privileged and proper milieu, I wanted to ask a slightly different question: what should we make of the distinction between the engineer and the *bio*engineer which seemed implied at the BIOFAB? If the first challenge is to make biologists more like engineers, what will it take to make engineers attend to *bios*. The question that Canguilhem raises about the relation of a living being and its milieu certainly applies to the work of the BIOFAB at the level of the artifacts under consideration. In this register the question of whether or not mechanistic or genetic understanding of standard parts is sufficient to the challenge of making standard *biological* parts is certainly worth raising. But that is a question that will need to be sorted out by the BIOFAB technicians and directors. The answer will no doubt be a matter of degree. This question of the *bios* can also be asked in relation to those of us who are being asked to help invent a program for the construction of standard parts. What is the relation between the privileged and proper milieu for us, and how will that difference determine whether or not we become dispositionally capable of manufacturing materials for a parts-based biological engineering? In the short run at least the answer to that question seemed to turn on the challenge and possibility that the bioengineers would be able to take a stance toward their work which simultaneously satisfied the style and mode o both directors. Could they find a way to embody a single subject position formed of multiple expectations of what counts as good and serious work?

II. INDETERMINACIES

CHAPTER 4

Governance and Veridiction: The Specter of Valuation

> *When anthropologists nowadays speak of "value"—particularly, when they refer to "value" in the singular when one writing twenty years ago would have spoken of "values" in the plural—they are at the very least implying that the fact that all these things [goodness, desirability, and meaning] should be called by the same word is no coincidence.*
>
> —David Graeber[180]

Each year the Synthetic Biology Engineering Research Center is subject to a site review conducted by its funder, the National Science Foundation's Engineering Research Center (ERC) Directorate. This two-day event typically takes place in late February or early March and is held in conjunction with a center-wide two-day retreat. In 2010 the SynBERC retreat and site review took place six weeks after the BIOFAB began operations, and while protocols were still being settled. The events constituted the first public presentation of the BIOFAB's initial operations and work plan. They also provided the setting for a first public articulation of what the BIOFAB was envisioned to be both as part of SynBERC and as an independent facility and what the BIOFAB directors expected the facility to produce and accomplish. It was also an opportunity to attempt to establish the terms according to which the facility might be valued—by the NSF ERC directorate, by industrial partners, and by scientific peers.

THE ERC DIRECTORATE

The annual site reviews are designed to both typify and ensure compliance with the NSF's ERC Directorate, their mode of governance, and what they take to be programmatically good, proper, or desirable.[181] These programmatic, although clear in principle, had the effect in practice of contributing to confusion about what the BIOFAB should be, how it should operate, and to whom it should ultimately be accountable. The confusion was intensified by the difficult exercise of justifying an operational program for the auditors in such a way that, despite what was apparent dissonance with the auditors' values, the justification ultimately would be accepted, allowing the program to continue. And all of this in the face of peers' judgment of whether what you are saying is true and doing worthwhile.

The ERC program was created in 1985 as a mechanism for more sharply orienting U.S. academic engineering to the end of better facilitating the needs of industry, and thereby the competitiveness of U.S. companies. Neither aspect of this orientation—making engineering relevant to industrial needs, nor doing this in a nationalist fashion—is particularly distinctive or remarkable, and could be said to have been an overriding preoccupation of the National Science Foundation from its inception. Updating the emphasis of their program in 2011, the ERC program announcement augmented its core mission, emphasizing the need to foster and support international connections and collaborations as a means of further expanding and ameliorating

the needs of engineering-dependent U.S. companies, an augmentation reflective of the multinational character of research.

The programmatic distinctiveness of the ERC turns on its aim of generating and stabilizing connections among and between three emphases. The first consists in providing support for researchers trying to animate efforts to engineer "complex systems." This focus on complex systems is aimed at providing the infrastructure needed to consolidate what might otherwise be heterogeneous and unrelated research undertakings. Which is to say that the ERC program is designed in such a way as to encourage researchers at U.S. universities to imagine and make connections among types and scales of technologies to the end of producing technology platforms. Designated support for work on complex systems has included the animation of centers for "Revolutionizing Metallic Biomaterials," for inventing "Biorenewable Chemicals"; programs for "Smart Lighting," and "Wireless Integrated MicroSystems." The second emphasis of the ERC program consists in supporting educational strategies that imbue U.S. academic engineering with curricular emphases oriented to industrial relevance. Their emphasis is on fostering an ethos within universities (and from there, programs for k-12) characterized by the assumption that worthwhile capabilities in engineering are those whose value is susceptible to economic calculation in the sense that students can become part of the "engineering workforce." The language used in the calls for funding as well as in the ERC program handbook calibrate the worth of research and educational programs to notions of industrial translatability. The third emphasis follows the second and concerns the generation of what the ERC imagines as an "educational pipeline," running from k-12 science programs to graduate education and post-doc mentorship to the development needs of U.S. industries. These three—an objective emphasis, a pedagogical emphasis, and a durational emphasis—are connected in and through the prospect of creating new platforms for industry. In this way, the ERC Directorate imagines a future of engineering as an extended translational effort to turn engineering education into professional schools in which students and senior researchers are able to produce, are made able to produce, complex engineered systems that can serve as the basis for new industrial technologies.

In its programmatic outlines SynBERC would seem to be a good fit for the ERC program. Its schematic self-definition is design precisely to demonstrate and facilitate the possibility of moving across levels of engineering complexity in order to integrate these levels into a broadly applicable industrial platform. Indeed, its organizational form—parts, devices, chassis, test-beds, human practices—is a direct transposition of a model for how to compose such a platform. In its programmatic outlines SynBERC is concerned with a question of education and the imitations of exiting practices among trained bioengineers: a core claim, after all, is the need to develop standards, techniques, and know-how that will shift the trained capacities of bioengineers away from things *biological* and more toward things *engineering*.

Two aspects of the site review process, however, have proven cumbersome for SynBERC, and, in a consonant fashion proved problematic for the BIOFAB as well. The two aspects are connected. The first concerns the effort to compose a site review team of peers from universities and industry. The mechanisms of scientific peer review are fraught with contradictions even under well established and rationalized settings.[182] The combination of the intensification of specializations and the limitations of conflict of interest generates situations in which the one whose work is being reviewed is sometimes better able to determine the significance of the work than others outside the program, project, or paper being reviewed. These

familiar difficulties are further troubled in the case of SynBERC by the fact that synthetic biology as a brand and a heterogeneous ensemble of projects is relatively new, and that most of the key players in the U.S. are either members of SynBERC or have close enough affiliation to disqualify them from serving on the site visit team.

The second aspect of the ERC review that has proven cumbersome for SynBERC concerns the strong governance role played by the Industrial Advisory Board (IAB). The ERC Directorate requires each center to animate an IAB. In broadest terms the role of the IAB is to help guide the center in producing technologies that can be judged industrially valuable, to provide funding toward the long-term fiscal independence of the Center, and to conduct SWOT analyses (strengths, weaknesses, opportunities, and threats) for the NSF, which factor significantly in the annual assessment. Informally the power of the IAB in the life of the Center shows itself in the question and answer sessions during the review. IAB frequently question the industrial value of work being presented by various SynBERC labs. It shows itself more formally in that the members of the IAB are invited to engage in closed-door meetings with the review team during which they discuss the results of the SWOT analyses and are able to make off-the-record recommendations concerning the funding and direction of the Center.

The situation is marked by a double asymmetry. On the one side, the scientific leaders of a new, and therefore not-fully-constituted engineering endeavor are being reviewed by a committee whose estimation of the endeavor actually depends to a significant degree on the authority of those being reviewed. Secondly, members of the industrial community—industries from existing biotechnology companies with settled business models predicated on existing technology platforms—are authorized to determine the value of an undertaking whose self-formulation is centrally predicated on the notion that current ways of practicing bioengineering are unsuitable to achieving key gains. Add to this the fact that terms of valuation for synthetic biology more broadly remain unstable. During the first year of the BIOFAB's operations such terms were particularly turbulent as the amount of venture capital contributed to synthetic biology sharply increased. Synthetic biology has been figured as a playful refactoring of living systems, with iGEM as the exemplar, as a matter of humanitarian consequence, with Amyris' artemisinin work cited, and, with work on biofuels and other petrochemical replacements as the exemplar, as a matter of prosperity. To cast things in biological terms: the fitness landscape for synthetic biology is not yet predictable—though certain dimensions have begun to settle, as I will indicate in the last section of this chapter.

All of this turns the site reviews into a valuation game in which the tacit rules of play are unclear and unstable. What should practitioners say about their work, how should their work and presentations be adjusted, and what will be taken to count desirable or otherwise relevant? In February 2010, six weeks after the start of operations, these questions were particularly pressing for the BIOFAB.

FROM OPERATING UNITS TO OPERATING SYSTEMS

From the first BIOFAB meetings in January through the weeks leading up to the retreat and the site review, Endy regularly reminded the experimental team that the events would be a first presentation and test of the facility's value and credibility. In this context, his usual insistence on productivity was sharpened. From early February on Endy focused energy and attention on the question of what sort of proof-of-capacity the BIOFAB might be able to demonstrate by the time of the review. Minimally, such proof would need to consist of an initial

plan of operation for the design, production, and analysis of genetic components, and hence a demonstration of organizational capacity to produce "datasheets" for standard biological parts. Such proof would also need to include a first-generation architecture for the context within which the BIOFAB would be building and testing its parts—Mutalik's EOU. In terms of software, it would need to include a "sequence refiner," a tool for automatically editing genetic sequences so as to be compatible with one or another BioBrick assembly standard. And in terms of human practices, Endy wanted a draft of the first report "What is a part?" to be available for circulation. Importantly, Endy stressed the need to demonstrate a capacity to be a "public benefit facility." The specifics of what such a demonstration consisted in needed to be settled so as to underscore that we were "a service to our community."

Endy arrived at a meeting in the first week of February with a proposal for how the BIOFAB should proceed. He suggested that the value of BIOFAB's work be graphed on two axes. The first he referred to simply as "community service." He stressed that whatever the BIOFAB produces it will need to be taken seriously (i.e. meet the needs of) an existing "user community." If this were the only axis on which the facility's value was to be graphed, "we would simply ask SynBERC and iGEM what they wanted us to characterize and deliver datasheets on those components." Such an approach, however, risked only "reinforcing existing projects." A key aim of the BIOFAB, however, is to facilitate forward engineering. In this light, the BIOFAB should also be evaluated by its ability to take a "qualitative leap forward," as he put it, adding "we are defining and developing a future game changer with regard to bioengineering."

Endy further proposed that what the BIOFAB is really and ultimately aiming to deliver is not standardized parts per se, but a standardized "Expression Operating System." The parts that the facility manufactures would be standardized to the extent that they could be functionally composed to operate within that system. Endy's proposal was noteworthy on two counts. It was striking in the first because it entailed literalizing the analogy between genetic and computational operations. An operating system in computer engineering is a kind of multi-scaled technology platform: it functions to both manage the computer's hardware and provide the programmatic environment within which applications can be executed. Endy was certainly not the first to propose that the cell's genome, the entirety of its genetic compliment, serves to "operate" a cell like an operating system operates a computer. That he would propose framing the BIOFAB's production capacities and deliverables on the basis of such an analogy, however, entailed committing the organization to the sufficiency of an analogy between the algorithmic units of operation within a computer's operating system (which could be added together to form operating systems of increasing scale and complexity) and the biochemical elements that are involved in genetic expression.

Endy's reframing was noteworthy in the second place because it was the first time (at least in a BIOFAB meeting) that Endy had discussed the BIOFAB's work as something involving or oriented to genome-scale engineering. Said more exactly, it was the first time in BIOFAB meetings that he had talked about the facility's work as a matter of genome-scale control of cellular operations. Importantly, he was not proposing engineering on the genome scale per se. The focus of the work remained to design standardized parts as the basic unit of operation. The difference was emphasis on the notion and proposition that these basic units could be daisy-chained in an additive fashion to the eventual "programming" of cellular behavior. Passing over insufficiencies in the analogy (which had been pointed out on a number of

occasions by his colleagues[183]), Endy introduced the notion of an "EOS" as both provocative and beyond the reach of the near-term resources and know-how. It was provocative in that it endorsed and promoted a simplified view of engineered biology; that, like compiled code, units of genetic expression can eventually be compiled into programmed genomes. It was beyond the reach of the BIOFAB in that (as Endy proposed in the meeting) it would require support on the scale of the genome sequencing projects: hundreds of millions of dollars of funding, multiple institutions and centralized management. The proposal that the BIOFAB would produce expression operating units leading to an eventual operating system provided a figuration beyond (though not inconsistent with) the BioBricks narrative, and provided the initial outlines of what would later become Endy's scripting of what a "game changer" on the "leap forward" axis of valuation might be.

Endy posed the question of how to operationalize work in such a way that the BIOFAB focused on the fabrication of parts that could be used by and would therefore be useful for an existing community, while also moving ahead with a vision of designing and building operating units. The simplest solution, in his view, was to plan on fabricating, measuring, and testing all the parts made by the BIOFAB within the designed EOU context. The BIOFB was proceeding at this point on the assumption that much of its work would consist in filling orders for the construction and refinement of needed parts and constructs from partner labs and organizations. This construction and refinement would be undertaken within the context of the EOU architecture. Refinements would fit the requirements of the BIOFAB's expression environment.

Endy remained insistent that progress toward the qualitative aims of standardizing functional composibility should be achieved through a mode of production which might generously be called *recursive rectification*.[184] That is to say, the aim should be to make something of a certain quality, see how it is working, and then adjust and refine one's mode of production. The task, therefore, was not to design experiments which taught us how things work. The task was to make things and to see how they work. The outside question was whether or not such a mode would lead to critique and rectification or whether production would follow from production. In any event, the near term task was to makes sets of "parts" and to assess what one had made, with the notion of an expression operating system pointing to a far horizon of intermittent refinement and engineering advance. "Bootstrapping" was a watchword.

The difference between designing experiments which taught us how things work and making things to see how they work might seem to be more or less negligible in practice. But it was immediately important in terms of orienting discourse and specifying the BIOFAB's activities. Endy reiterated his view that "we can't spend the next few months only building internal capabilities in terms of optimization of our own processes" and that "our goal is not to develop 'ivory tower' standards; this has to be something that we just get done." Whether or not anyone on the BIOFAB team was expecting, let alone proposing anything like "ivory tower standards" notwithstanding, Endy's emphasis reasserted his role as a pragmatic director committed, above all, to fabrication over exploration. The tacit diagnosis was that the primary impediment to success (even if success is just defined in terms of renewed funding) was "too much talk" and not enough "action." What this meant quite specifically was that Endy was perfectly happy for the BIOFAB to proceed by simply taking work that other labs had begun and refining it within the BIOFAB's proposed genetic architecture and mode of production—with all this would entail in terms of the animation of standards for measurement, analysis, the development of a database, the formulation of datasheets and so on. In Endy's terms, "buying

and repackaging someone else's work" is perfectly fine. After all, "every type of genetic element that we will be using has been studied by others; we have to simply take up one of these and go with it."

"Repackaging" of this sort represented one tactic for demonstrating "community service." To this end, Endy instructed Mutalik and Martin to spend the few weeks prior to the SynBERC site review producing a first set of measurements and datasheets for parts existing in the iGEM registry. Critics of the Registry often point to inconsistency in the quality and consistency of parts characterization. For example, Endy noted, "among those terminators which have been characterized, some show a negative termination efficiency (i.e., they are promoters!)." Such inconsistency, Endy emphasized, has become a primary point of blockage and frustration for many of the participating iGEM teams. Equally important is the difficult position that this frustration creates for the iGEM staff: although they are diligent about classification and coordination, they do not have the staff or resources to check whether or not all of the parts in the registry have sufficient information about how they will work under specified conditions and constraints. This means that there is the constant potential for incongruence among the design, composition, and functional success of the projects developed in iGEM. The BIOFAB could help take steps toward remedying this situation by better characterizing some of the registry's part collection.

Mutalik and Martin followed Endy's instructions, if with some hesitation. It was unclear whether or not the work of measuring and producing datasheets for select iGEM parts would facilitate or distract from the work of getting the necessary laboratory basics in place, from ordering materials to learning how to reserve time on the JBEI measurement instruments. As they proceeded, a number of difficulties emerged. The exercise of measuring a set of parts from the registry, as basic as it may be in terms of laboratory operations was, nonetheless, the first cycle of bench work undertaken by the BIOFAB researchers as part of the new facility, and there were kinks to work out. Less expected was a difficulty of the preparations for completing the iGEM datasheets, which got tangled in a technical conversation concerning the definition of BIOFAB protocols more generally. In refining his proposed EOU architecture, Mutalik raised the question of assembly standards. Which method of assembly should be employed to construct its first-generation EOU? Mutalik argued that the BioBricks assembly standard would not be optimal. He reminded us that the BIOFAB would learn to refine its EOU construction in such a way that, eventually, engineers would be able to connect multiple EOUs together. His focus was on how to structure the architecture of the elements within the EOU in such a way that functionally specific regions could be identified (e.g. "promoters," "ribosome binding sites," "insulators," and so on). Those regions could then be conceptually and physically modularized, libraries of each part generated, parts assayed in combination. Only then could parts be refined in such a way that the rough estimates of where one region begins and one ends might be molecularly specified and fine-tuned.

Mutalik's concentration on the internal composition of the EOU and its relative isolation from immediately adjacent genetic material meant that his efforts were concentrated on "upstream design parameters"—parameters concerning the requirements of a specified and immediate set of outcomes. He had not yet considered "downstream design parameters" in anything like a sustained way, but recognized the need for such parameters to inform the first-generation construct. The designation "downstream design parameters" refers to the fact that the EOU would not only need to be relatively genetically isolated and be characterized by an

internally consistent architecture, thus facilitating the work of building libraries of genetic parts, but it would also need to be designed in such a way that it could be useful across a range of combinations.

Mutalik's question, was: what method of assembly, what procedure for physically connecting segments of DNA should the BIOFAB use in constructing and composing the libraries of parts consistent with the structure of the EOU, and how would this method function once attention was turned to multi-functional uses of BIOFAB products? A first possibility was to use the BioBricks standard. After all, as Endy underscored on a number of occasions, the iGEM community is currently producing and using more "standard biological parts" than any other single community, and they use the BioBricks standard. Mutalik, however, was resistant to the idea of using the BioBricks standard within the EOU for a number of reasons. Most importantly, because the BioBrick assembly standard works by creating standard ends on the specified part it necessarily creates a "scar" at the junction between any two units. This "scar" consists of a string of several extra nucleotides at every juncture. Such a scar might prove problematic given that individual parts were already so small in terms of total base pairs. Given that the central aim of the EOU structure and the C.dog project more generally was to work toward increased predictability in functional composition of genetic expression, and given that even a single base-pair of DNA can have an effect on the mechanics of genetic expression, the insertion of even the small number of nucleotides represented by a BioBrick scar might have consequential effects.

Mutalik's specific technical questions regarding how to design in view of upstream and downstream parameters opened up a more difficult problem: who, exactly, should the BIOFAB have in mind when designing and fabricating its parts? The discussions concerning assembly standard, however, concretized and foregrounded the question. Arkin in particular had been conscientious about raising this question. His reasons were practical, as I noted in the previous chapter: how will we know what to make and measure if we don't have a sense of who will be using the BIOFAB's products? In response to the conversations about how best to design the first-generation EOU Arkin asked quite explicitly whether or not we want to design with the iGEM-type user in mind. Should the BIOFAB orient its first efforts to making biological objects that can be used by the widest possible number of users? Should an immediate goal be to lower the bar to entry, in terms of technical simplicity? Or should the BIOFAB work in something more like a "bespoke" mode, in which constructs are highly specified and highly customized? The latter would have the advantage of being both more suited to the state-of-play in the science as well as more suited to the resources available to the BIOFAB. The scientific questions concerning prediction of genetic expression remain pressing and in large part unanswered. The chief resource the BIOFAB has access to is excellence of thinking and design.

The alternative proposal, that parts be made for a more generally defined user revealed the difficulty that the BIOFAB wouldn't really have any clear idea of what types of genetic systems would be made using its library of parts, that, therefore, would not know what kinds of specifications to follow in terms of context, measurements, or analysis, and therefore it did not really have clear or pressing criteria for what it should make its first production priorities. One difficulty was that the idea for a BIOFAB had simply not been sold as a high-design facility. It had been sold as a fabrication facility, a factory, a "machine-shop" for synthetic biology. Crucially, the difference between a fabrication facility and a bespoke design shop turned in large part on the question of valuation. A commitment to the former would not necessarily be credited

as worthwhile by the people who prefer the latter. More crucially still was the fact that a failure to choose between the two left the BIOFAB staff in the operationally difficult and scientifically tenuous position of trying to exemplify the virtues of both types of venues.

VALUATION 1: FROM PIPES TO PROGRAMS

In the days leading up to the SynBERC retreat the question of how the BIOFAB would be evaluated, formally and informally, became a frequent topic of conversation. Discussions centered on whether or not an emphasis on "community service" might suggest that the BIOFAB was trying to be all things to all people. An emphasis on "revolutionary step forward" in the name of an eventual "expression operating system" it was proposed, would further enflame rivalries over branding, might be taken as evidence that the BIOFAB would be more manifesto-by-analogy than scientific detail. More complicated still was the problem of the fact that SynBERC's advisors and reviewers would be likely to evaluate the BIOFAB on the basis of whether or not the facility was likely to help address SynBERC's internal needs—and hence the looping conversations about who the BIOFAB should serve and which audiences it should seek to establish credibility with.

Toward the end of one meeting in which these conversations on SynBERC, credibility, and valuation were central and in which there was a significant measure of discomfort concerning the coming event, I suggested to Arkin that the retreat, whatever the BIOFAB's reception, constituted an important scientific and ethical opportunity for the facility. That opportunity, I suggested, consists of an occasion to test the various SynBERC PIs as to where they placed the BIOFAB within what might be thought of as the "fitness landscape" of synthetic biology—which kinds of projects are taken to be scientifically credible, which are taken to be salient in terms of funding opportunities, and which aspects of the BIOFAB's work might people respond to in terms of follow-up for possible collaboration. A difficulty, I conceded, was how to connect the immediate and partially articulated responses to the BIOFAB presentations—body language during presentations, follow-up questions in the formal discussions, informal conversations offered later, in a hallway or over drinks—with the ongoing struggle of each of the SynBERC PIs to negotiate the challenge of formulating their own relation to synthetic biology in strategically advantageous fashions.

Arkin's response was more considered than I had expected. These questions of power and boundary maintenance, and the strategies individual researchers and institutions animate in order to establish norms of credibility, disciplinary legitimacy, and department status were, Arkin confessed, something of an analytic hobby. They were professionally important, to be sure. Arkin, like all university investigators has had to learn to master the art of re-conceiving his labs research agendas in view of what work is currently getting supported through funding and job hires. He had, he intimated, perhaps spent more time analyzing how his colleagues and former students manage these dynamics than some others. In fact, he told me and the others who had not yet left the Friday group meeting, he had been considering giving a presentation at the SynBERC retreat which addressed some of these matters, albeit in an indirect manner.

Moving to the whiteboard Arkin drew four squares and numbered them. While drawing the squares Arkin explained that he thought fostering a self-described synthetic biology lab within a medical school environment was even more difficult than doing so within schools, such as his home institution UC Berkeley, with molecular biology and bio-engineering programs. The reason for these difficulties are numerous and arise from institution specific norms of good research, the break-up of disciplines and departments, the focus on medical outcomes of

research, including therapies and pharmaceuticals, the high money and status stakes associated with these institutions, and so on. In each of the four squares he wrote numbers, one through four. Each of these squares, he explained, represents a research unit for the lab of one of our SynBERC colleagues located at a medical school. Each of these four, he explained, can be analyzed according to which administrators, departmental norms, and industrial partners within the medical school they are designed to satisfy if not impress. They can also be analyzed in terms of timing and timeframe; each research unit includes projects that can be achieved in fairly short order, projects which indirectly provide cover for more long term interests of the lab. And finally, each can be analyzed in terms of what the researchers in the lab really seem to care about. These are the projects that often need the most protection. These are designed to have components that address problems "along the way" that can plausibly be argued to have benefits for other kinds of endeavors.

In an environment of micro-politics such as this lab in this medical school, Arkin emphasized, the probability that things will be described in terms of "synthetic biology" remain rather low. Rather, as can be seen with companies such as Amyris Biotechnologies, or LS9, emphasis will be on the "tools and processes" of synthetic biology which will help solve other kinds of problems. If synthetic biology is simply a term for certain tools and techniques that might help produce molecules or mechanisms of interest, so much the better. Such an emphasis on synthetic biology as a collection of tools (rather than a discipline, a way of thinking, a new configuration for genomic and post-genomic research, etc.) allows for flexible tactics of foregrounding and backgrounding: on the one side, it allows researchers to leverage funding opportunities connected to the term synthetic biology; on the other, it allows researchers to assure deans, department heads, and colleagues that "we're not really taken in" by suggestions that things are radically new, or by the idea that "biology really works like that."

The retreat was held on a Monday and Tuesday. The schedule provided time slots for each of the SynBERC test-beds and research thrusts, including the BIOFAB, to report on work undertaken over the course of the previous six months. What this meant in practice was that each of the test-bed and thrust leaders would provide a brief statement on research priorities. Then two or three graduate students or post-docs from labs that had been slotted in that test-bed or research thrust would be given five to ten minutes to report on their own work. An ostensible reason for the two-day retreat was for researchers to get a clearer sense of work taking place in other SynBERC labs with the hope that such clarity would provide a basis for possible future collaborations, or, if not collaborations, then at least possible connections. The unstated reason for the two-day retreat was to provide a kind of dress rehearsal for the presentations that could be given to the National Science Foundation site review committee, a rehearsal that would allow for last minute rectifications or eliminations.

The NSF expects that its investment in SynBERC is producing a kind of net-sum that exceeds the value of any of the individual parts. And so the SynBERC PIs have become adept at the exercise of performing integration. This adeptness is in part the result of four years of conducting the exercise; it is in part the adaptation of the professional requirement that high-level scientists be able to frame their specialized work in broad and instrumental terms; and it is, in part, an honest reflection of actual points of intersection among and between the work of the labs. However adept the PIs, the performance of integration in a situation which is actually somewhat fragmented is an undertaking one might think strange for those formally committed to scientific integrity. It might be thought strange in that it requires each of the PIs to actually say

very little of substance about the actual work of their labs. In the place of such substantive detail are restatements of research priorities in relation to problems of common interest. Given that all of the PIs enjoy a significant measure of authority in their respective fields, these overviews are simultaneously astute and more or less unassailable. Members of the site review committee usually ask for clarifications; members of SynBERC's Industrial Advisory Board often indicate where a given PI's work might be more relevant to commercial interests. But these responses have almost never risen to the level of the direct critique. The PIs accept that they are all performing an exercise meant to ensure another year's funding. As such, none of these adjustments, rectifications, and nods to integration is to be worried about too much. This may explain why one PI, when I asked him why presentations weren't responded to in a more serious fashion, simply smirked and said with a tone of mild resignation, "SynBERC is a soap-opera." It may also explain why both the BIOFAB and Human Practices presentations, which were delivered with earnestness and even eagerness, subsequently became targets of mild derision and open aggression.

Arkin was the first of the BIOFAB team to present. Although his presentation was much more circumspect with regard to the questions of institutional ethos and micro-politics that contribute to the determination of the current valuation of synthetic biology (at least within universities and among SynBERC researchers), he surprisingly focused his comments on the self-evident but under-discussed fact that funding and support for synthetic biology is context dependent. Elements of this context, he said, need to be mapped out so that decisions can be made about priorities and future directions. Arkin proposed that current projects can be situated in something like a vector of valuation. [185] To this end, Arkin's presentation provided an analysis of the parameters, elements, and values of such a vector, and indicated how the BIOFAB's proposed work might be situated in that field. In this way the significance of the BIOFAB's undertaking might be measured against other current endeavors. Such measurement, as his presentation strove to demonstrate, indicates why the BIOFAB's work should be taken seriously, and also why it is not yet being taken seriously enough.

The first PowerPoint slide of Arkin's presentation presented a quadrangle with a title that read "sensing magnetic north." An image of a compass was positioned in the middle of the quadrangle, with north pointing to the upper right hand corner. Within the quadrangle was a subtitle reading: "synthetic biology world." The left and bottom sides of Arkin's quadrangle represented two axes, each with poles on either end. The axis running along the left side of the quadrangle had at upper end the designation "programs" and at the lower end "pipes." The axis running along the bottom of the quadrangle had, at the left side and connected at the "pipes" corner, the designation "discovery." On the right side, on the opposite corner from "programs" Arkin had indicated "design." The term "pipes" indicated projects within which the main objective was to engineer a metabolic pathway for the production of a molecule of interest; the primary task of which is to "fit the pipes" such that a given input on one end produces a desired output on the other. The term "programs" indicated projects which aim at functional control of inner or intra cellular behavior. The terms "discovery" and "design" were simplified indications of the mode by way of which progress on either "pipes" or "programs" was being undertaken. In view of these axes and their poles, Arkin proposed that most of the existing work in synthetic biology could be mapped on a plane, with relative positions to the terms indicated. Projects mapped in the corner of the plane where "programs" and "design" came together were those consistent with "magnetic north."

In the mid-lower-left quadrant of the plane Arkin specified two kinds of projects that though closer to "pipes" and "discovery" require minimal capacities for "programs" and "design." The first he designated "metabolic retro-synthesis," a strategy for metabolic engineering in which the biologist begins with a molecule of interest, and then reverse engineers a metabolic pathway capable of producing that molecule. The Keasling/Amyris platform technology was clearly the exemplar of this kind of project; and it was not lost on anyone in the room that this kind of project was only "one the way" to north and not the orienting exemplar per se. The second kind project listed in this quadrant of Arkin's plane was designated "library optimization." The designation could be taken to stand in for aspects of any number of projects. It was clear, however, that Arkin's designation was focusing on efforts to create libraries of materials and to design optimal relations among those materials in combination. Such efforts might reasonably be attributed to work associated with the iGEM competition and the MIT Registry, although both of these efforts aim at the eventual facilitation of designed programs. More important, however, was the notion that optimization of libraries was not yet the optimal kind of project in synthetic biology.

Having presented and described the axes on his plane, and having specified projects that can be mapped onto it, Arkin clicked to his third slide. This slide introduced two crucial additional variables to his mapping and analysis. The first was the introduction of a "Z" axis for Arkin's plane. This axis, Arkin explained, represents value. Any project on the plane could be measured in terms of its value, a value visually indicated by a column rising out of the plane to a determined height. Arkin acknowledged the fact that, as of the time of his presentation, almost all of the investment in synthetic biology was going into projects in his lower-left quadrant, and particularly to projects fitting his "pipes" description. To use the term introduced in this chapter, funding and support was going to project that could be described as platform technologies that deliver a molecule or biological function of interest. Moreover, and equally important, this support is going to work that is as much a matter of discovery as it is design, which is to say that the majority of funding is not going to work which specifically targets animating more general capacities for the design of programs. While recognizing the worth of these capabilities, Arkin nonetheless underscored that capabilities characterized by successes in the upper quadrant were yet again more worthwhile. These included developing the capacity for decreasing the cost and increasing the quality of DNA synthesis through the combination of rational design and programmed cellular synthesis devices. They included the creation of parts whose function in combination could be predicted not only because libraries had been optimized, but because the rules of design and composition had been worked out to a sufficient degree.

I noted that Arkin's third slide added two important variables to his analysis, the first being the Z axis. The second important variable was the insertion of a large black banner across the middle of his plane, bisecting the lower left and upper right quadrants. Along the middle of this banner read the words "valley of death?" Although espousing projects that combine an emphasis on programs with an emphasis on design, Arkin acknowledged that it is not clear how one should go about formulating and fostering such programs. Current work, as his diagram tacitly demonstrated, is concentrated on projects having to do with the discovery and design of metabolic pathways, chains of chemical reactions in the cells that produce a molecule of interest, hence "pipes." According to one of the slides later in his deck, Arkin acknowledged the fact that most projects today aim at creating microbes that serve as "chemical factories" and that it is not at all clear (technically, socially, commercially, or in terms of safety or security) how one effectively gets "beyond the bioreactor." Said differently, Arkin underscored the fact that there

are few proposals for how one gets from the optimization of libraries for the retro-synthesis of metabolic pathways to the creation of an interoperable set of design rules by way of which one could genetically program the behavior of cells. Whether or not it is feasible to get across the "valley of death" in terms of the limits of work with biology per se was not a question that was posed. Rather, the question was: how do we justify and organize research initiatives in such a way that we can begin the work of finding means of populating the upper right quadrant of his plane.

Arkin's fourth slide was not altogether surprising. It once again showed Arkin's valuation quadrangle. This time the projects, the Z axis, and the banner were gone. In its place was a red arrow running from the lower left corner toward the upper right. Along this arrow were words reading "C.dog/Cellular Expression System." The proposition was clear visually, and Arkin spelled it out: the C.dog project of the BIOFAB is one possible means of shifting work from the optimization of libraries to the production of "building blocks"—the genetic system and its elements—required for facilitating the design of cellular programs. Such building blocks, as Arkin's subsequent slides outlined, would consist in the creation of a "basis set" of genetic elements and the rules for how to assemble them into complex systems. The term "basis set" has proven to be central to Arkin's stated hopes for the BIOFAB's work, even if he only touched on it in his presentation. Defined broadly, in algebra a "basis set" is the minimal number of variables needed in order to predict any other variable in a vector. In the case of Arkin's presentation and the work of the BIOFAB, a "basis set" would consist of the minimal number of designed genetic components needed to produce the functional cellular states desired in a "genetic program" (that is, in Arkin's terms, "scalable genetic engineering.")

BETWEEN LIBRARIES AND SERVICES

It is worth noting that there was very little direct response to Arkin's presentation, at least not during the session, or, as far as I was able to ascertain, in the informal discussions that followed the session. There was, by contrast, considerable discussion of Endy's presentation, which followed Arkin's. Endy like Arkin emphasized that the C.dog project was oriented toward the production of libraries of parts that would be defined by a key property: the control of genetic expression at scale. However, where Arkin's presentation focused on the question of value within a kind of fitness landscape of other projects, with some attention to the engineering details of how such a property might be achieved, Endy's presentation focused much more directly on the question of how the BIOFAB might be of more immediate value to the SynBERC and related communities. Endy began by presenting the BIOFAB's operational infrastructure as a service system. SynBERC labs and others, Endy announced, could submit requests for part characterization and refinement and the BIOFAB would return a datasheet in due course. As more mature infrastructural capabilities were developed, he further suggested, the BIOFAB would be able to provide rapid prototyping of designed genetic circuits, on the analogy of the way in which the MOSIS service had provided prototypes of circuit designs for silicon wafers. Individuals would not need to have the capabilities and know-how to construct a circuit, per se. They could focus on design and let the BIOFAB produce the test-case.

Perhaps more remarkable—or, I should say, perhaps what was more remarked upon—was Endy's appeal to a series of analogies and precedents for the work of the BIOFAB, which by then had become familiar to the BIOFAB team. Endy began with a series of slides that moved from the creation of catalogues of standardized parts in electronic engineering to the possibility of such catalogues in the early efforts of the MIT Registry and the iGEM competition. The

progression of slides suggested that the BIOFAB was a facility to extend and professionalize these early efforts to develop a BioBricks technology platform. In this way Endy invited the SynBERC community to imagine the BIOFAB as a service facility that would provide interested labs with data or materials needed to construct iGEM-like projects, including the prototyping of designed circuitry. And despite several slides outlining the challenges and opportunities connected to the work of successfully "tuning" parts toward the eventual end of creating an "expression operating system," Endy's presentation implied that the BIOFAB was generating the infrastructure for scaling and regularizing bio-scientific capacities that more or less already existed. The advantage of the facility, then, was not that it could generate new problems or propose new solutions, but that it could take care of a certain amount of labor on behalf of the SynBERC and other labs. To put it in terms that could be fitted to Arkin's valuation quadrangle, Endy's presentation suggested that the BIOFAB would "optimize rapid library assembly" and provide more "sophisticated high-throughput characterization."

Having struck these notes, Endy's presentation ramified in several ways, not least of which was that the substance of Arkin's proposals was more or less lost as a framing justification for the BIOFAB's efforts. Endy's presentation struck some as trying to be all things to all people. On one side the result of this was that there was a perceived license among the retreat participants to push back on the BIOFAB's self-definition. On another side the result of this was that certain members of the SynBERC Industrial Advisory Board who had been part of securing the funding for the BIOFAB complained that the notion of a "customer service" facility seemed to betray the pragmatic justification for the BIOFAB's creation, namely to help integrate the Center by creating parts for the various SynBERC projects. Another ramification was the intensification of dissatisfaction among some SynBERC PIs with having Endy play the role of spokesperson for synthetic biology generally and for SynBERC in particular. Endy's framing of the BIOFAB as something like an extension and professionalization of prior BioBricks work was taken by some to be something of a rehearsal of the least defensible "slogans" about synthetic biology—that it's "easy to engineer," that it "works like Legos," that it is "open-source biology," and so on. None of which Endy said in so many words. Nonetheless, two SynBERC Principal Investigators—neither of which had taken much time to talk with me on previous occasions—found time to corner me between breaks and advised me to intervene in the politics of the BIOFAB's self-presentation. If the BIOFAB was catering to the iGEM version of synthetic biology, as far as they were concerned, it could not be a venue for serious work. All of which, it perhaps goes without saying, only served to intensify the unstable valuation dynamics which Arkin and Endy had been concerned with in the lead up to the SynBERC retreat in the first place.

HUMAN PRACTICES: FROM VALUE TO WORTH

A brief word is warranted about the Human Practices presentations at the retreat and site review, the presentation that I made as part of the BIOFAB introduction as well as the presentation made by Paul Rabinow, then the leader of the Human Practices Thrust at SynBERC. The problem posed in this chapter concerns valuation, and at the site review that problem fell as much Human Practices as it did to the BIOFAB. Both Human Practices and the BIOFAB faced difficulties with regard to divergence between the practitioners and the NSF with regard to what was to count as a good problem and a worthwhile mode of self-formation. The difference is that these divergences and the tensions they generated were taken up an explicitly thematized by the Human Practices as an explicit part of its self-constitution.

The SynBERC retreat presented me with the challenge of giving articulation to the work that Endy and I had agreed I would conduct, but to do so in view of the horizon of research questions I was most interested in addressing. This challenge in this setting intensified my sense of tensions among obligations and interests. The assignment was to frame my work in terms that the biologists and engineers in the room would, at minimum, understand to be relevant to the strategic orientation of the BIOFAB. At the same time, I needed to situate the stakes of the overall experiment. That is to say, I needed to relate my effort to contribute to the development of the BIOFAB to a broader set of problems concerning the design of collaboration ethics and science today. Put differently, my task was to articulate a program of production and engagement that was relevant to the BIOFAB's operations in its details but calibrated to a broader set of experimental stakes.

I stated in very broad terms that the BIOFAB, whatever one made of it in scientific or organizational terms, presented a test of many of the core claims about the kinds of capabilities it was hoped synthetic biology might be able to actualize. To the extent that such capabilities were likely to ramify across domains such as health, security, or ownership, it was necessary for synthetic biologists generally, and members of the BIOFAB specifically, to think seriously about, and to prepare for possible negative outcomes of its work. My task, as I explained it, was to undertake the work of preparing for such outcomes. This preparation, I suggested, would require ongoing analysis not only of the BIOFAB's work, but the circulation and use of the BIOFAB's work. The challenge in my assessment was to begin to put into place both the organizational mechanisms as well as an organizational ethos to contribute strategically to outcomes judged to be positive and to be responsive to any outcomes judged to be negative.

This preparedness work, I explained, would be taken up in two phases. The first phase would be to produce a series of short reports in which key questions were to be articulated and possible responses outlined. These reports in hand, the next phase would be to continue thinking through problems that had been *diagnosed* in the reports, only now moving in a *strategic* direction. This distinction between a diagnostic and strategic mode of engagement had been a key determination of the Human Practices experiment at SynBERC. The "first wave" of Human Practices work, as it had been designated following terminology introduced by the Weiss lab at MIT, had focused broadly on the question of whether or not or how synthetic biology posed new problems. Consonantly, the Berkeley Human Practices group had shown how this question had oriented much of the work-to-date focused on synthetic biology by policy analysts, bioethicists, scholars in science and technology studies. An initial task in moving beyond this first-wave work was to design forms for and help to constitute venues within which it was possible to turn diagnostic determinations into strategic practices. How to bring about remediation remained a question and a matter of inquiry and experimentation. The BIOFAB, I proposed, presented one possible site for carrying such experimentation forward. It is a mark of the growing stultification of the Human Practices experiment that despite my efforts to frame my work in a fashion directly related to BIOFAB goals, the salience of my proposed work remained unclear to almost everyone in attendance, perhaps most importantly to me.

If my presentation tacitly raised the question and challenge of this shift from a diagnostic to a strategic mode, the Human Practices presentation offered by Paul Rabinow addressed it directly. Rabinow had been asked to provide a summary report of Human Practices work from the past year of SynBERC activities, to do so as part of a session entitled "SynBERC's Foundations," and to complete his presentation within a brief ten minute frame. Rabinow chose

to frame his report in terms of the key shift in Human Practices engagement from first-wave diagnostics to second-wave strategics. To do this he began with a quote from German political economist Max Weber: "It is not the 'actual' interconnection of 'things,' but the 'conceptual' interconnection of 'problems' which define the scope of the various sciences. A new 'science' emerges where new problems are pursued by new methods and truths are thereby discovered which open up new points of view." Weber's quote, Rabinow proposed, gives articulation to an insight tacit in a review paper on synthetic biology that had been published earlier in the year. That paper, entitled "Synthetic biology from the first wave to the second wave," Rabinow explained, suggested that the main blockage to advances in synthetic biology was the notion that the key task and challenge was a bottom-up approach to constructing individual biological parts. Such an approach, the review had insisted, had reached a critical limitation with regard to designing functionally complex systems. New design strategies were called for, according to the review, strategies which tried to leverage key aspects of living systems in a top-down fashion. That is to say, the challenge is to find biological domains which offer the possibility of managing complex cellular function. The task was to then to design or redesign specific biological parts and devices in the hope of designing synthetic systems which help achieve such a possibility. Such a second-wave shift, Rabinow argued, indicated movement away from a goal of working on the "actual" connection of "things" to the "conceptual" interconnection of "problems."[186] Such a shift entailed reframing work in synthetic biology in such a way that progress on the "actual interconnections of things" could be opened up and foregrounded strategically as "the conceptual interconnection of problems." [187] Such a shift was already proving a catalyst for the production of new work in Human Practices. Just as a shift from things to problems, which might or might not gain traction on the technical side of things, had already proven to be fruitful for the work of the Berkeley Human Practices group.

Such work was characterized by emphasis on anthropological engagement and conceptual analysis characteristic of projects. Above all, Rabinow stressed, second-wave Human Practices work needed to remain second-order in character. That is to say, it needed to be calibrated to careful empirical inquiry guided by rigorous conceptual formulations, but to the end of "observing observers observing," to use Luhmann's dense but helpful phrase. A strategic mode on the part of Human Practices should not be confused with the means-ends work of simply providing first-order deliverables. Such an approach thus requires a close adjacency to what is actually going on in the situation at hand, and thus could be included as an integral part of a research setting such as SynBERC or the BIOFAB, but it also requires the freedom of experimentation characteristic of any scientific undertaking worthy of the name. Second-wave Human Practices work could not know in advance of actual anthropological engagement or ethical assessment what kinds of strategic remediation of current practices might be both worthwhile and possible. Hence, the question of what the outcomes of second-wave work would eventually consist in, and, therefore, how it might be valued not only as desirable but also good and meaningful was also an experimental and therefore an under-determined question. Respect for such experimental care in the calculation of value needed to be made part of the enterprise.

CONSEQUENTIAL VALUATIONS: POWER AND RELEVANCE

Three weeks following the retreat and site review, SynBERC received the NSF site visit team's assessment. From SynBERC's point of view the assessment was positive: it recommended continued funding for the center. The assessment was less than positive for the BIOFAB, and was uncompromisingly negative with regard to Human Practices. The

assessment's executive summary included six "threats" to SynBERC's future. Two of these pertained directly to Human Practices and one to the BIOFAB.[188]

The introduction to the evaluation report acknowledged that the "BIOFAB is just beginning." As such the reviewers resisted premature judgments in taking up the task of discerning, "exactly how its role in and value added to SynBERC will develop." The wording is crucial: the extent to which it was seen to add value to SynBERC's overall mission was the only standard by which the BIOFAB was evaluated. In terms of Human Practices, the assessment stated that renewal of SynBERC funding was dependent on the removal of Paul Rabinow as head of the Human Practices thrust. The attack on Rabinow and his work was blunt and uncompromising. The justification for this attack was unconvincing, even contrived; it is clear that Rabinow was removed from his leadership position on something other than the merits.[189] This seemingly capricious attack is explained at length elsewhere, and will be returned to again briefly below. It suffices here to note that the we were blindsided by the attack on our work. Indeed, the SynBERC administrative staff wrote: "We are surprised by the nature and urgency of this criticism, which was not raised during the site visit, our conversations with the SVT members, and the previous years' reports."[190] In any event, the criticism of Human Practices was not dissimilar to the BIOFAB in that it was predicated on the proposition that the work of the thrust was not sufficiently "relevant" to the operational needs of the Center. More specifically, the report stated that the integration of questions of "bio-risk" into the everyday practices of SynBERC labs had been requested and remained lacking. As to Human Practices within the BIOFAB the report said very little. What was said, however, could be taken as a warning that standards of SynBERC's operational relevance would be imposed in my case as well.

The NSF's evaluation emphasized that the chief value of the BIOFAB lies in its "critical role" within the SynBERC organizational structure. The BIOFAB was funded, the evaluation stresses, to "enrich the capabilities of SynBERC to achieve its mission through the provision of parts." Elsewhere it adds that "the new BIOFAB facility is designed in part to provide the missing interaction with the test-beds." The evaluation also recognizes that the BIOFAB is designed to produce "parts and provide services to academic institutions and industry beyond the current capabilities of SynBERC programs."[191] The actual value of the BIOFAB's operations beyond SynBERC for the site review team, however, remains ambiguous and did not seem to count. In this regard the broader framings of the BIOFAB mandate to become a public benefit facility could not really be made to count either. At several points in the report this broader remit is strongly foregrounded. In its extra-SynBERC relations, the "BIOFAB is the arm of SynBERC best positioned to serve not only as the technological/manufacturing glue for integrating SynBERC's research effort, but also serve as the most important relational surface to the larger biotech interests beyond SynBERC."[192] And yet, despite statements such as this, it is clearly the relevance of the BIOFAB to SynBERC's organizational needs that serves as the criterion on the basis of which the value BIOFAB would inevitably be calculated.

On precisely this point, however, the reviewers seemed concerned. In the executive summary to the report the reviewers wrote: "While the critical role of the BIOFAB in the strategic plan of SynBERC as a parts fabricator is clear, there were also clear indications during the visit that its role may be understood differently by the Center Director and the leaders of the BIOFAB."[193] The report does not elaborate on these "clear indications," and one can only guess what exactly the reviewers are referring to. It is certainly the case that Endy's presentation of the BIOFAB at the site review did not foreground the facility's relation to SynBERC. Indeed, the

relation to SynBERC was basically put on equal footing with other "founding partners." In any event, the reviewers warned that "this difference in understanding of the role of the BIOFAB is a weakness and potentially a threat because it highlights the possibility that the BIOFAB could become independent from and even compete with SynBERC. The separation of the BIOFAB from SynBERC would clearly be detrimental to SynBERC and the BIOFAB."[194] For the BIOFAB to imagine itself in such a way that would indicate any measure of independence from SynBERC, per se, is thus, for the reviewers, simply unacceptable.

If the "difference" in understanding is a taken as a warning that future funds might be in jeopardy, the warning was rather strangely toothless. Indeed, the report recognizes that that NSF has only committed two years of funding and that the BIOFAB would need to establish its own funding base after that. Such an alternative funding base would certainly consist in large part of monies provided by industrial partners. But even on this point the report is circumspect. The BIOFAB is warned not to solicit partnerships that might compete with SynBERC's Industrial Advisory Board.

In its more detail assessments of the BIOFAB's vision and nascent operations, the report is more or less positive. It stresses that the value of the BIOFAB both to SynBERC as well as to other institutions, academic or industrial, turns on its ability to function as a "build-design" service facility: "the goal of the BIOFAB is to provide a service facility for parts manufacture, standards development and testing (measurement and production), data sheet production (design, refine and measure), CAD/EDA, the application of human practices measures, and rapid prototyping." The wording of this goal is worth pausing over in that it comes directly from Endy's presentation. Indeed, Endy's presentation offered primarily a "service facility" account of the BIOFAB's operations. Likewise Endy's presentation was consistent with the "operational model" recommended by the report which read, "internal (SynBERC) and external clients (partnering institutions, fully external organizations) clients would request a part, part characteristics, or a set of parts made to performance specifications. BIOFAB would design and maintain a database of parts, develop design algorithms and technology for fabricating them, and would advise clients on best uses, best practice, and safety/security issues."[195]

Absent from the site review's evaluation of the BIOFAB was any mention of the C.dog project or the question of what broader capabilities for "programming DNA" the BIOFAB might or might not bring into being. Unlike the presentation Endy gave as part of the SynBERC retreat, however, he did not emphasize the goal of "taking the central dogma off of the table as a research topic." Arkin, for his part, did not present at the site review but only at the retreat; he left the description of the BIOFAB entirely up to Endy. This meant that Arkin's assessment of the valuation landscape of synthetic biology and his assessment of the real worth of the BIOFAB's undertaking was not officially registered for the site review team. What this omission meant effectively is that any notion that the worth of the BIOFAB's efforts should be based on the prospect and possibility of developing a technology platform was simply not taken seriously as part of the evaluation. The report had expressed concern that the members of the SynBERC Industrial Advisory Board did not really value the SynBERC test-beds—the components of the SynBERC undertaking which most approximated something like platform technologies. The only exception to this relative lack of interest in the test-beds were those aspects which had a relation to Keasling's other efforts on biofuels.

While noting that the IAB did not really value the SynBERC test-beds, the report stressed that the IAB was interested in "foundational parts and devices" being produced as part of the

various SynBERC undertakings. In this light, the report suggested, the BIOFAB might, in the end, be the most valuable part SynBERC in terms of its relation to industry—"the most important relational surface to the larger biotech interests beyond SynBERC," as I've noted. The only catch and hesitation is that the members of the IAB were concerned that the work of the SynBERC labs might not be freely available for their organizations to take advantage of. Hence, the IAB had stressed the need for the BIOFAB to take the lead in developing "Freedom to Operate" protocols for the open circulation not only of its own materials, but any of the materials produced in SynBERC more widely. Indeed, among the few specific recommendations made to the BIOFAB one that was repeated at several points was the need for the BIOFAB's parts and datasheets to include "clear delineation of IP issues attached to individual parts, in the form of a database of derivation-genealogy, publications, and patent associations keyed to each part, ought to be valuable for the industry clients."

The exclusion of any reference to the C.dog project in the report is crucial and needs to be underscored. It means that any residual scientific agenda that might have informed the vision for BIOFAB operations as an internal measure of the value of its work had been taken off of the table in the setting of the official review. As I've noted in the previous chapters, in its original proposal and in its first weeks of operation the BIOFAB had already suffered a kind of operational impasse as a result of the differences and relations between the goal of "producing standardized parts" and producing parts capable of "controlling transcription, and translation." Endy's response to this impasse had been to insist that work should proceed building on past precedents. Such precedents, minimally, consisted in optimizing procedures for building libraries of parts. Such procedural optimization could be taken as a first step toward the eventual refinement the parts in the library in view of functional composability.

Arkin's response had been to insist on the need to move from combinatorial libraries to the design of programs. Such a move turned on the production of a "basis set" of standardized parts. One could imagine a scenario in which the optimization of libraries was a first and necessary step on the way to a basis set for synthetic biology. But such a scenario would have to be self-conscious about the fact that the library, per se, however calculable its elements were in relation to one another, was not sufficient for the long-term goal of rational engineering. At least not sufficient in Arkin's view. The BIOFAB might only ever take a few minimal steps toward the production of parts marked by "orthogonoality," "composibility," "connectivity," and "homogeneity," but those minimal steps, at least according to Arkin's presentation, were the measure of the facility's real worth.

None of this, of course, was considered in the NSF's valuation. The C.dog project and the goal of creating an "expression operating system" was apparently not deemed relevant to the aim of integrating SynBERC's thrusts and test-beds, nor (and more importantly) to the aim of achieving "industrial relevance." As the NSF put it: "While the quality of the research within the thrusts—parts, devices, chassis—is impressively original and high quality, there remains the challenge of systems level integration across all levels: rational design tools, modular assembly methods, assuring/defining the range of interoperability of component, safety, and industry relevance." The NSF deemed this to be "of significant concern" in that it held SynBERC's success to be ultimately dependent on, and measured by, the extent to which "the biotechnology industry [comes] to view the enabling technology not only as useable but also as relevant."

This view of things pointed to a curiosity and a concern for the BIOFAB (and for Human Practices as part of the BIOFAB). The curiosity was that by failing to take the stated goals of the

C.dog project seriously, the report was essentially writing out of the agenda the very work of standardization which would make the operational goal of filling service orders (for SynBERC or others) feasible. The report stressed that the operational model should consist of a rather unambiguous sequence: customers should be able to "request a part, part characteristics, or a set of parts made to performance specifications." In order for parts to be made to performance specifications, however, some progress on standardization and forward engineering, progress toward calculable design, would be needed.

And hence the concern. Progress toward calculable design, as discussed in the previous chapters, entails moving beyond current efforts to achieve physical composibility to better regimes of functional composibility. Such an achievement requires something other than simply the scale-up of existing technologies and know-how. It requires, in other words, a foregrounding not only of the work of making sure parts are connectable—the 'actual' interconnections of 'things' to use Weber's phrase. It also requires that these parts be functionally composible at scale and in context. Such a requirement, as has been widely discussed in synthetic biology literature, remains a chief difficulty marked by any number of scientific problems. Hence, the challenge of designing and manufacturing parts "made to performance specifications," is a challenge requiring a foregrounding of the "conceptual" interconnection among "problems."

It is precisely this work, however, that the site review team seemed to place outside the scope of "industrial relevance." And this concern, as Arkin creatively framed it in his presentation—the difference between simply producing libraries of parts and producing libraries capable of facilitating rational design—can be characterized as a "valley of death." It is a "valley of death" in the first place because no one really knows, technically or organizationally speaking, how to move—or whether it is even possible to move—from optimized sets of parts to a generalized basis set. It is a "valley of death" in the second place because funders, industry among them, do not take the funding of the creation of such technology platforms for synthetic biology as seriously as they do the funding of "pipes" that will generate molecules of interest—or at least they didn't at the time the site review team composed their report. Hence, to use "industrial relevance" as a determining factor in the valuation of the BIOFAB's work was to basically exclude (at least at the level of formal criteria of evaluation) the possibility of looking to the C.dog project as the primary aim and goal of the undertaking.

The determination of relevance in a game of valuation is difficult business under most conditions, and all the more so in relation to scientific and ethical work. The dimensions of this difficulty have been the subject of concerted thinking, on the part of first as well as second order actors, for at least a century. The difficulty begins with instability in the notion of relevance itself. In familiar usage "relevance" simply means "connected with the matter in hand" or "closely relating to the subject or point at issue." Such familiar usage, however, tends to cover over the fact that the determination of what gets to count as "closely related" is often far from obvious once serious thinking gets involved, and therefore making this determination entails the exercise of power. Etymologically, the term "relevant" has two crucial meanings. The first is "to lift up" or "to lighten"; the second is "to ease" or "to relieve." The question that must be asked is: are the criteria of relevance being made determinate, and to the extent that they are, what is being eased, lifted up, or lightened? And more important, for whom?

The determination of relevance in a game of valuation is difficult business for a second reason, alluded to earlier in this chapter. Value, the core of term valuation, is a term used to characterize three kinds of social facts: conceptions of that which is taken to be good and

worthwhile; economic determinations of desire predicated on what one party will give up to another party; as well as an analytic designation pointing to meaningful difference.[196] It is a term, therefore, whose senses are mobile and which are difficult to tie to depersonalized assessments of worth. The exercise of power in the determination of relevance increases the difficulty all the more. In the case of the BIOFAB, the exercise of power in the review constituted a move away from what had been presented as counting as worthwhile technically, scientifically, organizationally, and ethically. The NSF report did not proceed in a mode that could have taken seriously Arkin's arguments that the worth of the BIOFAB lies in its efforts to cross the "valley of death" in a move from optimized libraries to designed basis sets. Such arguments were tacitly ruled out of bounds in the name of SynBERC's organizational needs and IAB's determination of what counts as relevant for current industry needs. And, of course, it should not escape notice that such a determination of relevance and thereby of the terms of valuation also functions as a possible mechanism for producing ramifications in terms of work priorities, the logic of operational design, and—not least of all—the specifications for what kind of individuals will be suited, technically and dispositionally, to carrying out these priorities and these designs.

Which, I propose, brings us back to the themes of Rabinow's presentation. Rabinow's assessment was that any worthwhile engagement with the technical advances in synthetic biology would require formulating the "conceptual" interconnection of "problems" and not only tracing out the "actual" connection of "things." The interconnection of problems, after all, defines the scope of a new science and therefore should orient efforts in synthetic biology and in Human Practices alike. Rabinow's assessment was also an argument for what should be taken to count in the register of valuation—an argument that the significance of synthetic biology and Human Practices turns on experimentation and inquiry, and that the chief concerns could only be established in advance of actual work in the broadest outlines.

In this light it is not surprising that he was summarily dismissed in the NSF evaluation. That evaluation proposed that the Rabinow group's approach was inconsistent "with NSF's original guidelines for addition of this thrust in SynBERC." What the report meant by "inconsistent" was that the Berkley group was not sufficiently emphasizing matters of "bio-risk." What the report meant by "bio-risk," however, was not made clear. The evaluation did not mention or even take into consideration that Rabinow and the Berkeley Human Practices lab had published a number of articles and book chapters on questions of synthetic biology and security, including an article in *Nature Biotechnology* published only two months before the review. It did not mention that the Berkeley group's emphasis on inquiry and concept work had, in fact, been praised as exemplary in prior reports. What it did mention, and mention repeatedly, was that the work of the Berkeley Human Practices lab was not taken to be relevant by those responsible for overseeing SynBERC's work, including SynBERC's Industrial Advisory Board. That relevance—ethical, political, economic, or political—could be determined in advance of scientific work was simply taken as a matter of course.

No doubt the same could be said of the NSF's assessment of the BIOFAB, although the BIOFAB was never really vulnerable to the same kind of dismissals as Human Practices, given the centrality of its core efforts to SynBERC's stated aims. The BIOFAB was a venue proposed as a mechanism simply to fill orders for SynBERC PIs, after all. Whether or not such production was feasible without having first passed through the gauntlet of research and experimentation, was clearly not a question which would be posed at the formal levels of audit and valuation. That it was, in fact, a principle and pressing question within the BIOFAB, both for the technicians as

well as for me in Human Practices, was, following the retreat and review, all the more clear and all the less resolved.

CHAPTER 5

Pilot Project: The Time for Serious Design

The interplay of cultural, aesthetic, and scientific norms, and the experiments with new social and spatial forms that would instantiate them, make up an essential feature of modernity.

—Paul Rabinow[197]

The SynBERC site review foregrounded and intensified a crucial aspect of operational indeterminacy: who was the BIOFAB ultimately accountable to and why? On a simple material level, of course, the BIOFAB was accountable to the NSF's ERC directorate, and indirectly SynBERC's industrial advisors. But as I showed in the previous chapter, the NSF's metrics of evaluation were inconsistent with the director's long-range vision for why a biofabrication facility is needed, and therefore how to proceed. Put differently, following the meeting it was all the more clear that as the BIOFAB pursued its program it would need to be vigilant about what work it would take seriously, and whether and how to incorporate the NSF's expectation that the BIOFAB frame its work as an intra-SynBERC service.

Members of the BIOFAB team now understood that the operational questions of determining seriousness, value and relevance would likely entail significant ramifications for their eventual scientific status and possible vocational futures. Becoming the kind of facility capable of satisfying the SynBERC IAB seemed likely to entail the cultivation of considerably different priorities, dispositions, and habits than becoming a facility capable of satisfying Arkin's vision for "designing biological programs." As one member of the BIOFAB team put it following the review: "Actually, no one really seems to care what we're doing. But if we make things that are no good, than everyone will think we're not worthwhile. And if we just make a few good things then maybe, by word of mouth, they'll start taking us seriously." The question, of course, was: what, operationally, would the BIOFAB take as counting as "good" and, further, what would the work portfolio, regimens of accountability, and standards of success actually consist in? How would the conduct of research be governed? And would positive word of mouth really be sufficient for extending the BIOFAB's funding and positive reputation? As Max Weber insisted almost a century ago, merit is only occasionally a determining factor in the valuation and support of technology and science.

Endy had framed matters of seriousness, value and relevance in terms of the two goals of "serving the community in incremental ways" and "taking a leap forward" beyond the status quo. The task, he suggested, was to design a production strategy which brought these two into a coherent relation. What this amounted to in practice was to insist on producing large numbers of "parts," characterized in a consistent fashion, with the outside expectation that such production would ultimately facilitate a process of refinement toward standardization (i.e. a "leap forward" in control of genetic expression). Arkin, for his part, had distinguished the challenge and possibility of the BIOFAB's stylizing and forming itself as a "bespoke" design facility, with the

goal of approaching scalable production. The latter, he insisted, could always be "beaten" by other institutions willing to put in more resources. Additionally, in his public comments Arkin distinguished between the work of optimizing libraries of genetic components and the need to move toward the eventual production of a "basis set" for the rational design of biological programs. Such eventual production would not need to be at odds with the near-term goal of producing lots of parts. It would, however, require a regime of critical self-reflection and analysis indicating the way toward increased rationality in the design of genetic systems. That is to say, making more and more refined libraries of parts did not, necessarily, amount to making progress toward design understood as the capacity for forward engineering. Understanding the difference between these sets of distinctions and why they have proven to be operationally significant forms the core of this chapter. The key to these differences turns on the question of what counts as good design for synthetic biology. To paraphrase Rabinow, writing on the question of design in another context: the framing and orientation of the BIOFAB's work, and hence the questions of value and relevance, has been determined in large part by the (often unarticulated) interplay of cultural, aesthetic, and scientific norms. [198] In this light, the design of the BIOFAB as a program for the creation of standardized parts and the ramifications of this program for the kinds of scientists each of us was being asked to become, can be understood as an experiment with new biotechnical and anthropological forms adequate to those cultural, aesthetic, and scientific norms.

Endy's and Arkin's broad characterizations of the worth of the BIOFAB's undertaking provided, but failed to provide sufficient orientation to the difficult and consequential problem of how work would proceed. At best, their characterizations served to generate further questions about who it was the BIOFAB really needed to please. These further questions usually took the form: who is going our parts? In the broadest terms, Endy continued to frame the BIOFAB as a "public benefit" facility. The question of who, actually, constituted "the public" in this formulation and how they were going to benefit was usually answered in terms of "free and open access to anybody, commercial or non-commercial." But emphasis on the goal of accessibility tended to obscure the reality that operational priorities were likely to be judged more worthwhile by some, less by others. What would it mean, concretely and operationally, if the imagined public was an iGEM team from Davidson College who told us they would like to have access to better characterized parts, but parts that they themselves could characterize using widely available technologies? Or, what would it mean, concretely and operationally, if the imagined public consisted of participants in the proposed CAGEN competition—researchers with advanced capabilities who would need materials and knowhow commensurate with state-of-the-art technologies and design standards? Or, would the imagined public consist in the creation of a new community of users, users willing to take up and experiment with whatever tools and technologies the BIOFAB created and hence a community that could not be specified in advance? Endy would no doubt resolutely answer "all of them!" to such a question. But how "all of them" was likely to be served by the same facility, and hence how the BIOFAB's workflow should be designed and evaluated, was (at least for the BIOFAB team) not yet clear.

The site review intensified these indeterminacies for an additional and important reason. Several of members of the BIOFAB team, including Mutalik, Rodriguez, and I had relatively long-standing relationships with the SynBERC research community. Several of the SynBERC researchers had made it clear to one or another of us that they were either uncertain about or indifferent to the worth of the BIOFAB's undertaking. Others suggested that although the existence of a production facility for synthetic biology was, in principle, worthwhile, it was

nonetheless scientifically "boring"—and to that extent not actually worth serious investment by those capable of working on something more interesting. These reactions, sometimes expressed directly, sometimes only tacitly suggested, put Mutalik, Rodriguez, and me in the uncomfortable position of having to defend the BIOFAB's strategic plans and principle aims. That this defense was offered up to colleagues and friends without having an altogether clear sense of what the BIOFAB intended to become made the situation all the more uncomfortable.

For my part, I could navigate this discomfort by appeal to a kind of anthropological disinterest; however scientifically worthwhile the BIOFAB proved to be, I was there to observe and think through its significance and ramifications. But this response was far from ingenuous. The Human Practices experiment, after all, was predicated on the notion that anthropological engagement was a strategy for carrying forward a more adequate mode of ethical engagement. Or, as Endy put it in his presentation to the SynBERC reviewers, "Bennett is not embedded in the BIOFAB; he is part of the BIOFAB." To this extent, I, like Mutalik and Rodriguez cared about whether or not the work of the BIOFAB was scientifically worthwhile, and equally important whether or not it (and by extension we as participants) would be taken seriously. In my case and in the case of Mutalik in particular, this discomfort was made all the more acute by the fact that we could easily have been doing something else with our time. After all, Mutalik could have simply chosen to continue his research in the Arkin lab, and I could have simply continued in my position a part of the Rabinow Human Practices lab.

To introduce an ethical distinction, indeterminacies at the level of the BIOFAB's strategic orientation and the question of relevance, circulated at the interpersonal level to generate the affective play of esteem and scorn. Using an older ethical vocabulary one might be tempted to say that the dynamics of honor and shame were at stake. But the SynBERC retreat and review was neither that grand nor that serious. The question of how the BIOFAB's work would be evaluated did not turn on whether or not each of us would experience the pleasures of "high respect, or reverence, accorded to exalted worth or rank" or "the painful emotion arising from the consciousness of something dishonoring, or indecorous."[199] The affective register, rather, was played in something of a minor key. The question was whether or not, or to what extent our work, collectively and individually, would be considered to have a particular quality of worth and therefore that our efforts would be unlikely to be derided.

One response to the discomfort produced by this situation could have been to simply stand shoulder to shoulder with Endy in his public response to the BIOFAB's critics: "it's you're problem and not my problem." As I've already noted in previous chapters, several of the SynBERC PIs seemed to have a conflicted if not dishonest relationship with Endy. Few seemed to take his research seriously (though of course none of them were willing to press this publically). One SynBERC PI had commented that Endy's mantra—"we'll know we've arrived at engineering success in synthetic biology when designers no longer have to understand the underlying biology"—was confusing at best, insulting at worst. On another occasion, after a synthetic biology event sponsored by the NIH, a different SynBERC PI suggested that he found the analogies used in Endy's presentations to be simplistic and annoying. More strongly still, another SynBERC PI, when asked about the work coming out of MIT in synthetic biology, had suggested that Endy's doctoral students had not conducted thesis research worthy of the name. And yet, despite these off-the-record deprecations of Endy's scientific credibility, the broader community of synthetic biology researchers, especially those in SynBERC, had benefited from the enormous amounts of time and energy Endy was spending trying to bring synthetic biology

into a place of instrumental work, if not scientific credibility. The fact that Endy stylized himself as caring less about synthetic biology's scientific credibility than its engineering potential, in my view were tolerated by his colleagues to the extent that they could, when necessary, distance themselves from his rhetoric.

A relative lack of scientific credibility, however, could not be as easily negotiated by the members of the BIOFAB team, which made the informal criticisms encountered by the BIOFAB team at the SynBERC meetings all the more difficult to absorb. If some members of the BIOFAB team did not yet trust that Endy was sufficiently capable of understanding the difficult biology underlying the BIOFAB's stated aims, then it is hardly surprising that they did not know how to articulate and defend Endy's version of the BIOFAB's goals to their doubting peers. As Endy would later say about the BIOFAB team, referring to his vision for the facility: "I'm not sure they get it." His comment was more or less on target. They did not really get it. But this was in part because following the site review no one on the team was really sure what "it" was supposed to be. And to this extent, they certainly were not yet prepared to defend "its" worth to their peers or to take it as their own.

REORIENTATION

In the debriefing meeting following the retreat and site review some members of the BIOFAB were willing to discuss theses tensions and discomforts. Martin expressed the least concern for the ambivalent responses of the SynBERC community. His work was closely focused on operational details and the work of scaling production and measurement, with all this entails in terms of cloning protocols, software bottlenecks, organization of data and the like. To this extent, and given that such operational details are the concern of most labs with limited time and resources, he found many in the SynBERC community ready to engage and willing collaborate. Rodriguez expressed more caution, though indirectly. He reported that the various software and database engineers in attendance had furthered a series of ongoing disagreements about the role and strategy of software development in the success of synthetic biology. These disagreements ranged from technical questions such as which programming languages to use, to conceptual problems such as the way to handle the ontology of parts, to the question of which protocols should be used to standardize the sharing of experimental data. Rodriguez cast these tensions in the light of productive, if divergent, commitments. But it was clear that his work for the BIOFAB was being examined and evaluated against a set of protracted difficulties and simmering conflicts over credit, ownership, and sharing among the small cadre of software developers with professional commitments to synthetic biology.

My response was also cautious, but more direct about the problem of power and definitions of worth and relevance that the BIOFAB was likely to continue to face as part of the wider SynBERC community. Framing things in partially positive terms, I proposed that it was worthwhile for the members of the BIOFAB team to have circulated the halls of the SynBERC retreat to get a feel for the discord evident in informal exchanges, discord which is almost never made explicit and dealt with at a formal level. I, however, cautioned that this unaddressed discord was actually dangerous for the BIOFAB in that it was likely to reinforce a sense of confusion and even distrust concerning what the facility was proposing to accomplish. I also reported that I had had conversations with several SynBERC PIs about the work of the BIOFAB. This was noteworthy in part because this was the first time in four of SynBERC events that these particular PIs had gone out of their way to engage with me about anything substantive. Although most of these exchanges involved veiled and indirect criticisms, at least one PI expressed

concern in remarkably straightforward terms. He told me that he did not think that the SynBERC PIs trusted the work of the BIOFAB and that this lack of trust was connected to the fact that they did not understand, at least not yet, how or whether the work of the BIOFAB was going to be useful to the work of their labs. Trust was linked to utility, and relevance and value turned on the possibility of fostering such linkage.

Mutalik, for his part, was the most plain spoken. He admitted frankly that he found the event overwhelming, and was not sure what to make (or what he would be expected to make operationally and scientifically) of the "four boxes" according to which Endy had described the facility's work. Moreover, and more importantly, Mutalik expressed concern over the difference between the BIOFAB's internal deliberations about its strategic orientation and research portfolio, and the way in which the BIOFAB had been portrayed by Keasling and the NSF site review team. Specifically, he was concerned about the fact that the NSF clearly thought the BIOFAB's purpose was to solve SynBERC's four year old problem of non-integration between the Thrusts and the Test-Beds. We were being expected to clean up SynBERC's mess, as he put it. And Mutalik was concerned this would, in the end, take us down. True to his usual forceful stance, Endy's response on this point was to suggest that we tell SynBERC what we need to be rather than capitulating to what they think we need to be. Not that there was a clearly articulated agenda on the SynBERC side of things either; expectations were under-defined and Mutalik was right that this made them dangerous.

Mutalik further insisted that he did not want to spend his time in the coming months "cleaning up iGEM's house," as he felt he had done in the weeks leading up to the SynBERC retreat. Rather, extending the analogy, he wanted to "build a new house of his own." The wetware team had presented very little completed work at the SynBERC retreat. What they did present was the good-faith effort to help rectify the lack of sufficient characterization of some of the parts in the iGEM registry. As I described in the previous chapter, Mutalik and Martin had spent several long days over the two weeks preceding the event providing baseline and consistent characterizations of a set of promoters taken from the iGEM parts collection. The aim was to provide data on a number of BioBricks parts whose information and therefore usefulness was characteristically underdeveloped. Mutalik and Martin had taken up the work with a certain reluctance. Both were interested in pushing forward with the facility's work on EOU development and a first generation of parts to test the EOU as a workable construct and architecture for our parts development. In the wake of the SynBERC retreat Mutalik was clear: whatever the strategy for producing large numbers of new parts, he did not want to simply rectify the iGEM collection. This is not to say that Mutalik was not interested in making materials that would be useful to the iGEM community. The point, rather, was that the characterization work done for iGEM had involved using the host and genetic contexts required by the Registry. This meant that any work for iGEM was necessarily work not done on refining the designed genetic context of the EOU or work building libraries of parts consistent with that designed genetic context. It was, in other words, a situation which indicated that Endy's double goals of service to the community and a "leap" forward toward and EOS were not as easily reconcilable as one would hope.

THE PILOT PROJECT

Mutalik's last point had the clearest implications for the BIOFAB's work, which seemed to resonate with the BIOFAB team: the BIOFAB's attention and efforts should be spent producing a technology platform that was essentially distinct from (though not necessarily

incompatible with) past work with BioBricks; to the extent that we contribute to the refinement of the BioBrick model or the refinement of parts from the Registry collection, it should be within the context of the BIOFAB EOU. Endy seemed positively impressed by Mutalik's insistence and over the ensuing weeks quoted Mutalik several times on this point. One answer to the question "who are we making these parts for" was, of course, "the iGEM community—the biggest single community of parts makers and users in the world." The proposal was to remain committed to producing libraries of parts that might be useful for iGEM teams, but to use the BIOFAB's "standard rigs" for everything it made and characterized—even parts requested from affiliated partners. This way work on and with the EOU architecture could become the centerpiece of the BIOFAB's effort to create a set of foundational capacities.

The proposal had immediate organizational effects. Endy no longer conducted meetings in terms of separate BIOFAB divisions: software, wetware, measurements, analysis, human practices, etc. Rather, he began to structure things according to two "core capacities." First was C.dog. Work on the "central dogma" was no longer talked about or treated as one project among others, even as the most important project among others. The C.dog project, instead, was the first core capacity that the BIOFAB was delivering as a public benefit facility. This meant committing the BIOFAB's efforts to making the EOU the standard context for the construction, measurement, characterization and eventual refinement of all the components made at the BIOFAB. It also meant recalibrating the priorities of the wetware (now called the "experimental") team, software team, and human practices. The question "what should we be working on," Endy proposed, should be answered in terms of contributions to C.dog.

In this light, Endy asked Mutalik to reconceive the principle experimental priorities and to use the architecture of the EOU to map out categories of deliverables ("which parts are we going to make"), the division of labor in relation to these deliverables, as well as the experimental protocols and timelines. Mutalik's first efforts to produce such a map were rejected by Endy as too complicated and not yet focused sharply enough on the kinds of "products" that C.dog would ultimately (i.e. hopefully) consist in. Mutalik, who had spent considerable time and energy reformulating the experimental plan, once again felt frustrated. Arkin, in an attempt to rectify what he perceived as a communication problem, proposed a kind of reverse-engineering model for mapping the BIOFAB's production priorities. Beginning with drawings of the range of "rigs" (i.e. designed genetic expression cassettes) the BIOFAB would need to proceed with its work (e.g. rigs to test the insulating capacities of the EOU, rigs to test the relation between different kinds of parts, rigs to test different combinations, etc.), Arkin outlined the different classes and libraries of parts that would be generated within these rigs as well as the "juncture elements" that might need to be experimented with and refined in order to eventually rework both the expression cassettes and the parts.

Endy, not yet satisfied, proposed that he and Mutalik meet and simply draw up the road-map for "C.dog version 1" together. After several exchanges Endy and Mutalik presented three PowerPoint slides describing and defining what C.dog might eventually be. The slides were simple, and—we were told—presented only a first attempt to conceptualize how the BIOFAB work would be organized and oriented. The title of the first slide simply read "BIOFAB." On the slide were two items arrayed under the heading "C.dog Pipeline Development." The first item was titled "Stage 1 – Process Prototyping via E. coli." This item indicated that the stage one work would entail two "outputs." The first output was a refined version of the "C.dog process";

the second was designated as "E. coli C.dog parts set." The second item displayed was headed "Milestones/dates." This was followed by "TBD."

The second of the three slides was titled "Big Picture Goal." This slide included a single prominent sentence with two asterisk-designated clarifications. The sentence read: "Develop the capacity to rapidly engineer* standard biological parts that enable the programming** of the central dogma, at scale, within any target organism; such parts set should comprise and define the best available 'expression operating system' for each target organism." The two asterisk-designated clarifications read as follows: "*'engineer' means to design, construct, test, characterize, distribute such parts"; "**'programming at scale' means the reliable forward engineering to the greatest extent now possible, at the scale of ~2 dozen molecules."

The third slide was the most elaborate. It was titled "Expression Operating Unit" and had two representations of the EOU architecture as Mutalik had designed it. The two representations were laid out in a kind of piano-keyboard fashion with an upper row of keys designating the parts of the EOU and a lower row of keys designating the junctures between each of these parts. The caption read "above graphical depiction to serve as vehicle for quickly and clearly explaining framing and current progress." Below this first was a second representation, identical in form. This representation, however, was grayed-out with only two "keys" colored in. The caption read "for example, our work to date has been with promoter and translation start parts, and has not included any part-part junction engineering work." The representation indicated that, as work progressed on each of the parts or junctions, it would be colored according to progress made.

The three-slide presentation was significant in that it moved the BIOFAB team beyond a kind of representational impasse, and provided something closer to a reconciliation of the broad framings of the BIOFAB's work that Endy would be articulating in other settings, and the actual work plan that would be used to animate the daily life of the lab. It was less successful in providing a direct way forward in terms of experimental planning. From Endy's point of view—to simplify but not, I hope, to misrepresent—the next goal consisted in simply manufacturing the libraries of parts that would be included in the first iteration of the EOU. After all, bioengineering literature was full of elements that could be produced, measured, and characterized in the EOU architecture. The BIOFAB did not, at least in its early stages, need to design or invent new parts, per se. It could simply provide more consistent characterization of existing materials.

Mutalik (with Arkin's support) suggested that production might not be able to proceed in such a straightforward fashion. Although any number of other labs had produced parts whose designations were consistent with the designations marked out in the EOU (e.g. "promoters," "insulators," "5' UTRs," etc.) how each of these parts was defined and annotated was far from consistent. Moreover, most of these parts had been characterized as individualized units and not as units conceived in combination. While there were many part libraries that had been made by other labs, there were fewer combinatorial libraries of the sort that the BIOFAB was proposing. After all, the challenge was not just to build and characterize biological parts; the challenge was to build and characterize biological parts that could be reliably used in combination. That is to say, the principle problem was the problem of functional composition. Arkin and Mutalik pointed out that very little work had been done designing even simple combinatorial libraries in order to test the BIOFAB's most basic premises, namely that genetic sequences could be imagined as relatively independent units that had relatively consistent functional performance in

combination with other units. Although there is considerable data on many of the kinds components expected to form part of the first EOU—segments of DNA that expressed a promoter function, or served as a site of the binding of ribosomes in the initial shift from transcription to translation—there were, they argued, less data on how these components are likely to behave in combination. The question was: could the BIOFAB proceed in a fashion that basically treated each "part" as a unit that could be trusted to function in a relatively independent manner (i.e. consistently) when put in combination with other functional elements, or was there something about the relation between those elements that would determine the performance of each part?

Mutalik and Arkin proposed designing a simple set of experiments to address this question, even if just in a provisional and limited fashion. Mutalik proposed that these experiments could function as a kind of "pilot project": a simple combinatorial library that would allow the BIOFAB to test its basic premises, begin to work out its protocols for measurements and analysis, and to produce a first model for how to assign "scores" to various parts in combination—all with an eye to the question of functional composition. Mutalik proposed building a combinatorial library of 12 widely used promoters and 12 widely used 5'UTRs (with controls) in combination with a "reporter gene"—a sequence of nucleotides corresponding to the production of a protein whose expression levels could be measured as an indirect approximation of the activity levels of the promoter-5'UTR combination. The aim was to compose and measure these constructs and to analyze them such a way so as to be able to determine not only the total activity of the construct, but the "average" activity of each of the elements across all of the constructs which contain that element. In this way a "part," though measured in combination might be assigned an individual value—a value computed as an activity score "independent" of the combinatorial relation, but (hopefully) predictive of that relation. In this way the BIOFAB team might be able to determine whether or not, or to what extent, each of the elements in the combination functioned in a manner relatively and calculably independently of the others—a warrant for proceeding with the construction of much larger combinatorial sets.

Though the design of the pilot project was quite simple, the results were nonetheless striking. Working from the raw data Guimarães, a visiting student in the Arkin lab at Berkeley and the BIOFAB's de facto analyst, began with a simple algorithm wherein the total activity score of a given construct was imputed to each of the parts combined in that construct. Assuming a multiplicative relation between each promoter and each 5'UTR Guimarães assigned a value to each part such that, when the two parts were multiplied, gave the total activity. The challenge was to determine whether or not the value could be assigned in such a way that the activity score derived in one construct was consistent with the scores derived in other constructs. And indeed this proved to be the case. Guimarães was able to determine an "average score" for each promoter and 5'UTR. The reliability of this scoring was determined by building a "part-activity model" to predict the score of any one part in the library when combined with any other. The model proved to be remarkably accurate, predicting the activity of any given part in combination with any other part at an 85% accuracy rate. Put differently, the assumption that each of the parts could be assigned an individual value and that such a value allowed for predictable performance levels in combination with the other parts in the library proved accurate in all but five cases. Moreover, it was subsequently discovered that in four of the five cases in which the model did not accurately predict the outcome of the combination, the sample parts had undergone mutations, which might account for why they were the "outliers."

Guimarães' analysis was received with tempered enthusiasm. Enthusiasm for the reasons mentioned: the project suggested that parts could be conceived and scored as relatively independent; as such, these parts could be ranked according to their relative performance strengths and their function when composed could be predictably calculated. More important was the reliability of Guimarães' model. It suggested that the experimental determination of a given parts "score" in combination with any other element in the library would provide enough information to reliably determine its "average" score and therefore its likely strength in combination with any of the other parts in the library. For example, as the BIOFAB team created new promoters, actual combinatorial constructs would only need to be made with one or two 5'UTR / reporter genes. The activity scores determined by these one or two constructs would be enough to predict the likely performance of the promoter with any of the other 5'UTRs. The labor-saving possibilities were immediately evident for the experimental team.

The enthusiasm was tempered, however, for a number of reasons. First was the fact that the prediction numbers from the model seemed too good. Guimarães' and others were expecting that it would be unlikely that the promoters and 5'UTRs could be scored on a simple multiplicative model. Guimarães' for his part thought that there would need to be a third factor included, namely the structural interactions between the two parts. Hence, when the model showed that a value assigned to a given part, derived from a given construct, was predictive of the score-in-composition with other constructs, Guimarães' was surprised and pleased, and cautiously optimistic. Further analysis and experimentation confirmed that the results were trustworthy, at least within the genetic and host contexts within which the experiment was designed. Second, the reporter gene used to test the relation between the parts was green florescent protein, GFP. Given that GFP is commonly used, it was a reasonable selection for the test construct. GFP, however, has two limitations. It is commonly understood that GFP may not behave like other genes of interest. More importantly, the use of florescence to score the activity of the composite parts is a measurement system fraught with all the difficulties of such indirect methods. The test construct after all, did not measure the activity of the parts directly, how could it? Indirect measurement is the proverbial name of the game in biology, and a limitation which many bioengineers are working on, including many researchers in the Arkin lab. It is a limitation which the BIOFAB will live with for the time being, but which shows itself in the fact that the parts scores are derived indirectly.

Third and more consequentially, was the fact that the success of the project and the analysis as a proof-of-concept might prove to be more limited relative to the overarching BIOFAB goals than it might appear. Although the multiplicative model certainly demonstrated that you can treat the promoters and the 5'UTRs as more or less independent (i.e. you don't need another factor in the prediction which is the idiosyncratic interactions between any two parts), this independence can easily be overstated. When asked about the generalizability of these results, Guimarães was careful to point out that although the promoter may in fact function in ways that are relatively context independent, this is likely not true of the 5'UTRs. It is generally known, he explained, that a given 5'UTR forms a specific structure with the protein coding sequence which follows it. The fact that the pilot project used the same coding sequence for every construct meant that the "independence" was really an independence of the promoter from the 5'UTR/GFP. It did not demonstrate the independence of the 5'UTRs per se. In other words, if we had randomized the GFP, then we likely would have changed the behavior of the 5'UTRs and therefore would have had to account for Guimarães' "third factor."

The value of the project as a proof-of-concept for the BIOFAB's ongoing work may also be limited by the fact that the model "black-boxes" any molecular or contextual explanation of why it is that the promoters and the 5'UTRs function the way that they do. I say "may be limited" because this black-boxing indicates a key point of disagreement in the BIOFAB about what counts as good design in bioengineering and therefore what will count as a worthwhile and satisfactory outcome of the BIOFAB's work over the long run.

On the morning Guimarães circulated the results of his analysis I stopped by his desk to congratulate him on the first output of his work with the BIOFAB. He smiled, but with a non-committal shrug. Pausing before responding to my question of whether or not he was happy with the results he offered a hesitant yes. The hesitation, he explained, was that while the results were worthwhile they were not altogether scientifically satisfying because the results provided predictable combinations of parts, but did not explain what it was about those parts that caused them to function as they do. A further experimental question, he suggested, might be: what are the relations between these results and predictions, and the actual physical characteristics of the biological components in question? His models could predict combinations of parts in the study, but it could not explain what was going on materially such that the predictions themselves could be predicted. It should be noted that as confirmation-experiments progressed, Guimarães became increasingly enthusiastic.

This black-boxing might not be a problem for the BIOFAB. It might be enough for prospective engineers to have access to an optimized library of parts, whose functions in composition with other parts in the library can be predicted. As long as these combinations are reliable under specified conditions, what else does an engineer need to know? Put in more technical terms—terms which began to circulate in the wake of the pilot project results—the question can be framed as whether or not the BIOFAB needs to simply characterize a collection of parts and train models that tell us something about how that collection will work under specified conditions, including different combinations, or whether or not the BIOFAB should be striving to produce a bioengineering equivalent of a basis set? One problem is that a black-boxing approach of the kind characteristic of the pilot project might not be sufficient for the calculable engineering of other elements involved in genetic expression. The junction between a specific 5'UTR and a specific coding sequence, for example, is likely to form a structure that is a function of the relation between those two elements. That structure, in turn, is likely to affect the performance of those two elements. Hence, a given 5'UTR is not likely to have a consistent (i.e. independent) performance score in combination with just any protein of interest. This relative lack of independence challenges a black-boxing approach. If the BIOFAB were to simply continue to generate libraries of parts without reference to the underlying causes, it would need to be able to include coding sequences (i.e. "genes of interest") as parts of its libraries and generate composition scores for these sequences. But such an approach would be unfeasible; there are simply too many genes of interest to directly measure in the BIOFAB's library. Alternatively, the BIOFAB could try to design mechanisms that function as a buffer between the 5'UTR and a coding sequence, and which "override" any secondary structures that might form. If it is not possible to design such a structure, then the BIOFAB team will need to face up to the possibility that the rational engineering of genetic expression at scale will require more than a combinatorial library. It will require an understanding of the relation between genetic sequence and context, as Arkin signaled from the outset. It will need some explanation of how expression works, so that rules of design can be derived from those explanations. That is to say, it will need to move beyond black-boxing.

The pilot project should have put the question of how far one might be able to go in designing a technology platform for the rational design and control of genetic expression by simply producing libraries of components and analyzing the performance relations between those components on the BIOFAB's agenda in an explicit and direct fashion. It did not. It did, however, put the question on the agenda in an indirect fashion. The question showed itself in Arkin's and Endy's respective responses to the pilot project results, and what each of them expressed as key next questions, problems, and aims. The differences in these responses, I should note, was never explicitly recognized in the BIOFAB meetings, and therefore was never made a formal part of discussions, planning, and project scoping. Rather, it was not made part of the agenda except where I pressed the point. At several points I suggested that differences in response to the pilot project were likely to generate indeterminacy and might even be sites of potential discord in the BIOFAB's scientific and production priorities. Independently and individually, Arkin and Endy responded to my questions by trying to provide greater clarity about what they each took to be the important next steps. Such clarification, however, really only served to underscore the difficulty that I was trying to point out.

The real question, it seemed to me, was whether or not the BIOFAB was hoping to produce (or even be plausibly on the road to producing) a basis set for bioengineering. This question seemed worth posing at the time in that it allowed me to specify what I took to be conceptual, strategic, and stylistic differences between Arkin and Endy in terms of the design of the ongoing BIOFAB program. No doubt my specifications presumed more significance in the differences than there really was. It is the case that whatever unresolved discursive differences between Endy and Arkin, the work of the BIOFAB was going to have proceed apace. If operationally less significant than my formulations made them out to be, they were, nonetheless significant in terms of the self-understanding and priorities of the BIOFAB experimental team. In this light it struck me that stylistic differences, however tacit and possibly non-remediable, should be made explicit in order to be sorted out by the BIOFAB team. In this way it might be possible to more efficiently formulate and prioritize work, and also help determine the otherwise diffuse norms and forms of the subject positions the BIOFAB team was being expected to invent and embody.

WHAT NEEDS TO BE KNOWN: ERROR RATES & PREDICTABILITY

The circulation of the results of the pilot project, including the results of Guimarães' analysis, generated energy and activity. In view of the results, the operations team produced an operational pathway of how the project was conducted and where production appeared to be bottlenecked. Working from this pathway the software team began to develop sequence design and correction as well as data-management algorithms to be used in better automating workflow. Similarly, the pilot project provided a dataset for the production of first generation BIOFAB datasheets. These datasheets could include descriptions of genetic, host, and environmental context, measurements, and results of the prediction model—all to be made available through the facility's website. In this way the work of imagining, forming, and circulating data and datasheets could become a real-time priority. And with an experimental proof-of-concept the BIOFAB experimental team could begin to generate vectors containing the EOU architecture, vectors within which libraries of parts could be produced.

The workflow algorithms proved to be a major undertaking, and as of the writing of this thesis they were still being refined and (much to the frustration of the team leaders) the workflow was still lacking the desired characteristics of standardized organization, regularization of

protocols, and, where possible, automation. And, after considerable discussion and the realization that it would be some time before a "data client server" could be sufficiently designed and put into place for the automated generation of datasheets, the data was simply posted to the BIOFAB website through links to Google spreadsheets—"better out than delayed through endless discussions of format," Endy insisted. Most crucially, the completion of the pilot project did not lead immediately to the work of constructing libraries of additional parts. Rather, it served to return conversations in the weekly meetings to questions of how the facility should be imaging its work priorities and what it was and was not yet achieving.

In a telling set of exchanges, Arkin insisted that we should not describe the data in terms of "promoters" and "ribosome binding sites." The BIOFAB, he stressed, did not yet have a precise definition of a "part," let alone criteria for what exactly counts as a "promoter: or "RBS." The boundaries of the segments of DNA which had been physically combined in the pilot project were not yet rigorously defined and normalized. "Why is it that this category of objects is called 'ribosome binding sites,'" Arkin asked? "They don't have the same number of base pairs. They don't have any kind of refined structure." What we know we have, he insisted, "is a segment of 5' DNA that has a kind of ribosome binding site function in there somewhere." The pilot project, he stressed, produced relatively clean and reliable data. It did not, however, establish a refined set of terms that could be generalized.

Arkin's insistence on precision is telling in that it indicated something about what, in his view, would ultimately qualify as intellectually and scientifically satisfying. Arkin, as he often reminds the team, was trained as a physicist and chemist. As such, he usually continues, he wants to know what physical constants are actually in play. The pilot project, "black-boxing" the underlying chemistry and physics, was not yet satisfying on these grounds. That is not to say that Arkin was disappointed with the design or results of the study. Quite the opposite was true. At the Friday meeting of the week the pilot project results were first circulated, Arkin provided a run-down on what he thought was most significant about the project. By way of introduction Arkin shared with the BIOFAB team the results of an ongoing project from his lab which demonstrated, in a rigorous and specific manner, that when it comes to the mechanisms of genetic expression, "every base pair matters." These results, he seemed to be indicating, not only reminded the researcher to give proper attention to the molecular detail of things, it also reminds us that interpretation of experimental work requires the capacity to discern what can actually be concluded and what cannot. The importance of this otherwise typical expression of scientific care lay in the fact that it tends to cut against the grain of the way in which abstractions and generalized claims are made in synthetic biology—parts, devices, chassis, and the like.

Arkin's emphasis on scientific prudence and care provided the segue to the results of the pilot project and the modeling work that Guimarães had carried out. Guimarães was absent that afternoon so Arkin shared the diagrams of his modeling efforts. Arkin acknowledge what Guimarães had noted, namely that the modeling work was limited by the fact that it treated each component in the combinatorial library as an abstract and independent unit, and thus did not tell us anything about the underlying biology. That being said, he stressed, the project was nevertheless quite remarkable in that it predicted the behavior of components in combination with an 85% success rate. When I mentioned that Guimarães had actually expressed a certain reservation about the fact that the project relied on "black-boxing," Arkin laughed and said "that's because, like me, he's really a biophysicist." Black-boxing aside, Arkin was excited by

the fact that parts could be treated as though they were independent and predictably "scored" in combination. This was a key to rational design in bioengineering.

Discussing the results of the pilot project earlier in the week, Endy had emphasized a related but slightly different point. The pilot project and Guimarães' analysis was important for synthetic biology and relevant to the BIOFAB's long-term aims not only in that it allowed for predictable functional composition. It is also important in that this prediction is predicated on a certain consistency of individual components across different combinations. Given that predictability in Guimarães' model required treating the parts as independent variables, Endy's point might have gone without saying. The emphasis Endy wanted to lift out, however, was the fact that the project seemed to indicate that some parts functioned in a manner relatively indifferent to genetic context. Parts that are more rather than less context sensitive are crucial, Endy stressed. These allow for the compilation of a kit of possible components to be reduced, and for context to be treated as less determinative of the functional workings of a designed system relative to the use of those parts.

Endy told the team that he wanted to prioritize two next steps. A first was the development of a part's "de-rating score." Given that some parts seemed less context dependent than others, the question could be posed of how to devise a score of quality and reliability. Such a score would allow future users of the BIOFAB parts to consider the relative consistency in the performance of a given component in the design of genetic systems. Endy asked the BIOFAB team, and Guimarães in particular, to think how it could develop something like a "de-rating score" for all of the parts it produced. A "de-rating score," he explained, is used in the engineering of electrical circuits to indicate how well a given component is likely to perform outside of the contextual conditions for which it was originally designed. For example, a given device is designed to dissipate a certain electrical current at a given temperature. The de-rating score indicates how the device's performance is likely to change as temperature changes. Endy argued that potential users of the BIOFAB's components would like to have a quantified score of the consistency of a given part's performance across changing conditions. The needs of most engineers, Endy suggested, was for parts that worked in a fairly reliable manner across a range of contexts and, as such, the absolute scores for those parts as determined by actual measurements in all of those contexts (with all the labor that such actual measurements entailed) could more effectively be ignored if the BIOFAB provided a rating systems for how much a given parts performance was likely to remain constant across different combinations with other parts. To this end, Endy asked the team to prioritize a plan for deriving such a de-rating score for the parts in the pilot project.

A second next step was for the BIOFAB to select or design a next-generation set of reference objects to be circulated with the BIOFAB generated parts collections. Reference objects, as I explained in chapter two, are genetic elements whose *in vivo* performance can be used to normalize measurement standards across laboratories. The key to the use of a reference object is that it can be used to determine a ratio with another comparable part of interest (a promoter, for example) in one laboratory context. Then, when that part of interest is used in another lab it can be once again measured against the reference object. In principle, differences in experimental conditions can be accounted for and effectively ignored if the ratio between the part of interest and the reference object remains the same. In short, a reference object allows you to trust that what is being measured in one lab is comparable to what is being measured in another lab. The production of BIOFAB reference object was a priority for Endy, and had been

from the outset. The work of Kelly *et al.* on reference promoters was one of the key precedents Endy appealed to in the orientation of the BIOFAB's work.[200] Now that the BIOFAB had a first combinatorial library, however basic, it needed reference objects against which to score the activity of the parts. In this way the BIOFAB would be prepared to share what it had made.

In light of the conversation with Endy, those of us at the Friday meeting asked Arkin what he would propose as a means of establishing something like a de-rating score. (We would ask him about reference objects at a later meeting). Arkin's first response was to adjust our understanding of how de-rating scores function in other engineering domains. De-rating scores, he suggested, are not salient until the basic functional characteristics of a component have been established and regularized. A key to the de-rating score of an element in an electrical circuit is that it behaves in a specific way under "normal" conditions. Once the functions in a device have been refined, then any variable in that function might count as candidates for possible de-rating. Moreover, de-rating requires that everything in a system remain constant except for one element. Physically this requires a constant environment, which is difficult to achieve in any thoroughgoing fashion in biology. The pilot project, he reminded us, did not actually established refined functional elements in such a way that a worthwhile (i.e. useful) de-rating score would be derived. What we have in hand, he insisted, was a collection of DNA fragments that contain different functional elements and a model for how the elements in this collection function when assembled.

Perhaps more to the point, a score for contextual tolerance was not, in his view, the most pressing need for future engineers. The most important thing is establishing a model for the predictable functional composition of parts. Biologists interested in forward engineering need to know how several elements are likely to function when combined in context. As long as the combination scores are relatively predictable it does not matter whether or not each of those parts functions in exactly the same way in other contexts. That is to say, predictable combination does not need a de-rating factor per se, at least not as a first order requirement. It is the case with the pilot project that the relative independence of each part facilitated the design of a model for prediction. In this way, it is also the case that each part's value is relatively consistent across combinations. That is excellent and worthwhile for scaling work. But what if this wasn't the case? What designers need is not relative consistency and inconsistency of part function across combinations, but real knowledge of how that part is likely to function in combination, whatever the variation.

What the pilot project and Guimarães' model shows, Arkin repeated, is that a finite library of components can be combined and recombined in a relatively predictable manner. Equally important are the operational considerations of such predictability: it suggests that not all combinations in a library necessarily have to be tried out in order to have a fairly good idea of how they will work together. It might, rather, only require trying enough of them to train up a model to tell us how the rest of them would work. This, he insisted, is a key to how our work will be successful in the long run. Genetic context is in large part a question of how a given functional unit of DNA will act when physically composed with other units of DNA. Physical composition does not, of course, tell us everything we will need to know about genetic context. Physical "connections"—interactions among genetic elements that are not directly composed—for example are not accounted for by this approach. Questions of host context and environmental context are not controlled for either. The pilot experiment, in this respect, is as simple as it can be, and only functions to get us going. No matter how simple the experiment the BIOFAB had

established its first set of objects that could be rationally combined under specified constraints. That outcomes predicted by the model so closely matched the actual physical measurements is the "score" that forward engineers would most welcome. For this reason alone, Arkin concluded, the results of the experiment should be considered "pretty cool."

RELATIVE MEASUREMENTS

As an indication of affect the term "pretty cool" no doubt falls into a register of minor significance. It is not for that reason a throw-away term, analytically speaking. The expression bears paying attention to because it indicates what caught Arkin's attention, and therefore what he took to be worthwhile. Moreover, given his scientific authority for the members of the BIOFAB team, and the importance of that authority in affecting the team's sense of scientific integrity, Arkin's positive response, even when expressed in such everyday terms, carried with it the effect of focusing attention and orienting concern.

Curiously the term was expressed again during the following Monday's meeting in discussions of the pilot project—this time by Endy. Whereas Endy had been absent from the Friday meeting, Arkin was gone the following Monday. Following the normal procedure for the Monday meetings, Endy had each of the team members report on the results of their work from the preceding week. Given the threshold in his efforts with the pilot project, Guimarães was invited to go first and to take what time he needed to carefully walk us through his results. Guimarães rehearsed in detail the PowerPoint slides that Arkin had briefly shown on Friday. He explained how he had trained his model from project data, where it seemed to be more and less trustworthy, and what the few outliers consisted in. Guimarães explained that the black-boxing approach used in training a model from a fixed library seemed to be insufficient in a handful of cases. Where his multiplicative two-component model did not predict the data, he suggested, a third factor might be needed. This third factor consisted in the effects of the relation between the two components. In order to account for those effects, the black-box would need to be opened, as it were. Nonetheless the prediction results were striking.

Endy was pleased with the progress of the project. He pressed Guimarães to clarify a number of points concerning his methods and what he, Guimarães, thought were the possible limitations of the results. Endy's response, however, was perhaps more tempered than Arkin's. He actively focused on the outliers in the set, and despite the small number of these, took them to be serious and troublesome. He stressed that future users of BIOFAB parts would need performance specification to be exacting; as such exceptions to rules needed to be rigorously accounted for. Guimarães responded to Endy's concerns the best he could, and, without much more discussion the meeting shifted to the operations report from Martin.

The previous Monday Martin had been specifically asked by Endy to address the question of how the data from the pilot project might be used to construct relative measurements. Martin had reviewed the Kelly *et al.* paper to ensure he understood the equations and methods proposed. Working from these methods Martin selected one of the promoters out of the pilot project library—a fairly well-characterized and widely-used promoter from the so-called Anderson Library—and used the measurements of that promoter to establish a baseline value in relation to which the measurements of the promoters could be compared. In this way he assigned a relative score to each of the promoters in the library in terms of their relation to the performance of the Anderson promoter.

Martin's presentation of the data was concise and well-figured. Creating a kind of visual homology with the other pilot project results, Martin displayed his relative measurements using the same analytic grid that Mutalik and Guimarães produced to show the average part scores, both actual and predicted. Martin walked us through the initial results of this effort to re-characterize the pilot project data. Following Kelly *et al*. he explained that relative measurements required a number of assumptions, not least of which is that the experimental conditions used for the reference object were essentially identical to those used for the part of interest. On the assumption that the pilot project protocols had been carried out in a more or less consistent fashion, the BIOFAB could simply use the ratios with the Anderson promoter as a relative measurement of part performance.

Endy's response was immediate. This, he told us, was "really cool." He went on, speaking in a notably serious tone, "No offense, but this is the first time I've felt like anyone gets what we're doing here." Endy's comment was striking in that the BIOFAB had, after all, been accumulating staff and animating its research project for almost four months at the time of the meeting. What was it about relative measurements that constituted "getting it" in a way that had not, to that point, been exemplified? If striking, it was also disconcerting. It was disconcerting in that no one on the BIOFAB team really seemed to understand why the notion of relative measurements was so important to Endy and therefore to the work of the facility. Martin in particular at several points prior to that meeting had explained that he could not understand how relative measurements would advance the work the of BIOFAB—and this after spending considerably more time considering the notion than anyone else on the BIOFAB team. Martin noted that the work of constructing the test rigs for the relative measurement would seem to be just as much labor as simply determining the actual measurements of the artifact in question.

That no one on the BIOFAB technical team appreciated the notion of relative measurements, at least in relation to the BIOFAB research priorities was somewhat baffling. It had been on the agenda from the outset. The notion had formed a core part of the original BIOFAB proposal as one of the key precedents justifying the feasibility of the BIOFAB's aims. In a section of the proposal entitled "Preliminary Results," work with and on methods for relative measurement were cited as the second of "three recent results that detail the process by which many standard biological parts and devices can be made, characterized, and openly distributed." Consonant with this proposed emphasis, Endy had almost always included the need to develop "reference objects" for relative measurements as part of the BIOFAB's proposal. His accent on the importance of relative measurements for the BIOFAB's work, however, seems to have been lost or was simply not understood.

Part of the reason for this may be that in designing and scaling up the C.dog project the notion of relative measurements had simply been taken as relatively less important. A small experimental team has only a limited number of work cycles, as they say. An additional reason, however, was—to put it frankly—that prior work with relative measurements in synthetic biology was not yet taken seriously. Both in the proposal and in his direction of the BIOFAB's work, Endy made frequent reference to the work of Kelly *et al*. Endy referenced this article with the Canton *et al*. piece as kinds of touchstones for work in parts-based synthetic biology. Or, to put it in terms Endy himself would not have chosen, he would reference them as bio-scientific *equipment*—aides to practice which the team needed to have ready-at-hand.

The Kelly piece had clearly not been taken up as equipment in this way by BIOFAB team, despite Endy's regular encouragements. Endy's editorial response to an early draft of my

first "Human Practices Report," for example, stressed that the main thing missing was an adequate recapitulation of Kelly's work. I subsequently produced a brief summary and reference to the Kelly work in a later draft, including it in a short section on previous efforts to deal with the problem of context-dependence in biological engineering. In reviewing that later draft Mutalik was surprised to see the Kelly reference in the same paragraph as references to stars of bioengineering such as Hermann Bujard and Frances Arnold. He asked rather bluntly: "do you really want to include this guy?" My rather lame response that I had included the reference at Endy's request ended the exchange. Nonetheless, Mutalik's good-faith criticism exhibited the distance between Endy's commitment to the usefulness of relative measurements and the BIOFAB team's understanding of why they should be considered central.

The proposal that relative measurements are needed for parts-based synthetic biology was initially developed by Jason Kelly as part of his thesis work under Endy in MIT's bioengineering program. In this work Kelly had put forward an assertion central to the rationale for the BIOFAB: that managing complexity in the design and composition of biological systems is made easier with standardized parts. Such standardized parts, however, were lacking insofar as an integrated community of users had not yet decided on a standard by way of which measurements could be reliably made across differing biological and experimental conditions. Such a state of affairs was hardly surprising, Kelly acknowledged. Standard measurements for engineering in biology have proven a practical problem (e.g. despite the wide use of the so-called "Miller units" in measuring the abundance of protein in a cell, differences in substrates used in measuring make those units more or less incomparable). They have also proven to be a "cultural problem" (Kelly's term). For example, standards for measurements have been developed in relation to the specifications of a given biotechnology application.[201]

These problems are exacerbated by the fact that in biology, unlike other domains of engineering, slight variations in measurement conditions, such as where the cell is in its phase of growth, or in experimental conditions, such as how much and what kind of medium is being used, may produce major differences in the properties being measured. A first step toward remediating this problem, Kelly suggests, is to introduce techniques for relative measurements using an *in vivo* reference object. Though he does not define the term, Kelly contrasts "relative" measurements from "absolute" measurements (on Endy's account, it should be noted, such a distinction is itself relative; an important point that I will return to). "Given the complexity of living matter," Kelly writes, "the relationships between the measured properties of biological parts and experimental conditions may be difficult to determine (at first)."[202] Hence, it might be more useful to develop techniques for calculating "the measurement of relative (or ratio) properties rather than absolute characteristics." "A relative measure," Kelly goes on to explain, "is the ratio of the measurement of some aspect of the object being characterized in comparison to a standard reference object that is measured under the same conditions."[203]

The details of Kelly's experimental efforts to develop such techniques are less important here than the general nature of his strategy. Kelly chose "promoters" as his first class of objects in relation to which a first generation reference standard might be attempted. His first step was to establish a standard protocol for defining the "absolute activity" of the promoter, a standard that relied on the correlation of the somewhat controversial notion of "polymerase per second" or "PoPs" with the synthesis of green florescent protein. His second step was to characterize his reference promoter in relation to this protocol. Protocol and characterization in hand, researchers, Kelly proposed, could essentially factor out variations in measurement conditions by simply

characterizing their own promoters against the activity of his reference promoter. The key was to measure the reference promoter under the same conditions as those within which the researcher's promoter of interest is measured.

Kelly and his colleagues contrived a "kit" for using his reference promoter, and sent them out to a number of different labs. These labs, in turn, measured his reference object under the conditions within which they were working their own objects. The results of the experiment seemed promising, as Endy reported in the BIOFAB proposal. In Kelly's words, "We found that the absolute activity of BioBrick promoters varies across experimental conditions and measurement instruments. We choose one promoter (BBa_J23101) to serve as an *in vivo* reference standard for promoter activity. We demonstrated that, by measuring the activity of promoters relative to BBa_J23101, we could reduce variation in reported promoter activity due to differences in test conditions and measurement instruments by ~50%."[204]

The Kelly experiment, and therefore the conclusions to be drawn from it, depended upon a number of premises. If there was resistance among the BIOFAB team to reproducing those experiments it, in part, because not all of these premises were trusted. Hence there was some question as to whether or not the work of creating and measuring the constructs needed to derive relative measures was worth the experimental payoff. More crucially, there was some confusion about what it was the BIOFAB would actually gain by developing reference objects in this fashion. The Kelly paper seemed to indicate both direct and indirect value to the use of reference objects. In the near term, these object are worthwhile in simply helping to overcome differences in experimental conditions when trying to share designed biological parts across labs—making sure that what I measure in my lab can be compared to what you measure in your lab. The worth of the experiment according to Kelly and his colleagues lies principally in the fact that measurements across laboratory conditions are often not comparable—for dozens of possible reasons. As Arkin has put it in relation to another project in which his lab compared the results of enzyme assays: the principle differences in measurement turned out to be the people who were conducting the experiments.

In the longer term, however, there was the implication that these relative measurements would also be useful for rational design and forward engineering. As engineers grow accustomed to understanding the performance of genetic objects in terms of their relative performance vis a vis a reference object, they might get a feel for how to use these relative measurements to anticipate the outcomes of their designed systems. A principle and widespread problem in bioengineering is that there are no good means for direct *in vivo* measurement of individual aspects of genetic expression. Indeed, quantifications of the performance of genetic elements of any reliable sort are currently a principle lack in bioengineering. Relative measurements, even if only offering performance ratios, would seem to at least offer a step in the right direction.

BASIS SETS

Although Kelly *et al.* demonstrated the worth of developing standards for relative measurements as a strategy for ensuring the reliability and comparability of reported measurements of the performance of genetic elements across laboratory conditions, questions persisted among members of the BIOFAB team as to how these measurements might also be useful for dealing with the core design challenges of the C.dog project. Most central was the question of whether or not, or how they might be useful as a means of helping to realize long-term goal of specifying the rules for the forward engineering of gene expression.

At the following Friday's meeting I posed this question to Arkin. Arkin hesitated in answering the question, stressing that he had not been present on Monday. He did, however, tell us that he had given the question quite a bit of thought in other contexts. And, he admitted, he remained something of an "agnostic" on the question of how relative measurements might or might not be helpful for the challenge of design and forward engineering. He then reframed the question in terms of the hoped-for outcomes of the BIOFAB's work: How should someone proceed who is interested in making components for others to use "off the shelf" to build a genetic circuit? First and most importantly that person will need to make a part that can be quantitatively defined by some mean and variant in a stationary state. So, the question is, how should we do this? Biologists have multiple processes for measuring activity and lots of equations for analyzing that activity, which means that the BIOFAB should be able to know exactly how much of a given molecule is being produced over a given period of time in relation to a given set of conditions. And this should give us a kind of "universal object," namely a part that can be quantitatively characterized: so many units of X with mean and variance.

In the abstract this might seem to be pretty straightforward. "Here are pieces of DNA that encode this function – make a protein and it does something – you know what's going on in a jar of cells. You know what's going on in a circuit; they know what's going on." What should the units of measurements be? When Arkin studies an object, he explained, he wants to know exactly how many numbers per volume. "But numbers of what?" Ideally numbers of molecules of a protein of interests. "But when we're talking about measuring a biological part, we're not always talking about the sequence of DNA that encodes for the protein. Rather, we may be talking about elements of the machinery that drives genetic expression." In this case, if we want a measurement that gives us a mean and a variant we have to ask again: a mean and a variant of what? "What amount? The amount that turns on the circuit?" What might that be?

Kelly's protocol indirectly measures the mean and variant of the functional element of interest indirectly by use of a green florescent protein, concentrations of which can be read by an optical scanner. By placing a promoter upstream of the coding sequence for green fluorescent protein (GFP) we could use the rate of GFP synthesis as an indirect measure of promoter activity. We could then use a quantitative model to relate observed GFP synthesis rates to promoter activities reported as PoPS." Such an indirect and correlated means, however, does not give Arkin what he really wants—actual numbers of molecules. GFP after all, Arkin reminded us, is itself an indirect measurement, and using it to measure non-coding elements of genetic expression requires assumptions about correlated activities. GFP is read by an optical scanner that hits each molecule of GFP with a laser. This means that what the scanner reads is really only the amount of photons reflected back and detected. Given that "all of this is embedded in a cell embedded in a population of other cells—the photon can be bumped around, can inspire other photons—alpha photons become beta photon, and this all gets converted through some optics to numbers. How do we know what the numbers converted by the optics is related to the number of proteins in the cell?"

When using a reporter gene like GFP, it is difficult to account for variance in measurements between and among labs and even within a single lab. Measurement conditions can be controlled for up, to a point, and instruments fine-tuned. The number of factors contributing to variance can also be determined: "Settings on the machine, the media, the number of cells in the media, the physiology of the cell, and some variations in the photons themselves." Strategies for standardizing all of this would require carefully calibrating one's machine so as to

effectively "map at least how many photons are coming into the camera; you could figure out a conversion of light that was equal to a certain number of molecules being present. But we do not have such a thing—that would allow us to establish the exact relation between an instrument reading light to a weight—a certain number of molecules." Nonetheless—and this is the point that Arkin wanted to underscore—a basic challenge remains: the need for a quantitative standard that maps the readings of a machine to a physical unit such as weight, number, or concentration. "We need," he stressed, "measurements of physical constants." For physical constants "we have the equations," and these equations are "backed by a model of reality." That the notions of "physical constants" and "models of reality" were unproblematic Arkin seemed to take as a matter of course.

Arkin had effectively shifted the grounds of the question at hand: the question of the worth of relative measurements for standardization and forward engineering turned on whether or not they facilitated knowledge of physical constants "backed by a model of reality." If not, why should the BIOFAB bother with them? Taking examples from computer engineering and chemistry, he pressed the value for design of physical constants over relative measurements: "Physical theories and numbers are behind the design of chips; and these theories and numbers are connected to physical constants that can be accounted for. We are in a situation in which we want measurements of physical realities." Pressing on, he added: "Why do we have molecular measurements in chemistry labs? Why is it important to have things like weight, efficiencies, etc.? It depends on the exact numbers of things. This is why I get suspicious of people designing in relative measurements. I need to know what the thresholds are that allow for functionality. These are not relative thresholds. The properties I'm interested in are not relative measurements."

Offering something of a concluding thought Arkin added: "My tendency is to drive toward getting physical constants as much as possible. But this takes a lot of work. Some in synthetic biology want relative numbers to drive design to pass over all of this work. Perhaps this is the difference between the views of a physical engineer versus a practical engineer."

Several days later I asked Arkin to expand on this last point. The question, he suggested in somewhat opaque terms, depends on how you treat the notion of an "abstraction." Is an abstraction a concept that helps you reduce work or is an abstraction an object that is produced as an outcome of work? If it's the former than you can use an abstraction—say the notion of a part or even a part feature—to black-box the question of physical constants. This can be very useful. In the pilot project, for example, it allowed the BIOFAB to train a model to predict the outcome of any combination of promoters and 5'UTRs in a library. Sequence analysis could effectively be ignored by simply treating each of these as an independent part. The fact that the model was so successful established that the underlying hypothesis, namely that the two parts could indeed be treated as independent, was more or less sound. Obviously, such an approach can get you a long way, allowing would-be engineers to leverage the predictive properties of the model and the library to design composite objects. The trouble, he suggested, is that such black-boxing can limit the designer to only being able carry out forward engineering with the components in the library that have been trained to the model. If the library were comprehensive enough, both in terms of part type and variation, and if the model continued to work effectively beyond the simple two-part predictions, then black-boxing might suffice much of the time. But with the expectation that ultimately either libraries won't be comprehensive enough or that some components in an "expression system" won't be susceptible to being treated as independent, then

engineers will need to know what's going on "behind" the abstractions so as to eventually identify the underlying rules of functional composition. Once those rules are in hand the work shouldn't be limited by the constraints of any one library. Engineers would be able to design in view of how a component conforms to physical constants—like transistors in a circuit.

Put differently, said Arkin, the collection and the trained model associated with it does not yet represent what he really wants: a *basis set* for synthetic biology. A basis set in mathematics, he explained, is a set of vectors, a coordinated set of numbers on an axis, that when combined linearly can give you every possible position in a given vector space. Analogically, a basis set in biology would be the collection of rules for analysis and design that would account for the use of any genetic element. The advantage of such a basis set for building a predictive model is that it does not only give you some combination of genetic elements which you've already physically constructed, observed, and characterized. Additionally, it would be able to give you a prediction of any possible combination of similar elements. The question and problem then is: how do we define standard biological parts in such a way that their physical characteristics can be calculated as a basis set?

The possibility of a basis for synthetic biology, in Arkin's view, is what makes the notion of an EOU and the relatively simple work of the pilot project conceptually significant. On the one side, an EOU presents a minimally controlled genetic context within which the BIOFAB can build and characterize a suite of components. The expectation is that by controlling for and thereby limiting the number of contextual variables contributing the function of a given component the BIOFAB libraries will allow for the calculation of a performance score for each of those variables in relation to the others in the library. In this way the BIOFAB will be able to provide biological engineers with a catalogue of components that work in a specified and reliable manner, albeit within a defined genetic, host, and environmental context. Equally significantly—and this was the crucial point relative to the possibility of basis sets for genetic expression—by limiting and regularizing the contextual variables and expanding its library, the BIOFAB team will actually be generating broad and consistent data set concerning the interrelations of the mechanisms involved in genetic expression. This data set, beyond the black-box, should provide the opportunity to more carefully analyze the relation between the physical constants involved in composition such as the sequence of base pairs in each component in relation to and in combination with the sequence of base pairs in other components, or the structures created at the junctions of these components when combined, in such a way that the BIOFAB may eventually be able to identify the physical parameters (i.e. rules) that might give us something like a basis set. However minimal and relatively un-complex this exercise, it nonetheless further opens the possibility of achieving a crucial aim: an understanding of the rules of composition in such a way that a linear combination of genetic elements can be made to function within a predictable and manageable range.

In this light, the term expression operating unit is, Arkin has pointed out, both *provocative* and *consistent*. It is provocative insofar as many other bioengineers are working on similar kinds of objects; these researchers are content using what has become a common term for this class of objects: a genetic expression cassette. And if provocative this has little to do with either the "expression" in EOU or "unit." The provocation adheres in "operating." The term sustains an analogy to computer programming. An operation in programming is the basic functional unit in an operating system—the program on which all of the other programs installed on the hardware are able to run. Using the term in this context suggests that the BIOFAB (or at

least its directors) is imagining a cell to be like the hardware of a computer and the genome to be like the operating system. Genetic expression, the name EOU suggests, is the basic operating function of the genome. Hence, the operation of the system depends in a basic and direct fashion on the operation of each one of these functional units. The task and challenge of the C.dog project is to build these units in such a way that their function in combination will one day be predictable and functionally coherent. It is in this sense, then that Arkin thinks the name EOU is not only provocative but consistent. It is consistent in that it conforms to an imagined future in which the motifs and relations in the genetic activity of a cell can be imagined as modular and the rules structuring the functional relations among those modules specified and standardized. Such an imagined future entails the pragmatic hope of optimizing combinations among a defined set of objects—a threshold that certainly cannot be taken for granted. Additionally, it is an imagined future in which the modularized and deconstructed genome persists as a collection of composable units and rules for composition that, together, can be treated as a basis set for the design and composition an operating system for the functioning of a living cell.

ACCIDENTAL NOMINALISM

Between mid-June (a month or so after the completion of the pilot project) and mid-August two summer interns joined the BIOFAB team. Each was assigned a limited sub-project within the larger framework of the C.dog project. The first was assigned to the software team and spent several weeks helping to refine the algorithms produced by Martin and Rodriguez for specifying and error-checking sequences for the design of BIOFAB's parts. The second was assigned the task of animating the BIOFAB's reference object project. Working under the direction of the operations team, this intern was asked by Endy to address two problems. The first was broad and somewhat open: can the BIOFAB create a library of reference objects for relative measurements that helps reduce variation in reported parts activity at a rate better than the Kelly study reported >50%? The second, which was actually the methodological basis for the first: what are the experimental conditions that industry uses in relation to which a library of reference objects might be made?

Endy instructed the intern to talk to various BIOFAB industrial partners and inquire as to the key conditions of industrial operation (e.g. pH, oxygen levels, temperature, volume, etc.) that were likely to have an impact on genetic expression. With this list of variables in hand the intern was to begin the work of identifying two sets of promoters. The first set included promoters that exhibited a range of activity connected to each of these operational conditions. The second set included promoters that seemed indifferent to these conditions. Having produced these two sets, the task was to select out those promoters which would seem to be the best reference objects for context-specific conditions. The eventual goal was to circulate the selected reference objects with any BIOFAB parts in order to "reduce the complexity of measuring and sharing information of promoter activity," as Kelly *et al*. had put it.

The reference object project progressed just fine for a 10 week internship. The intern made acceptable headway on the tasks assigned. Tellingly, however, after his departure, very little was done to pick up and extend these initial efforts. Such a failure is due in part to the fact that the BIOFAB technical staff is small. Martin, who had been coordinating operations, was preparing to leave his appointment to start graduate school at Stanford, noted that with so few work-cycles on such a small staff, other things were simply more pressing. More to the point, in my view, was the fact that most of the BIOFAB team (including Martin who oversaw the

intern's work) still did not really understand why the BIOFAB should be using up any work-cycles thinking about the problem of relative measurements.

The ambivalence on the part of the BIOFAB experimental team made it all the more difficult for me to sort out what, if anything, was significant about the impasse over relative measurements. Martin, Mutalik, and Arkin were unenthusiastic about relative measurements. None of the three accepted that it should be a key element of the BIOFAB's work. At the same time, this lack of enthusiasm, and the place of the notion of relative measurements in relation to the pilot project, brought to the surface differences between Endy and Arkin in terms of their respective feel for good design in synthetic biology and "the interplay of cultural, aesthetic, and scientific norms" in their respective sense of how the BIOFAB's program should proceed. [205] I have concluded that the topic of relative measurements is not really the core of the BIOFAB's production agenda; however, it does provide one surface on which the programmatic differences (programmatic understood in the sense described in chapter one) between Endy and Arkin were being played out.

Although the stylistic differences between Endy and Arkin were obvious, I had difficulty specifying these differences in such a way that they might be depersonalized and introduced as a design, operations, and ethical problem within the BIOFAB—a task I had taken upon myself to carry out as part of the human practices contribution to an ethical remediation of the BIOFAB's experimental work. Given my inability to provide a satisfactory capsulation, I decided to simply put the question to Endy. I asked: "why do you think Arkin is agnostic (at best) on the question of the relation between relative measurements and the C.dog's goals; and why do you think that the technical team remains unconvinced of their importance for the BIOFAB's work?" Before responding Endy paused. He then turned away from me, reached over to his lap-top, which was sitting on the table beside him, opened his email and pulled up a message he had just sent to the BIOFAB team. The message was a response to a document Mutalik had recently composed scoping out the next phase of the C.dog project. Endy showed the one-line response he had sent to Mutalik earlier that morning. Written in all caps was: "what about reference objects?!"

Endy then addressed my questions by first telling me that I needed to begin with a different question. He insisted that at this stage the only honest response to my question (do we think relative measurements will be helpful for prediction; will they help us make basis sets) is: who knows? And who cares—at least for now? "The point," Endy said with a note of exasperation, "is that we're about to create a library of parts and we're going to start sending data on those parts to labs all over the world. What if they can't reproduce our results? What if they call us up and ask us what the problem is? How are we going to know if someone who doesn't get our results is crazy or if we fucked up?" He underscored that the BIOFAB must devise some means of knowing whether or not the difference in measurements is the result of screw ups in our work or screw ups in their lab. Relative measurements, he concluded, will help us with this.

Picking up on the suggestion that an orientation toward the eventual creation of basis sets should determine the worth of relative measurements Endy again responded: who cares? "We're going to make reference objects, we're going to test them, and we're going to send them out to be used against the datasheets that we produce." Betraying a note of frustration, Endy rehearsed what had become something of a touchstone over these early months of the BIOFAB's operations: the task is to make parts and circulate them. Then questions about the underlying rules of composition can be asked. But the point is to make and circulate.

I proposed to Endy that his frustrations on this point reflected commitment to a qualified version of the "engineering ideal in biology"—a phrase taken from a book on the American biologist Jakob Loeb.[206] Endy said he had read the book, and did not seem particularly interested in the comparison. Instead he again paused. He leaned back in his chair and looked at the ceiling. He asked: "Why shouldn't relative measurements lead to the formation of a basis set? Really what is the difference between a relative measurement and any other kind of measurement?" Adding intensity to his voice: "What does Arkin really mean by a physical constant? Is he talking about rates? If so, how are rates really measured? Speed of light? But speed of light is measured in meters per second. What is a meter? It's this." Endy spread out his arms. The point, Endy stressed, is that we take speed of light to be a physical constant because we've learned to trust it. It is "this much." We have a feel for it. But a meter is in this way no less of a physical constant than a ratio between the performance of one kind of promoter in a given system and another kind of promoter. The only real difference is familiarity which has come from long use.

Endy asked: "have you read *The Morals of Measurements*? Look it up for an account of how measurements really work."[207] Endy turned to his computer and looked the book up online and emailed me the link. The truth of the matter, Endy insisted, is that a relative measurement is unsatisfactory to many engineers because it is unfamiliar. Most engineers from other disciplines can simply take for granted that the standards and materials in their fields are there—as if they have been there all along. But these were new at some point. People fought over them. Endy then turned and pulled up a copy of Jason Kelly's dissertation, which he had sent to me a day earlier. Scanning through the PDF he stopped on an image of the British ohm—the rod designed to calibrate electrical current in the 19th century. The rod was produced by a single manufacturer, who, by controlling the specifications could reassure those who tested their currents against it that their measurements would be exactly like everyone else who tested against other copies of the ohm.

At that point in the conversation Mutalik and one of the BIOFAB technicians, arrived for an appointment with Endy. I told them that we had just been talking about relative measurements and why it is the BIOFAB team did not seem either interested or convinced. Mutalik looked mildly embarrassed, no doubt because of the email he had received earlier in the day from Endy. Endy then said: "I was just telling Gaymon that I think measurements of any kind are relative, relative to a norm of shared experience. Gaymon and I could decide that the plastic barrel on that table was going to be our unit of measurement and then he could go measure the Berkeley campanile and I'd go measure the Hoover tower at Stanford. We'd then call and report how many barrels high each of the towers are." All measures, he went on, started out like this: standards chosen, agreed on, experiential, and ultimately accepted as simply part of the physical constitution of things.

Some weeks later Endy reported to the BIOFAB team that he and Arkin would be meeting to talk through the use of relative measurements at the BIOFAB. Neither Endy nor Arkin reported the results of that conversation. Several weeks further on, the BIOFAB was once again discussing how best to assign values to the components in the pilot project library, including how to account for both the mean of each part across the library, the relative deviations from that mean in each specific combination, and the error rates between the actual measurements of combined components and the measurements predicted by the BIOFAB's model. At one point someone in the meeting commented on the criteria of ranking among the promoters in the pilot project set, asking: "what counts as strong and what counts as weak; are

those designations only relative to the overall set?" The answer, of course, was yes. The strong were only strong relative to the other elements of the set, not relative to some specified criterion of performance. Arkin, acknowledging this limitation, responded in the positive; the ranking was relative to the set, as the scoring was inferred from the apportioned measurements of GFP. Endy responded by noting that "at this point, something is better than nothing." Arkin, with a note of concession in his voice replied: "yes, something is better than nothing."

DESIGNING REGULARIZATION

How might the relative differences between Endy's and Arkin's feel for design and for the place of measurements and standardization in what counts as good design be characterized? And, more to the point, are these differences significant? Apart from the mild turbulence they cause when explicitly noted, do they, in the end, matter? The honest answer is: it's not clear. They certainly have had some effect on the BIOFAB's activities. The team has not yet worked seriously on relative measurements, at least not in a fashion similar to Jason Kelly's prior work. The notion of relative measurements has indeed been foregrounded in the ongoing conversations about how the BIOFAB ought to assign quantitative values to the parts in the library collection. Most directly, these conversations have centered on what to do with the pilot project data. Six months after the completion of the experimental and analytic work, the pilot project is being "written up" for publication. This work of formulation and presentation has pressed the question of what "real engineers" will want to know about a given BIOFAB part in order to be able to use it. Arkin, in this context, has stressed the importance of error scores that show the difference between observed activity and predicted activity. Endy has again raised the question of how to quantify relative deviation from the "mean" scores. It is clear to all involved in these conversations that the variables and options are simultaneously far from complicated (the regression model has only two variables after all) and far from resolved. Crucially, this lack of resolution turns on the fact that the data for each part in the library is derived from a GFP reading. This reading requires an indirect imputation of value to the various components involved in the mechanisms of expressing that GFP; which is to say that the BIOFAB has no way of directly measuring the activity of any of the parts. The model being used, however, seems to satisfactorily support the hypothesis that the parts can be treated as though their activity is independent. But, again, when it comes to assigning the quantitative values by way of which the activity of these parts could be understood by potential users, things remain unresolved.

Differences in style as what counts as good design and useful measurements will have some obvious effect on how the BIOFAB sets up its datasheets and how it instructs potential users for interpreting and using the components in the library. For Arkin's part, he often returns to the point that the BIOFAB should, in the end, make all the experimental data available so that potential users can sort some of these things out on their own. More important than the effects of these differences on the datasheets, I propose, are the impasses created in terms of trust and subjectivation. On the side of trust, the conversations about measurements usually favor the proposals being made by Arkin. As one BIOFAB team member put it, these conversations are "interesting and stimulating." By contrast, this same person frequently notes that the demands Endy is making, at worst, "don't make scientific sense," at best "aren't interesting." It is perhaps not surprising that even the senior post-docs on the BIOFAB team are uncertain as to the best way of contributing to the conversations about how the BIOFAB should be proceeding. Most of the experimental team is inspired by Arkin's reworking of the problems, as I explained in the last chapter. To date, however, it has been Endy's insistence on product-oriented deliverables that

has generated both orientation and motion. The substance of that orientation and motion has been formulated, for the most part, by Mutalik, Cambray, and Rodriguez—all of whom have been put in the difficult position of having to exemplify the "good synthetic biologist" in this otherwise indeterminate situation. What stance to take up and which practices to cultivate?

Rabinow's statement quoted several times in this chapter is from an article summarizing a key distinction from a much longer work.[208] That longer work consists of a historical recapitulation and anthropological analysis of the notion of "society." Rabinow's shows how the notion of society was formulated in 19th and 20th century planning as that object by way of which the human condition might be engineered to the end of physical and moral amelioration. In his analysis Rabinow introduces a distinction between two modes of design and planning concerning society, which he designates "technocosmopolitanism" and "middling modernism." These terms, I propose, offer the first elements of an analytic frame within which the stylistic differences between Endy's and Arkin's approach to the work of the BIOFAB can be situated and understood. Said differently, Rabinow's typification of different modes of social engineering in the 19th and 20th centuries provides a kind of template for an analytic copy-change. I hasten to add that "the social," in the strictly technical sense that Rabinow examines it, is not what is at stake with the BIOFAB (despite persistent use of "societal implications" as a term defining what it is Human Practices should attend to). Rather, the chief point of conceptual connection lies in the fact that the BIOFAB's program must face the question of the extent to which the activity of living beings, characterized by complex and historically embedded systems, can be conceived as calculable, strategically intervened on, and made to conform to ideal norms of functionality and well-being.

In his article Rabinow explains that urban planning has had a privileged role in making visible an "essential feature of modernity": the interplay of cultural, aesthetic, and scientific norms in attempts to experiment with social and spatial form.[209] Its role is privileged because planning has constituted a programmatic attempt to formulate the means by way of which a society can successfully and stably "estimate, foresee, and assume its needs." A central aim of planning was regulation, a term entailing both adjustment and regularization. Regulation, Rabinow writes, can be cast as a need "in search of its organ and its norm of exercise." What is known is that regulation is needed; what is not known is what form and norm by way of which regulation might be effectively actualized.

For a number of years, Endy (and in a lesser and more indirect way Arkin) has been arguing for the need to establish programs for standardization in biological engineering. A key to this program was the creation of a fabrication facility for the production of refined genetic elements that can be meaningfully classified as standard biological parts. Such a facility would receive orders, make parts to specification, and return both material and data. Additionally, these fabricated parts would be refined in such a way that they not only met the functional specifications outlined by the party placing the order, but would also function coherently and co-operably with other fabricated components. The facility, in this way was not only generating standardized parts. It was also generating regimes of standardized practice. These regimes, at their most successful, could be imagined as standardizing the biological environment within which designed systems were operating. The motion was from fab as specialty shop to fab as industrial production to fab as an organ for actualizing the norms of standardized biological engineering. Put differently, in this vision of this Endy's plans called for a facility that could "estimate, foresee, and assume" the needs of parts-based synthetic biology.

A key difference from earlier moments of modern planning was that these efforts at bio-fabrication were not directly oriented toward the needs of "society," per se—however much the vision promised industrial and national prosperity as well as the amelioration of human and environmental health. Rather, these efforts were to be oriented toward the needs of an imagined engineering community and the "needs" of biological materials, insofar as regularized practices of design and composition were not yet in hand. This community, these materials, and these practices would constitute something of a social mechanism by way of which "real-world" needs might be more affectively addressed.

Perhaps a more important difference is that the key term in this vision for synthetic biology is standardization and not regulation (though adjustment and regularization were certainly assumed). And if standardization is the need of an imagined bioengineering community, then, following Rabinow, it is fair to say that standardization itself is "a need in search of its organ and its norms of exercise." Whatever else can be said about it, the BIOFAB's C.dog project is certainly a programmatic attempt to establish an organ for the constitution of standardization. One of the principle blockages to this constitution is, as I have suggested, its techno-scientific norms (of measurement, of context, of design, etc.), and the kind of practitioners who might be capable of giving these norms a form sufficient to Endy's view of the future—with all such norms and forms imply culturally, aesthetically, and micro-politically.

Endy's emphasis on relative measurements and Arkin's emphasis on the need for specifying physical constants leading to a basis set (and not just an optimized library) can be cast as varying programs (or at least programmatic elements) for constituting the techno-scientific norms by way of which standardized practices in bioengineering might be cultivated. Both these are embedded in a broader vision for bioengineering that can accurately be described as modern in the sense proposed by Rabinow, namely that they can both be justified "under the twin imperatives of industrialization and welfare." In this sense biological parts as well as the practice of bioengineering are understood as objects of knowledge and reform. For both Endy and Arkin and indeed for the BIOFAB, a key to that knowledge and reform turns on an additional twin imperative: production and quantitative measurement. Making libraries of components, it is supposed, will move the BIOFAB in the direction of providing answers to the problem of standardization. The correlation of large libraries with models predicting their values in combination will lay the groundwork for developing strategies for useful quantification. Arkin's vision for a basis set adds to this that success in optimizing libraries will provide the experimental data needed to successfully specify rules for forward engineering. Future standardization is thus a function of successfully passing through cycles of production, analysis, and experimental as well as operational rectification.

As a form of cultural and scientific production, the interplay of experimental production and quantitative measurement within the BIOFAB operates on a relatively minor scale, and will do so for the foreseeable future. Despite industrial partners who profess to be "excited" about the BIOFAB, funding remains relatively minimal and, as such, staffing and other facilities modest. For all of the attention that the BIOFAB has received it is, after all, a four-person team on the biology side of things. And yet as Rabinow emphasizes in his analysis of urban planning, programs of relatively modest scale may nevertheless introduce elements of organization and practice that subsequently become essential components of later apparatuses. In this light, the significance of opportunities to think through and give form to experimental norms need not only

be evaluated on in terms of the utopian hopes of their proponents, but might also be tested against their eventual ramifications.

"Middling modernism," Rabinow writes, exemplifies "the norms of industrialization, health, and sociality as well as the technological processes aimed at regulating social practices."[210] It takes as a core premise that these norms should be discovered in or realized through the sedimented historical materials of specific customs, cultures, and countries. Rather, "the 'human material' on which it worked" should be conceived as a universal subject "whose needs, potentialities, and norms could be discovered, analyzed and formalized by science."[211] Such a mode of planning and its correlated design strategies, as well as its confidence that living beings can be made to conform to universal norms, is consonant with many of the early statements about the potential of a parts-based approach to synthetic biology. This "first-wave" of work, as it has been called, emphasized the conceptual and practical power of abstraction hierarchies to black-box and thereby effectively ignore complexity and the idiosyncrasies of interactions between designed components and elements of cellular context. It has been noted by several observers that this first-wave work, depended in its design strategies on the analogies it drew "from the development of integrated circuits in electronic engineering as a means of establishing its research priorities as well as its principles for design and construction."[212] In a fashion similar to the design of circuits it was held that individual components could be made interoperable and thereby aggregated in a straightforwardly additive fashion. Such a project, as Rabinow says of middling modernism is audacious in that it rhetorically and experimentally treats as inevitable the proposition that new forms of biological engineering will be made possible through the labor of producing standards for practice and the refinement of materials. Such a vision is not exactly context-free. Rather, the vision is that experimental contexts (as well as the context of experimentation) can be controlled for in such a way that the biological material worked on and reproduced is no longer fundamentally dependent on sedimented evolutionary histories or naturally occurring environments.

"Technocosmopolitanism," in distinction to middling modernism, "can be defined as the attempt to regulate history, society, and culture by working over existent institutions and spaces—cultural, social, and aesthetic—that were seen to embody a healthy sedimentation of historical practices." In this regard, "technical dimensions of urban planning in Morocco would resemble those in Brazil…but the well-planned city would artfully integrate and strengthen topographic, cultural, and social specificities into its plan. The art of urban planning, and thus of a healthy modern society, was held to lie precisely in this orchestration of the general and the particular."[213] Crucial here is that the aim of regulation is achieved through the perturbation or refinement of existing mechanisms. Such regulation is carefully distinguished from control; the potentials of historically given materials and spaces are assumed to be, at least in significant part, a function of (and thus dependent on) those histories and spaces.

An important outcome of prior work in Human Practices was that the formulation of a "second wave of synthetic biology" was in several key respect consonant with the notion of technocosmopolitanism. Research programs in this second wave could be identified as exercising a prudent acceptance of the constraining effects of historical sedimentation in evolutionary systems, as well as the labor attendant to such acceptance. Such labor is defined in part by an attempt to work over that sedimentation by identifying select domains within the cell or cellular populations in which "biological complexity holds the promise of being manageable and potentially open to strategic leveraging."[214] Work on these "ontological domains," such as

signaling pathways, system-level controls for genetic expression, or environmental sensors, is characterized by an attempt to bring generalized techniques and technologies to bear on specific biological topologies. It is only after these topologies have been sufficiently characterized that something like a parts-based approach might be taken up.

Neither technocosmopolitanism nor middling modernism sufficiently captures the strategic orientation of either Endy or Arkin in their efforts to direct the work of the BIOFAB. However, I would argue that they do mark out analytic types in relation to which the work of the BIOFAB can be situated and more effectively monitored. Certainly in his framing of the BIOFAB's principle goals and eventual outcomes, Endy's efforts to direct the work of the BIOFAB is much closer to middling modernism than it is to technocosmopolitanism. The notion of standardized parts may not be tantamount to the aspiration of "creating New Man, purified and liberated to pursue new forms of sociality," but it does promise to create a suite of components that, if fashioned correctly, will contribute to the fabrication of a whole-genome operating systems, a system capable of controlling genetic expression in such a way as to direct of cellular and multi-cellular activities. These discursive and metaleptic resonances with middling modernism, however, may not prove to be operationally consequential. The daily work of the BIOFAB, after all, is marked by complications of designing even simple biological constructs. Indeed, the corrected (i.e. non-mutated) library set for the pilot project is (as of the writing of this thesis) only now reaching completion. The pilot project predictions are reliable because they are simple and the context is constrained. Everyone on the BIOFAB experimental team knows that although promoters and UTRs can be treated as independent, UTRs and coding sequences will likely form unexpected structures and therefore their "scoring" will vary from composition to composition. All of which suggests that the BIOFAB's efforts to produce an optimized library of components will not be universal in any serious sense. It may be worthwhile, but it will not be universal.

For his part, Arkin is less discursively sanguine about the universal possibilities entailed in the dream of standardized synthetic biology. Arkin, after all, led with the problem of context dependence. His responses and reactions to the BIOFAB team meetings inevitably can be cast as examinations of the limitations of the work at hand, the insistence that experiments be designed in such a way that ad hoc explanations can be minimized, and that conclusive statements about the work be rhetorically constrained out of deference to the broad horizons of what synthetic biologists do not yet know. That being said, Arkin remains resolutely focused on the possibility of a designing a basis set for synthetic biology. Such a set would not allow for the construction of "a new biology" to inflect Rabinow's description of the aims of middling modernism. It would, however, make possible a mode of bottom-up engineering that would allow for the rational re-design of living systems beyond the constraints implied in leveraging existing systems—from pipes to programs as he puts it.

Rabinow explains that both technocosmopolitanism and middling modernism emphasized a kind of zoning: the spatial and conceptual distribution of functions. The question was the extent to which the norms of such zoning were taken to be universal and applicable to all cases of social planning, or whether or not such norms and such zoning would need to take into account the specificities of a given context. In the BIOFAB such spatialization of function is a basic premise of its work; the notion of a standard biological part, after all, implies the ability to physically isolate functions so as to recombine them to designed affect. The pilot project was designed as a first experiment in establishing such a mode and effort as worthwhile. What is distinct about

these efforts is that they are not (yet) characterized by planning in anything like the sense that Rabinow's terms imply. Rather, they remain experimental in the straightforward sense that the norms of physical separation and combination are not known in advance of actually making and remaking conceptual and material instantiations.

The question for the BIOFAB, at least on the heels of the pilot project work, was how to quantify the components and their relations such that predictable interoperability become more rather than less likely. Minimally, as Guimarães' preliminary models had shown, such quantification could issue in predictable combinations of measured elements within a defined genetic context and a more or less controlled host and environmental context. Additionally, as Endy emphasized, quantification could consist in scoring the relative independence of individualized components across combinations. The aim here would be less to know how genetic context (i.e. the physical composition of zones of DNA) changes performance and more to know which functional zones remain performatively constant in the face of such contextual changes. In contrast to a relative measurement approach, Arkin proposed the need for experiments and measurements that took account of the physical constants at play in combinations. Such constants, "backed by a model of reality" would be susceptible to formation as a basis set. Design could then move from a matter of combinatorial libraries to model-driven prediction.

In any case, it bears remembering that for both Endy and Arkin the question of measurements, relative or otherwise, is posed in relation to the problem of context variability, context dependence, and the question of whether or not part-performance in context can, in the end, either be predicted or otherwise black-boxed away. The stakes of the question can be cast as a kind of interplay of art and science. The terms art and science here mark out a distinction between greater and lesser degrees of standardization, rationalization, and control. The game is to see how far one can go in moving the design of genetic expression beyond the artisanal crafting of "one-offs," to use the frequently evoked British expression. One-offs imply a kind of hyper context dependence in which all functional elements are designed to do just the right thing under just the right conditions: the design of proper elements for proper milieu as it were. The hope and the aim of the BIOFAB, whether by developing basis sets or libraries with reference objects, is to "take the central dogma off the table as a research question." Put more modestly, the aim—as it has been all the way through for the spokespersons of parts-based synthetic biology—is to create a situation in which a sufficient measure of determination has been established with regard to the problem of how to compose manufactured components into functionally worthwhile systems. Coupled with developments in computer aided design, the outcome of such a determination is to produce a ready-to-use toolkit whose applications are under-determined by design.

How to move forward is far from determined. Two variables that will be in play, however, are clear. The first is that a certain measure of confidence is being placed in the notion that routinization of operations, the production of substantial parts libraries (where "part" is defined as a genetic component that has a function associated with it), and the regularized use of Mutalik's EOU will create the conditions within which the problems of predictability, context dependence, and eventually part-refinement can be resolved. The hope that a rationalized conduct of work will lead to the development of rationalized strategies for design and composition. The second is that the work of the BIOFAB will inevitably involve trade-offs between the kinds of design strategies that one might associate with middling modernism and

those associated with technocosmopolitanism. Or, better than "trade-offs," we might venture that the BIOFAB will involve restylizations of existing biological elements and systems in the name of fashioning those elements and system as more functionally predictable and more contextually generalizable.

Such strategies, insofar as they are focused exclusively on the techno-scientific questions of measurement, scoring, and design will fail to take account of the problematic internal constraints of the BIOFAB's program, where this chapter started. These constraints are on some obvious level bioscientific: how will the facility's work be conducted and will it or won't it lead to hoped-for outcomes. On another level, and perhaps more importantly, these constraints also concern the question of careers and credibility. It concerns careers in that, as of early summer 2010 none of the team leaders—Mutalik, Rodriguez, Cambry nor, for that matter, me—understood what counted as good design and worthwhile scientific production. Arkin's verificational riffs remained inspiring (which certainly cannot be taken for granted), but not sufficiently directional. And the importance of Endy's emphasis on relative measurements continued to be lost on those who were actually conducting the daily life of the facility's wetware work. Neither trust nor curiosity could be activated as virtues that might have carried the team through this indeterminacy.

This meant that none of the team leaders understood how the work at the BIOFAB constituted a sound investment in our own professional (let alone vocational) futures. The question was perhaps less acute for me, in that whatever happened at the BIOFAB I would have materials for my anthropological experiment. But insofar as I cared about the question of capacity building and ethics, and how a participant such as myself contributes or fails to contribute to addressing that question, the indeterminacy and the internal constraints connected to it were burdensome. Further, and this is the other side of the internal constraints, indeterminacy about whether or not the facility's experiments were credible and worthwhile left open the question of who it was the BIOFAB should be serving. It is fine to distinguish between incremental service and a breakthrough technology. But such a distinction requires either refusing the status quo and justifying only the "moon-shot," or (as was the case at the time of the pilot project) operating as though service to the community in the form of just making a lot of parts would, ultimately, lead to the moon-shot.

But even if the goal was to serve a community, and even if that community was, in some respects only virtual (i.e. those self-selected engineers who will use the parts once they are made and circulated) one is tempted to ask: is it CAGEN or iGEM? Given Arkin's not infrequent reference to the former and Endy's regular return to the latter, it seems that the difference between the needs of these two communities might function as a kind of proxy for who it is the BIOFAB is actually serving. As the SynBERC scientific director put it on several occasions: usefulness is designed by who uses it. If the BIOFAB establishes protocols for relative measurements as a key tactic for characterization a different community will think the facility's work is useful than if the BIOFAB concentrates on physical constants. As Endy insists, of course the two are not mutually exclusive. The former might become the latter in the minds of enough users that a community becomes possible.

Put differently, what the pilot project did was expose the reality that whatever new social and scientific program the BIOFAB would eventually constitute, and whatever form the community of users might take, such forms would be shaped in significant part by "the interplay of cultural, aesthetic, and scientific norms." And this was the case not only in terms of the

experimental designs and engineering protocols. Also at stake was the question of the kinds of practitioners the BIOFAB participants were being asked to become, what work we were being asked to take seriously, which avenues of scientific curiosity we were being tempted to open and asked to close off, and which kinds of products it was expected they would be able to produce and circulate. That Endy's and Arkin's engineering styles and feels for design were contrastive does not mean that they were either necessarily divergent or discordant. They both, after all, exhibited "essential features of modernity," however re-stylized. That differences in style were not formally specified or reconciled, however, left the research team in the purgatorial position of not understanding how to appreciate and thereby operationalize or embody varying strategies and priorities. This, in turn, intensified the affect of discomfort concerning what the facility was really all about, how its work would be represented, and which imagined future would ultimately provide the criteria of success.

CHAPTER 6

Human Practices Inquiry: Deploying Monsters-Machines-Mechanisms

> *I think the modern age of the history of truth begins when knowledge itself and knowledge alone gives access to the truth. That is to say, it is when the philosopher (or the scientist, or simply someone who seeks the truth) can recognize the truth and have access to it in himself and solely through his activity of knowing, without anything else being demanded of him and without him having to change or alter his being as a subject.*
>
> —Michel Foucault[215]

On Thursday May 20, 2010, a team of researchers at the J. Craig Venter Institute (JCVI) led by Dan Gibson published a paper in the online edition of *Science* reporting that they had successfully synthesized, assembled, transplanted and activated the entire genome of a bacterium.[216] The work received widespread attention. Such attention is hardly surprising given that this paper announced the crossing of a major threshold of the Venter Institute's highly visible research portfolio. Specifically, Gibson *et al*. had produced a phylogenically distinct form of life—a cell genetically discontinuous from its parent cells. Their abstract read:

> We report the design, synthesis, and assembly of the 1.08–mega–base pair *Mycoplasma mycoides* JCVI-syn1.0 genome starting from digitized genome sequence information and its transplantation into a *M. capricolum* recipient cell to create new *M. mycoides* cells that are controlled only by the synthetic chromosome. The only DNA in the cells is the designed synthetic DNA sequence, including "watermark" sequences and other designed gene deletions and polymorphisms, and mutations acquired during the building process. The new cells have expected phenotypic properties and are capable of continuous self-replication.[217]

As the abstract indirectly indicates, the researchers appreciated—and provided a framing of—the broader importance of their work. The JCVI website expanded these indirect indications, introducing what would become the Institute's principle talking points: "While this first construct—dubbed *M. mycoides* JCVI-syn1.0—is a proof of concept, the tools and technologies developed to create this cell hold great promise for application in so many critical areas. The ability to routinely write the software of life will usher in a new era in science, and with it, new products and applications such as advanced biofuels, clean water technology, and new vaccines and medicines." Three crucial elements: proof of concept, digital design/software of life, and genomic novelty. All of which, not surprisingly, are taken to point toward a better—which is to say more instrumentally managed—biological future.

The publication of the JCVI paper produced immediate political and material ramifications. In the days that followed, the Energy and Commerce sub-committee of the US

House of Representatives held its first hearings on synthetic biology; within six weeks the US Presidential Commission or the Study of Bioethical Issues held its first hearings, hearings likewise centered on synthetic biology. And, in the days that followed, JCVI announced tens of millions of dollars in new investment partnerships; similar announcements were soon made by other biotech companies describing their work as synthetic biology. In this regard the Venter announcement contributed to a more general re-figuration of the worth of synthetic biology in which the promise of commercial prosperity was slowly moving to the foreground as claims about solving real-world problems that had once been articulated in something of a moral register were backgrounded.

Equally important, the paper opened the possibility of a reconfiguration of moral-theological imaginations concerning the status and identity of living systems as technological artifacts and the relation of biological artisans to those artifacts. That this *possible* reconfiguration has failed to *actualize*, that a reconfiguration has in fact not taken place is, I will argue in this chapter, ethically significant. It is significant in that although the JCVI announcement had the effect of determining what would become expert talking points, it failed to unsettle underlying assumptions concerning the ethical *status* of synthetic biology. This failure, as I will describe, is hardly surprising. Nonetheless, the fact that shifts on a scientific and discursive register did not affect shifts in an ethical register proved to be consequential for the governing of synthetic biology generally and for the BIOFAB in particular.

FROM VITALISM TO WHOLE-GENOME ENGINEERING

In the same week as the Gibson *et al*. paper was released online, the journal *Nature* published selection of responses solicited from a number of leading biologists, as well as from one philosopher and one bioethicist. Assessments differed as to what JCVI's accomplishment actually portends and why specialists and non-specialists should or should not care. Among those offering expert opinions was Harvard Professor and SynBERC PI George Church. In a fashion similar to the other responding biologists, Church congratulated the JCVI team, but underscored that this was not a game changing moment in synthetic biology. He stressed that the JCVI work was a *technical* and not *biological* breakthrough. And, in what read as an effort to preempt those who might over-interpret the significance of the Venter Institute's research, Church underscored that Gibson's team had not "created 'new life' and tested vitalism."[218]

Arthur Caplan, the much quoted University of Pennsylvania bioethicist, picked up a similar theme, but stressed a quite different point. Whatever Gibson *et al*. achieved technically, its ethical significance was precisely that they had, in Caplan's view, eliminated the notion of vitalism once and for all. Vitalism, according to Caplan, is the view which holds that "life could never be explained simply mechanistically," but must be understood by reference to "a vital force" which is an "ineffable current distinguishing the living from the inorganic."[219] Citing a litany of positions which he takes to be vitalist, from Henri Bergson and Louis Pasteur to "Christianity, Islam and Judaism," Caplan concludes: "All of these deeply entrenched metaphysical views are cast into doubt by the demonstration that life can be created from non-living parts, albeit those harvested from a cell." In this light, Venter is taken to be on par with the historically momentous and iconic figures such as Galileo and Darwin, in that the work of his Institute "would seem to extinguish the argument that life requires a special force or power to exist." Offering one last burst of high-praise: "In my view, this makes [JCVI's accomplishment] one of the most important scientific achievements in the history of mankind."

Where Church preempted criticisms from "vitalism" by stressing that JCVI had not actually "created life" and hence did not (or at least should not) really impact either the biological or moral imagination, Caplan argued in another direction, that JCVI *had* actually created life. The key is that they had done so in such a way as to demonstrate that life did not entail anything that might be taken as metaphysically special. In this respect the impact on both the biological and moral imaginations—and particularly on the perceived relation between them—was altogether central.

Reactions within the BIOFAB resonated variously with the emphases laid down in the *Science* commentaries. At the Friday meeting a day after JCVI's publication the BIOFAB team put the question to Arkin: what did he make of the Venter Institute's latest publication? Endy was absent from the meeting. The following Wednesday, however, he was scheduled to testify to the US Congress about the JCVI work and synthetic biology more generally; we would learn his views, or at least his publically formulated views, then. Arkin admitted that over the last day he had found himself arguing both sides of things—to those who seemed overly impressed he deflated, to those who seemed less than fully appreciative he talked things up. In all, however, he thought that the JCVI work should be taken seriously as a major threshold, and not, as some of his colleagues had suggested, only a kind of technological next-step in the development of synthesis. To be sure, the technical difficulty of what had been done could not be taken for granted; the ability to assemble a whole synthesized genome in a new host cell displays extraordinary ingenuity. The significance however, in his view, lay precisely in the notion and possibility of phylogenic discontinuity. "For a long time we've been thinking that what makes an organism phylogenically distinctive is its genetic inheritance. With JCVI's *Mycoplasma mycoides* bacterium, running on their synthetic JCVI-syn1.0 genome, phylogenics of an older sort shows its limitations."

Arkin held out his hand in profile. He asked us to imagine his hand as a branch on the *Mycoplama* bacterial family tree. Grabbing each of his fingers in turn, "imagine that each of these is a particular strain. Each is closely related to the others, but each is distinctive in some important respects." "Here's what JCVI did," he told us. Touching his first finger with the first finger of his other hand he explained that the Venter group had started out with one kind of bacterium. They sequenced the DNA in the genome of that bacterium, and spent a number of years trying to work out what elements it could functionally do without—steps toward a stripped down "minimal genome." Then they spent another significant period of time developing an *in vivo* method for assembling that minimized genome in yeast. Having done that—having chemically synthesized the basic oligos and inserted them into a yeast host, they were able to reconstruct the entire genome. This genome—the JCVI-syn1.0—they then transplanted into *Mycoplasma mycoides*, from which they had removed the native genome. After considerable trouble, they were able to get this genome to "boot up," as Venter would describe it during congressional and bioethical hearings.

"The synthesized genome originally taken from this bacterium" still touching his first finger, "was placed in this bacterium," touching his little finger. Within several populations doublings—"from about six to twelve"—the synthesized genome from bacterium will have replaced all of the molecules in the host cell. That means that within a very small number of population doublings, the cells resembled the first bacterium more than the second. The synthetic genome had essentially produced a new cell.

Arkin's framing anticipated the subtext of several highly visible and subsequently publicized exchanges between Venter, his colleagues, and critics in the following days. Surprisingly, colleagues and detractors alike would say that Gibson's team did not really "synthesize life," as many headlines had trumpeted. For the colleagues' part, the deflation seemed to be a way of heading off "over reactions." For critics (of which there were surprisingly few, as I will discuss in the next section), there seemed to be a impulse to steer things away from the question of whether or not synthetic biologists were challenging vitalism (contra Caplan). Venter's response to these reactions was noticeably coy. On the one side, he did not directly admit to having created synthetic life. A host cell had indeed been used, and the claim to have created life might have stirred more of a reaction than even Venter was looking for. Yet Venter declined to say that they had not created synthetic life. Rather, he simply repeated his version of what, technically, they had accomplished. He insisted both to congress and to the Presidential Commission that JCVI scientists had synthesized a genome which now ran the expression "machinery" of the cell they had put it into—a non-native cell that subsequently had each of its molecules replaced by "their genome." In a different exchange he used a metaphor from computer programming, insisting that the genome is the software that (eventually) builds its own hardware. Admitting that they started with an existing cell, but insisted that the molecules in this cell were replaced by the ones made from their genome. "No doubt," he added, "someday we'll figure out how to assemble the original host out of chemicals as well." Then, presumably, he could say that they had indeed created synthetic life. In any event, the point that Arkin wanted to press was that they had opened the door, technically speaking, to the need to formulate new ways of imagining biological relatedness—phylogenic discontinuity.

Endy never actually commented on the Venter work in a direct fashion to the BIOFAB team, which is somewhat surprising given that Endy was asked to testify on the significance of the Venter work before both the US Congress' Energy and Economics sub-committee and the Presidential Commission for the Study of Bioethical Issues. These public and formal statements, however, had an indirect "rebound effect" on the conduct and formulation of the BIOFAB's work. The Congressional hearings took place on the Wednesday following the publication of the JCVI paper. Endy was one of four biologists, presenting with Venter, Keasling, and Anthony Fauci, Director of the National Institute of Allergy and Infectious Disease. The line-up of testimonies reflected a clear hierarchy. Venter was the star; the hearings were held to discuss his work primarily, and synthetic biology more generally as a kind of after-thought. Keasling was there as the expert on synthetic biology and biofuels, and stood in as a kind of representative of the commercial potential of synthetic biology. And Fauci, an articulate and practiced performer, represented the government's interests in funding and contributing to new scientific research. Endy, although lacking the status of the other biologists, was nonetheless able to effectively position himself as something like the spokesperson for synthetic biology, per se.

Endy focused his short testimony (the expert witnesses are only given seven minutes to present) on what he framed as the key incapacity on the part of synthetic biologists. Although synthetic biologists are able to synthesize significant quantities of DNA, and even assemble whole-genomes, they are not yet able to design new genetic functions at that scale. At the Presidential Commission hearings Endy introduced the analogy of the printing press—it's one thing to print a book; it's quite another thing to write one. Endy had made this point on any number of other occasions, including in formulating the rationale for the BIOFAB's funding. Articulated in this setting, however, Endy's focus on the "biotechnology integration gap" (as he called it) ramified differently. By positioning the Venter Institute's work as exemplary not of the

desired next-step in synthetic biology, but as an exhibit of synthetic biology's chief incapacity Endy was able to leverage the success and profile of the Venter announcement in the name of a different set of strategic priorities. These priorities, of course, turned on the need to develop a technology platform for the design of functionality in genetic expression. What remained tacit in Endy's congressional testimony, but which he named indirectly in his testimony to the Presidential Commission, was that the BIOFAB was positioned as a first institutional attempt to formulate the terms of such a technology platform. Importantly, Endy's testimonies stressed the need for national initiatives, on the order of the government funded initiatives in nanotechnology, but coordinated in a fashion similar to the genome sequencing projects, to overcome this gap between capabilities in synthesis and incapacities in design. It is hardly surprising, in this light, that Endy's framing of the BIOFAB from this point forward, would no longer emphasize the themes of community support or the fabrication of standardized parts—though these remained elements of his narrative. The emphasis, rather, would be placed on the need and possibility of whole-genome engineering as a parts-based design problem. Or, using the analogy which had been activated in the lead up to the pilot project, what the BIOFAB was really about was the production of an expression operating system.

Niklas Luhmann demonstrated a decade ago that the role and function of experts is to establish and circulate talking points.[220] The *way* in which these talking points were picked up and extended, however, bears examination. The Venter Institute talking points cast the significance of the work in terms of the kinds of *artifacts* which the JCVI technology platform is capable of producing. These taking the talking points as key topics, thematized them in terms of the capabilities of the *artisans*. According to Church: we should not worry, because the JCVI biologists are not able to make life. Caplan: now that JCVI has done what it has done, our ability to think about life and its metaphysical status has been irrevocably changed. Arkin: the JCVI scientists were able to re-imagine the possible grounds of relatedness in biology beyond genetic continuity. And Endy: the JCVI biologists are not as capable as we might have hoped; for all their prowess we still lack the ability to design the genetic machinery that runs the cell.

To put this differently and to underscore a consequential point: the responses to JCVI's work, in different ways, exemplified a crucial ethical lesson that Georges Canguilhem had taught us fifty years ago: that the status and significance of fabricated objects lies as much in the maker as it does the object made. Crucially, this relation is not just one of responsibility, understood in a juridical sense. Rather, it is a question of ethical entailments: how does the production of certain kinds of biological objects require the development or neglect of certain capacities, and how does the production of certain object serve as a vector for constituting capacities? To the extent that Canguilhem's lesson is taken seriously, a principal ethical challenge lies in understanding the precise character of the relation between the bioengineer and the engineered artifact.

Canguilhem's lesson is all the more important—and this is why I raise it here—when we consider that as discussions of the ethical significance of Venter's work began to ramify in the wake of the JCVI announcement, his important lesson effectively began to fade. Assessments of the significance of JCVI's work centered predominantly on the object side of things: is the new bacterium safe, will it advance industry, can it be used to speed up or lower the cost of producing medicines, what might it offer in terms of environmental remediation, and so on. Such questions certainly cannot be taken for granted. But in their place, the question of which capabilities are actually being cultivated on the part of the biologists doing the work, how those capabilities can

be connected to questions of virtue, and therefore which relations, techniques, and experiences are being made to be especially crucial to the development of synthetic biology, were marginalized, or, at least marginal.

MONSTERS. EVALUATING MORPHOLOGICAL DIVERGENCE

Marginal but not altogether absent. Of responses that did in fact center on the ethical status of the biological artisan in relation to the biological artifact, some were typically polemic. Bishop Domenico Mogavero of Mazara del Vallo, chairman of the Italian bishops' legal affairs committee, expressed alarm. Bishop Mogavero was quoted as saying that the Venter Institute's work "is a potential time bomb, a dangerous double-edged sword for which it is impossible to imagine the consequences."[221] More forceful still was his admonition that "Pretending to be God and parroting his power of creation is an enormous risk that can plunge men into barbarity." The tenor of Mogavero's response was neither shocking nor surprising. Warnings against violating nature or playing god became normal in polemics concerning recombinant DNA technologies, the genome sequencing projects, and embryonic stem cell research. However familiar the polemics, the point is that Mogavero foregrounded the question of how the ethical status of the biological artisan and biological artifacts are mutually determinative.

Although the tone and emphasis of Mogavero's comments were not surprising, what should have been surprising is the fact that his were well outside the norm. Indeed, the official response from the Vatican's Pontifical Academy for Life emphasized that as long as JCVI's synthetic cells were "used toward the good, to treat pathologies, we can only be positive about their development."[222] Nonetheless the official Vatican stance might be characterized as somewhat untroubled and prudential. The undertone was: let's wait and see how these technologies are used. Noticeably absent is any commentary on the status or role of the biologist and the ethics of designing or engineering new biological organisms.

Considerably less polemic than the comments made by Bishop Mogavero was the response to Venter's work offered by philosopher Paul Wolpe at the first meeting of the Presidential Commission. I will return to Wolpe's testimony in the following chapters, but will emphasize one important point here. Wolpe's response was thematically similar to the Bishop's in that he foregrounded and emphasized the ethical importance of considering the capabilities, status, and practices of the biologists engineering living systems in relation to the living systems produced by biological engineering. We might say that whereas Mogavero emphasized the potential *monstrosity* of what was being undertaken by JCVI and other synthetic biologists, Wolpe emphasized the question of the ethical significance of the production of *monsters*. Wolpe's testimony posed the question of what lessons might be drawn for synthetic biology from the Jewish story of the creation of the Golem and Christian (Wolpe's designation) story of the creation of Frankenstein's monster. Crucially, he stressed, the ethical posture of Rabbi Loew in the story of the golem is one of humility and care; the ethical posture of Dr. Frankenstein is one of ambition and risk-taking. Wolpe connected the golem and Frankenstein stories to synthetic biology in order to better pose the question of how creating biological "monsters" might or might not be monstrous. In doing so, Wolpe foregrounded possible connections between the ethical status of the bioengineer and the ethical status of objects of biological engineering.

Wolpe's introduction of the two stories was articulate, appeared to well received, and was responded to by the Presidential Commission members as timely (though the same points had already been made in more extended reflections on synthetic biology by Laurie Zoloth and van

den Belt[223]). His presentation, however, did not cohere with the predominant ethical talking point. Given the legacy of the debates over GMOs, genomic patrimony, and embryonic stem cell research, and given that JCVI itself emphasized as a double achievement the production of phylogenically discontinuous organisms and the computer-aided mediation of non-living to living matter, it is actually quite remarkable that the themes of the monstrous and monstrosity—i.e. themes concerning the relation of the creation of "unnatural" entities to the morally inadmissible—actually *did not* figure significantly in discussions of the ethical significance of the Venter Institute's work. As one illustration of the fact that this relative absence is indeed remarkable, we might consider that when the Presidential Commission for the Study of Bioethical Issues released its final report on synthetic biology, it strongly cautioned that sound ethical debate must move beyond the tropes of "playing god." This despite the fact that few critics had actually responded to the Venter work in those terms. The relative absence of the "playing god" responses, set against the expectation of such responses might be taken as nothing more than a curiosity. It is, however, I would argue, significant because the failure of "the monstrous and monstrosity" to figure more prominently in responses to JCVI's work marks out what can be taken as a more general failure: the failure to seriously engage the question of the possible relations between the ethical status of the bioengineer and engineered.

In anticipation of the publication of the JCVI paper a reporter from *Science* contacted anthropologist Paul Rabinow to get his response. The long and detailed conversation resulted in a single but salient quote in the published article: "this experiment will certainly reconfigure the ethical imagination."[224] As Rabinow had explained in detail elsewhere, in the wake of the genome sequencing projects, people around the world began to think of "genomes" as holding definitive secrets about the identity of themselves, their plants, and their food;[225] the JCVI program indicated one way in which synthetic biology re-imagines biological life and identity on different grounds. The reporter may have quoted the salient point of the conversation with Rabinow, but the import of his statement was quickly lost in the article, as attention turned to matters of safety, security, and intellectual property.

I want to be clear: the question of the ethical imagination was posed. It simply was not been taken up in any serious as part of the expert talking points about the ethical significance of synthetic biology. Several prominent biologists clearly anticipated a negative reaction in the register of the ethical imagination. It was expected that civil society organizations, religious communities, and others would repudiate synthetic biology in the name of the inviolability of life, the hubris of manipulating living systems, and so forth. These reactions did not figure in the conversation, and the preemptive guard against them more or less covered the fact that there simply were not strong or sustained negative reactions to the Venter work formulated along these lines.

Why is it significant that themes concerning the ethical status of biologists and their relation to the creation of new biological objects, themes exemplified in the problem of "the monstrous and monstrosity," did not figure more prominently? The Venter work highlighted several elements of synthetic biology that, understood with some precision, at least invite reconsideration of older moral-theological questions and thereby might provoke some serious engagement with how synthetic biology might (or might not) reconfigure our ethical imaginations. At the Presidential Commission hearings, philosopher and long-time bioethicist Allen Buchanan was the first to directly attack the tropes of "playing god" and "violating nature." His PowerPoint presentation included a slide which, in the name of rational discourse,

specifically ruled such questions out of bounds. One need support these tropes to be troubled by the questions begged by Buchanan's attempt to circumscribe the range of themes which can be taken as rational and therefore legitimate. The first question is: who wants to activate these tropes? As I've insisted, it is a social fact that synthetic biology is not actually being represented using these tropes by either its critics or supporters. The second question is: what might be lost in Buchanan's effort to police the limits of permissible topics? I suggest that one loss might be any serious consideration of the relation of the ethical status and relation of biologists to their work.

Some questions concerning the instrumental value and possible material dangers of synthetic biology have been foregrounded in ethical deliberations of synthetic biology. Indeed, they have sometimes been treated as though they are the only serious considerations. One ethical demand of the day, I would suggest, consists in making room for other questions. Those reflecting seriously on the ethics of synthetic biology should make analytic distinctions that may help to formulate more precisely what it is that synthetic biologists are and are not yet bringing into the world, and how such efforts might be evaluated. Such precision, it seemed clear to me at the time, would help specify the limitations and possibilities of the BIOFAB's program understood technically, vocationally, and ethically.

One way to proceed is to examine developments in synthetic biology using notions of "monstrosity and the monstrous." Such an exercise is useful in the first place because, as Canguilhem has shown, it concerns precisely the question of the ethical significance of "morphological divergence," what Arkin termed "phylogenic discontinuity." It is useful in the second place in that it provides a genealogical pathway within which JCVI's work (and the work of synthetic biology) can fruitfully be placed. If it is the case that the instrumental questions of amelioration, safety, and prosperity have come to dominate discourse about the ethical significance of synthetic biology, this may be due in part because the work has effectively been placed outside of the genealogy which Canguilhem outlines. The question of monstrosity and the monstrous may strike the contemporary ear as anachronistic and thereby irrelevant. Nonetheless, as a number of contemporary thinkers have argued, it may yet be instructive. What does the creation of the organisms entail in terms of the ethical formation, stance, and responsibility of their creators? And to what extent might synthetic biology reactivate and recalibrate themes of the monstrous and of monstrosity? And why should we care?

Canguilhem writes: "What makes the value of living beings… is their consistency as a species," the fact that "the same engenders the same."[226] Gibson *et al*., in the first line of the abstract, stress that the bacterium they have created is in a discontinuous relation with its own species: "We report the design, synthesis, and assembly of the 1.08–mega–base pair *Mycoplasma mycoides* JCVI-syn1.0 genome starting from digitized genome sequence information and its transplantation into a *M. capricolum* recipient cell to create new *M. mycoides* cells that are controlled only by the synthetic chromosome."[227] Their work, read in light of Canguilhem's distinctions, would seem to introduce a fundamental inversion of, and challenge to, this account of the valuation living beings.

Canguilhem, specifying why consistency as a species should count so highly, states: "Slicing through the vicissitudes of the material environment, consistency expresses itself through the resistance to deformation and a struggle for the integrity of form." The value of life adheres in the possibility of retaining its integrity of form as a species despite the fact that in the case of any one organism the vicissitudes of the environment might prove overwhelming. And thus, introducing one of the key terms of his essay, Canguilhem explains the term *monster*

signifies not only a living being of reduced value, also, and more importantly, "it is a living being whose value is to be a counterpoint." The reason the monster is a counterpoint to the value of other living beings is that its existence reveals the precarious contingency of life as it is otherwise formed and experienced. "By revealing the precariousness of the stability to which life has habituated us," Canguilhem proposes, "the monster bestows upon the repetition of species, upon morphological regularity, and upon successful structuration a value all the more eminent in that we can now grasp their contingency." The crucial conclusion that he draws from this is that the counter-value to life is not death. The counter-value, rather, is monstrosity.[228]

So, we can ask: is JCVI's new organism, "the new *M. mycoides*" a monster, and does it exhibit the counter-value of monstrosity by revealing the contingency and precariousness of the stability of life? Strictly speaking, and following Canguilhem's definitions closer, the answer to this question would seem to be yes, in which case Wolpe's use of the Golem and Frankenstein stories would seem to be appropriate: using reworked elements of two different species of bacteria, JCVI produced a third which is the direct phylogenic progeny of neither of the first two. But the answer is less obvious when we consider that precariousness and contingency, far from being framed as counter-values to life, have, in fact, been figured as the very premises on the basis of which work in synthetic biology is being undertaken at all.

It is in foregrounding the proposition that phenotypic stability and continuity are only a habit and not a law that the possibility of remaking living systems is opened up. This contingency is what allows for the proposition, made by JCVI and most everyone else connected to synthetic biology: that living systems, once cast in an engineering frame, are ideally suited as technological platforms for address pressing real-world problems such as the production of fuels, and therefore also promise to be the basis not only for the expansion of the biotechnology industry, but for the fostering of a new "bioeconomy." In this light, it could be argued that far from producing that which is a counter-value to life, i.e. a monster, JCVI successfully established a new platform for the generation of those instrumental ends which are most highly valued: "a new era in science, and with it, new products and applications such as advanced biofuels, clean water technology, and new vaccines and medicines."[229] And this instrumental value—the ability to write the software of life, as the analogy would have it—turns on the disruption of morphological continuity, either by habit or by law. It turns on the assumption of that contingency as the nature of how living systems work. Or, more put more precisely, the assumption of that contingency as the nature of how living systems can be made to work. Which, of course, is a now an old evolutionary assumption.

These revaluations may not be altogether dissonant with Canguilhem's analysis. After all, he explains that the fearsomeness of the monster is precisely that it shows us something that had been true all along: the continuity of species is only a form of reassurance. Such continuity covers over the fact of contingency. But this contingency nonetheless, as Canguilhem shows us, has for much of the history of European Christian, philosophic, and popular thought, constituted a negative value in that it discloses the fact that we humans cannot persist as ourselves over time without the capacity to resist the vicissitudes of life's milieus. JCVI's work thus strikes a contrast. And their own framing of that work takes it for granted that a principle value of living systems is actually their plasticity and their relation of non-dependence on the parent-progeny relation. Designed morphological divergence opens up new possibilities for leveraging the capacities of synthetic DNA to make living things better and to make better living things.

The flexibility of living systems to become other than they are has become such an established norm of biological practice and value of biotechnical industrialization, that the term monster grates on the contemporary scientific ear. To pose the question of the monstrous might be taken to be out of bounds of reason. There is now a long history, after all, of removing living cells from the time and space of natural milieu and engineering them to perform just the right way under just the right conditions have long been a familiar technology of the life sciences. JCVI's promise of instrumental gain connected to the decoupling of a cell from its own parentage, or from any parentage for that matter, only extends and reinforces what most biologists already take to be the case about the evolutionary flexibility of living systems. Contingency, synthetic biologists might argue, thus does not reveal a monstrosity, but rather it opens a horizon of experimental possibility. As Arkin put it, rebuffing those who might be unsettled by JCVI's experiments: "all they've shown us is how nature works."

Strictly speaking, of course, JCVI has not just shown us the way nature works; they have shown us one way in which it can be made to work. JCVI confirms Canguilhem's insight that species continuity across the vicissitudes of the environment is a habit and a habituation turned by observers into a law. In the work of synthetic biology, the contingency of living systems is rendered as a collection of malleable design elements within a laboratory space is being made a habit and amenability of those systems to being used to solve "real-world" problems is being made a matter of habituation. And although these habits and habituations are matters of technique and technology, it bears keeping in mind that habit and habituation are *practice* terms, taken in the ethical and pedagogical sense of that word. It reasonably follows, then, that neither JCVI's efforts, nor the efforts of the researchers at the BIOFAB need to be understood as exhibiting what living systems do. Rather, these efforts indicate what living elements and their milieus are capable of being made to do. These biological artifacts—whether JCVI's bacteria or the BIOFAB's EOU—behave the way they do because they have been made behave in these ways. All of which might seem an obvious point to make, except that it underscores a key aspect of synthetic biology: taking up a design and engineering stance toward biological systems characterized by an orientation to their properties of contingency requires the cultivation of certain dispositions; and the cultivation of certain dispositions allows for the production of certain artifacts. Evelyn Fox Keller makes a similar point when she highlights the epistemological stakes of synthetic biology's attention to "parts, devises, and systems." Here I want to highlight the ethical stakes of this same enterprise.

So why introduce terms like "monster" or "monstrosity." If the morphological and functional flexibility of living systems is no longer a source of ethical distress, why propose a term so jarring, a term which strikes moderns as perhaps too inflammatory, too resonant with just those sorts of polemic critiques that biology needs to avoid if it is going to remain firmly a matter of Science and not slip backward into irrationality? The assumption that living systems are characterized by plasticity, and that neither their form nor function is overly determined, has been with us now, Canguilhem reminds us, since the formalization of biology and teratology as experimental sciences in the 19th century. And the assumption of plasticity and efforts to design technical means of experimenting with the limitations and creative possibilities connected to this plasticity have become an increasingly important norm of scientific practice. With the 19th century efforts to formulate scientific explanations of morphological divergence, the notion of monstrosity began to be de-coupled from the physically monstrous. Deformation, after all, can scarcely be held to be a monstrosity if it is just the interplay (however tragic or promising the results) of natural forces. Moreover, with the hope and promise of being able to control the

plasticity of living systems—a hope made manifest at least since Loeb's artificially induced teratomas—a monstrous form may, in fact, just be the normal form of some new possibility. For almost a century biological materials have been cultivated to serve a seemingly limitless array of experimental and industrial needs for seventy-five years.[230] Indeed, Canguilhem recognized that since the 19th century, "monstrosity appears to have revealed the secret of its causes and laws." The monster is no longer a monstrosity, but only the normal is an attenuated form. Henceforth, the transparency of monstrosity to scientific thought cuts monstrosity off from any relation to the monstrous." And, I might add, it sets the groundwork for cutting off the question of the ethical status of biological practice as having any immanent relation to the creation of new biological forms.

It was within an older theological imaginary, Canguilhem reminds us, that the monstrous and monstrosity were integrally linked. The monstrous, the existence of the monster, did not only constitute the fastening of the fantastical and the morphologically distorted. The monster also, and perhaps more importantly, constituted the ethical and spiritual form of deviations from an otherwise ordered cosmos. For the medieval theologian, following an Augustinian framing, the cosmos was the actuality of the God's providence for a finite creation in its history. Order constituted the very possibility of being; disorder was thus its negative value. Said differently, the actualization of disorder in material form can only be the tragic effects brought about by the willfulness of the created soul, the way of the flesh, or, cast more in more sinister terms, the work of the devil. Or, to use a somewhat more technical vocabulary, monsters were disruptions of the teleological impulse characteristic of the created and ordered cosmos. The point is that the cosmos has an order, and that order is given providentially. Disorder, then, carries juridical weight and juridical consequence. And hence the vocabulary of the monstrous and monstrosity. Monstrosity, after all, is not just a term indicating a formation deviating from a norm, but also a juridical term indicating a deviation from the law. We need not recapitulate theories of the disintegration of the notion of the cosmos and the politico-theological constitution of the universe to have a clear sense of how far the presumption of evolutionary plasticity and functional contingency are from an earlier scientific imaginary. Hence we don't need much persuasion to be convinced that the fading of the terms monstrous and monstrosity from view is only to be expected, and that their invocation constitutes an anachronism. The JCVI experiments in this sense, it could be argued, don't mark a return to the monstrous. They are rather a kind of exultant threshold of actualization of a long-present scientific impulse. The abnormal, to use Canguilhem's terms, has become the possibility of re-normalization.

The presumption of the plasticity of form and the contingency of function as norms of experimental practice, do of course, remain dissonant with certain communities and their moral imaginaries. The opening line of Canguilhem's essay that "The existence of monsters calls into question the capacity of life to teach us order," might seem less opaque when we keep in mind the now decade long debates over stem cell research. The Roman Catholic position on the status of the embryo and hence human embryonic stem cell research, for example, turns on the notion that the embryo is a potential person and that this potentiality is basic to the ordered biological nature of the developing blastocyst. The embryo, the Vatican has argued, is genetically ordered to a particular outcome—becoming a baby—and hence disrupting that outcome is ethically illicit. For the Vatican, the fact that the removal of the embryo from the body, the disaggregation of the cells of the early embryo, the placing of those cells onto media all combine to allow for biological possibilities that were never present until such experimentation was undertaken in no

way changes the fact that an order-of-things has been disordered. To quote Canguilhem once again, we want to have confidence that in life "the same engenders the same."

The same engendering the same is biologically familiar. Human gametes will produce human children. This familiarity establishes a confidence in life, a confidence noted earlier: that life, despite the vicissitudes of the physical milieu, is perfectly capable enduring as long as species remain consistent. Morphological divergence, in this light, is a harbinger of "the negation of the living by the nonviable." When the same engenders the other something monstrous has occurred insofar as a certain nonviability is introduced. This, Canguilhem proposes, is what links the monstrous to monstrosity, producing a "radical fear." "Why radical fear," Canguilhem asks. "Because we are living beings, real effects of the laws of life, and ourselves possible sources of life in our turn. A failure of life is a double concern to us, for such a failure could touch us or could come from us. It is only because we humans are living beings that a morphological failure is, to our living eyes, a monster."[231] The monster, the same engendering the other is a monstrosity precisely in that discloses the constant possibility that life may be "tripped up" at any moment as it strives to make its way successfully across its milieu.

But can the synthetic biologists generally, and perhaps the work of the JCVI in particular, really be considered monstrous on these grounds? As I have already noted, the value of living beings in synthetic biology lies precisely in their morphological contingency. The existential connection between the monstrous and monstrosity a connection made on the basis of our familiarity with the same engendering the same, is backgrounded in favor of a promised future in which "living systems are ideally suited to solve the world's most pressing problems." Moreover, the Venter Institute's paper stresses precisely that viability and not nonviablility is what makes their designed JCVI-syn1.0 genome and the new *M. mycoides* bacterium so attractive. The new *M. mycoides* bacterium may indeed exemplify the same engendering the other. But more important to the JCVI biologist is that the other is subsequently capable of producing the same. If the monstrous is the "vital counter-value" because it exposes the possibility of species failure and therefore the failure of living beings to inhabit their physical milieu, then JCVI's work appears free from the condemnation of being a monster on these grounds. JCVI's announcement, after all, not only emphasized that the only genomic activity in their cell was the activity driven by their synthesized genome, they also underscored that the new cells "are capable of continuous self-replication." Life's continuity can just as easily be ensured by the other generating the same as the same generating the same.

It turns out, perhaps not surprisingly, that for synthetic biology, whether the work at JCVI, the BIOFAB, SynBERC, or any other number of labs, morphological and functional contingent, although emphasized and foregrounded, is not the only value in play. In fact, the valorization that Canguilhem stresses, namely that the value of life "adheres in the possibility of retaining its integrity of form as a species," is equally prized if not equally advertised. The worth of the Amyris platform technology, to pick just one example, lies not only in the fact that they have been able to reconstruct in yeast a metabolic pathway which otherwise only exists in the bark of a Chinese Yew tree. It also lies in the fact that the cells within which they have engineered those pathways will subsequently "slice through the vicissitudes of the material environment," and express a species consistency "through the resistance to deformation and a struggle for the integrity of form."[232]

This consistency is crucial. The proposed value of the bio-economy is precisely that it is an economy of scale. Metabolic engineers are promising to produce new living forms that exhibit

the self-replicating properties of all living forms. This means, synthetic biologists should be able to scale the production of morphologically and functionally designed organisms by simply producing strains of these organisms that can survive in ever larger fermentation tanks. And indeed, to stress the point further, the precise problem that synthetic biologists face in the scalable production of designed systems is the fact that within the controlled settings of industrial production (think Canguilhem's "privileged milieu") there is a constant threat that the colony of designed cells will mutate and evolve. Which is another way of saying that once contingency has been foregrounded and leveraged at a design stage (i.e. "made the value of living beings") the value of species consistency once again is made predominant.

The positive value of life currently being formulated in synthetic biology thus consists in a set of strategically managed trade-offs between contingency and control at the design phase, and species consistency in the downstream functioning of the designed biological objects. Living beings, to repeat what has become a truism of the philosophy of bioengineering, are being treated as technologies. The subtly is that on the one side, the positive value of life lies precisely in the fact that it can be treated and imagined as though it were not constrained by prior vital forms: living systems rendered in the vocabulary of motifs, scaffolds, parts, devices, cassettes, etc. On the other side, however, one of the principle reasons life-as-engineering-toolkit is attractive is that living systems, qua living systems, can do things that non-living systems cannot do, such as self-replicate, respond, and adapt. Hence a kind of double motion from life imagined as plastic and pliable and life imagined as steady and reliable.

Put differently, imagined as a technology, life does not need to flourish. It only needs to continuously self-replicate in such a way that a specified set of functions can be designed and activated in response to a specified problem. The living beings produced, thus need to be only so vital and no more. The challenge is to achieve the ability to limit and manage vital processes, to design genetic systems so as to leverage the attributes of the vital, while operating with the regularity characteristic of non-living mechanizations. The goal is for the engineer to be able to design the engineered in such a way that its mode of being expresses the characteristics of both the vital and the non-vital. The apparent difficulties in achieving this goal delimited and managed vitality reinforce the tendency to reduce the ethics of synthetic biology to questions of environmental safety and bio-security. The "radical fear" produced by the Venter Institute's announcement (to use Canguilhem's phrase) did not issue from a sense of the *monstrous* as the negative counter-value to life. Rather, it issues precisely by the sense that such an artifact might cause *death*. Canguilhem's pair life-as-consistency/monstrous has become the pair life-as-contingency/death. Canguilhem stresses quite insistently that when dealing with the monstrous and monstrosity the counter value to life is not death but rather is the monster—a creatures whose mode of being exposes the fact of life's contingency and constant possibility of failure. With synthetic biology contingency is premise and discontinuity the goal. Death, and not the monstrous, is the counter-value to the normalization of the plasticity of life.

A triple fact: synthetic biologists are trying to produce biological materials which are other-than-the-same, in the sense that elements can be disaggregated from living systems, refined, and recombined in such a way that the designed outcome can subsequently function and even self-replicate in a reliable fashion. In view of death as the counter-value to these functionally specified artifacts, an additional aim is to produce engineered organisms in such a way that they won't actually be able to "slice through the vicissitudes" of the material environment. Rather, they should only be able to survive where the material environment has no

vicissitudes. Or, to put it another way, what counts as the positive value of life-as-technology in synthetic biology is precisely that which might in other places and under other circumstances count as the monstrous. In any case, what we can be certain of in view of all of this is that synthetic biology helps bring to actuality a new norm for the bio-technical in which the monstrous and the normal cannot be so easily distinguished. The question that must nonetheless be asked is: what kind of technology is this, and what is its relation to the question of the ethical significance of the relation between the engineer and the engineered, where this chapter began?

MACHINES. ARTIFICIAL CONSTRUCTS

A ready answer might be given by JCVI's own analogical vocabulary: that they have made a genomic machine. JCVI refers to the artifacts they have made as "the software of life." And in Venter's prepared testimonies to both the US Congress and the Presidential Commission he insisted that the real power of their work turns on the fact that "the genome is software that writes its own hardware." Such analogies to machines, however, are elusive and unhelpful. They are elusive in that they usually mistake an analogy for an identity. The suggestion that a genome relates to a cell like software relates to hardware is lost in the insistence that the genome is the cell's software operating on its hardware. The elision is hardly accidental and to call attention to the use of analogies highlights the fact that biology in this domain often lacks its own logic, and so must borrow another. Even if the references to software and hardware is taken seriously, it would apply to any cell, or at least any engineered cell, and therefore does not really tell us anything about the kind of thing that JCVI has made other than suggesting generally that their genome was synthesized and therefore, unlike the genome of a wild-type bacteria, may be considered machine-like. Machine in this case becomes more or less identical to the artificial. Such an equivalence is obviously difficult to sustain. Hence, it actually does not help us specify what is going on.

Minimally, we can say that what JCVI has done is to bring together an ensemble of technologies and elements of living bacteria in such a way that taken together they were made to function as an ensemble. By way of this ensemble, JCVI was able to conceptually and materially disaggregate a genome into parts (units of a whole), remove what they took to be non-essential elements of that genome, and then re-aggregate that genome in such a way that the resulting artifact could be said to function as though it were the machinery whose purpose and function it is to drive the vitality of the cell. Whether or not what they made can be said to be a machine, or even machine-like, is doubtful, as I hope to make clear.

The sufficiency of analogies to machines for understanding living organisms is a long-standing problem both in philosophy and in experimental biology. Sustained efforts to achieve context-independence in the design of biological components as well as emphasis on the goals standardization and modularization have produced a range of "genetic elements used as components of synthetic regulatory networks." [233] These elements have introduced refined capacities for inflecting and directing genetic expression—transcriptional, translational, and post-translational control. Moreover, and equally important, the technical achievements and organizational forms catalyzed in synthetic biology not only by discursive appeal to these analogies but also practical appeal to precedents in other domains engineering has been crucial facilitated the initial design and organization of synthetic biology as a large-scale project—the existence of the BIOFAB is only one example.

The limit of analogies to biological systems as machines, circuits, or computational technologies has been put in question by philosophers and biologists alike. These limits, for example, have featured in debates among systems biologists concerning the question of whether or not biological systems can be explained by appeal to the chemistry or molecular physics underlying complex biological systems. Other minor debates, such as whether or not biological systems will ever be susceptible to precise mapping in Boolean systems of logic, remain unsettled. And, for those holding to the notion that understanding the basic mechanics of biological systems is only a matter of time, unsettling. More to the point, although in synthetic biology similar debates have remained relatively rare, experimental practices indicate a problematizing of the computer analogy. Work by the Weiss lab, for example, takes as an explicit point of orientation the proposition that biological systems are not the kinds of things susceptible to the same kinds of modularlization and additive composition as other kinds of systems. The question then is: to what extent can these systems be modularized and rationally composed. Sydney Brenner, one of the few who has raised the question of the sufficiency of these analogies for synthetic biology, has argued forcefully that cells simply cannot be usefully imagined as a hierarchy of components and circuits. Cells consist of juxtaposed vectors of activity whose domains of interaction and non-interaction depend on the scaffolding strategies—physical and temporal—activated in the cell by way of which activities can be timed and functions coordinated. Researchers in the Keasling lab, to cite another example, though sympathetic to parts-based work, have given concentrated attention to the question of the non-additive or "promiscuous" features of living systems—enzymatic activities perform multiple functions on top of the same sequences of DNA. These non-additive characteristics beg analogy to either computer software or hardware.

All of which brings into focus a second salient difficulty conceiving synthetic biology on the basis of machines, one which will bring us back to the framing questions of this chapter, and, for that matter, the framing questions of this text. For all the references in synthetic biology to Richard Feynman's claim that you don't really know something until you've made it, many synthetic biologists, including Drew Endy and, up to a point, Adam Arkin, are not particularly interested in justifying their work by what it helps us understand about living beings. The familiar trope, as I discussed in chapter two, is to contrast engineering with "science." All work in synthetic biology is, of course, knowledge dependent. And, as scholars have shown, it is unhelpful to distinguish between those who study biology and those who engineer biology on the basis of whose work is more characterized by intervention, rationalization and manipulation. It is equally unhelpful to describe bioengineers as biologists who "only want it to work." That said, there is a point of emphasis and stylization that comes through in the organization of work at the BIOFAB and no doubt in other synthetic biology facilities as well. That emphasis and stylization turns on the (usually) tacit notion that working on and working over living beings with technique and technology can only be stymied by too much concern for generalized explanations. Such emphasis and stylization clearly has important consequences not only for the kinds of objects that are worked over, studied, and fabricated, but the kinds of practitioners and practices taken to be exemplary. As I noted in the second chapter, the appeal to synthesis as a mode of engaging with living matter is in the first place a practical and not only epistemological matter.

It is simply the case that Endy and Arkin are not particularly troubled by arguments suggesting that biological systems "don't really work like machines." And, it follows, they don't seem particularly troubled by the sufficiency or insufficiency of analogies to computational machines. And if they are not particularly troubled, it is less because they don't think

understanding matters and more that they don't think it needs to be given operational, that is to say practical, priority. Quite the opposite is true. Both Endy and Arkin have found it operationally useful to appeal to the machine analogy, as evidenced by the use of the terms EOU and EOS. The fact that Arkin in particular may not really "believe" that biological entities are not identical to other kinds of machines is less important than the heuristic and operational value of such comparisons. That is to say, the question of analogies and the language of machines only really enters in with regard to the practical test of the extent to which imagining genetic activities in terms of computational machines provides a framework for orientation and a lever for shifting work forward. To cite Arkin: the reason the BIOFAB might be able to get away with calling its primary object of interest an expression *operating* unit is that the fabrication of proteins by the genetic material's "use" of other molecules in the cell, such as polymerase and ribosomes, is "the genome's basic unit of operation." If it is the basic unit of operation, Arkin suggests in rather unaffected tones, "why not call the genome an expression operating system?" The game is one of production and limitation, practice and motion.

Canguilhem offers an analytic distinction and pair of definitions, which are helpful in this context. The distinction, captured in the title of the essay in which they it is formulated, concerns the relation and differences between "*machine* and *organism*." In proposing to define this distinction, Canguilhem poses a question pertinent to synthetic biology: why is it that in the history of biology and philosophy of science machines have so often been used to explain living organisms, while the reversal of that relation is relatively so rare? And further, and equally pertinent to synthetic biology, he asks: what beneficial clarifications might such a reversal hold?

Importantly, Canguilhem proposes that these questions cannot be satisfactorily answered unless and until we are willing to rethink familiar assumptions about the relation between technique and science, and between technician and technology.[234] Canguilhem begins by laying out the broad outlines of the difference between an organism and a machine. He writes: "In an organism—and this is too well known to need insisting—one observes phenomena of self-construction, self-conservation, self-regulation, and self-repair." In the case of a machine we find that: "its construction is foreign and presupposes the ingenuity of the engineer." Further, we find that a machine, unlike an organism "demands the constant surveillance and vigilance of the machinist." We can of course imagine machines which perform self-surveillance and self-repair. Such machines, however, only displace "the relationship of man to machine; they do not "alter its sense." The term sense is crucial, implying both direction and purpose. A machine, however well-designed, remains an artifact and therefore remains that which was made by an artificer.

Filling in the details of this outline Canguilhem writes:

> In the machine, the rules of rational accounting are rigorously verified. The whole is strictly the sum of its parts. The effect is dependent on the order of causes. In addition, a machine displays a clear functional rigidity, a rigidity made increasingly pronounced by the practice of standardization. Standardization is the simplification of models and replacement parts, the rendering uniform of metric and qualitative characteristics, which allows for the interchangeability of parts. Any part is equivalent to any other with the same purpose—within, naturally, a margin of tolerance that defines manufacturing limits.[235]

Thus an initial double distinction at play in determining the difference between a machine and an organism: the first that organism is self-constructed whereas a machine is constructed by another who is self-constructed; the second that the machine is functionally rigid and marked by the practice of standardization. These distinctions may seem too obvious to warrant much

consideration, "too well known to need insisting," as Canguilhem might put it. But in the case of synthetic biology they go directly to the ambivalent heart of the status of the efforts and artifacts under consideration. Synthetic biology can be defined as one experiment (one in a long series of similar biotechnical efforts) in attempting to recreate living systems in such a way that, to the extent possible, they can be made to behave in a machine-like fashion. This includes the task and the challenge of getting genetic expression to operate in such a way that, as Canguilhem explains "the rules of a rational accounting" can be "rigorously verified" in relation to clearly determined functionality. It similarly includes the task and challenge of designing techniques through which "the whole" can be treated as though it were "strictly the sum of its parts" and through which "the effect" of designed activity is "dependent on the order of causes" rather than other non-controlled variables.[236]

Elsewhere the Human Practices lab has argued that those like Endy, who strongly advocate a parts-based approach to synthetic biology, can be cast has having a dissonant design and engineering style with others in synthetic biology such as the Venter Institute, or the Church Lab at Harvard who emphasize whole-genome engineering, or the Weiss Lab at MIT or Arkin Lab at Cal who focus their efforts on cellular systems. The fact of this dissonance and its connection to the scale of objects under consideration should not be explained by suggesting that Endy is somehow more committed to the creation of machines that "display a clear functional rigidity, a rigidity made increasingly pounced by the practice of standardization" and than others. Venter, Church, Weiss, and Arkin, after all, also want "the simplification of models and replacement of parts." It is better explained by the simple fact that Endy, unlike the others, has dedicated his professional life to promoting the idea that what synthetic biology needs, to use Canguilhem's words, is "uniformity of metric and qualitative characteristics, which allows for the interchangeability of parts." In this approach "any part is equivalent to any other with the same purpose—within, naturally, a margin of tolerance that defines manufacturing limits."[237] The Venter Institute, by contrast, has not advertised nor advocated any commitment to such parts-based interchangeability. And no doubt they would be satisfied with designed elements that worked only in their system and not "equivalent to any other part with the same purpose." This difference, however, so often pointed to as marking out a fundamental breaking point among synthetic biologists, should not detract from the fact that—and this is the point I want to stress—all of these engineers, in one way or another, want to be able to produce living organisms that can be made to behave in more or less a manageable, that is to say, in a more or less machine-like fashion.

But here ambivalence enters in. Most synthetic biologists can actually tolerate living systems being less than fully manageable, at least up to a point. No one knows what that point will be; it is an experimental science after all, and acceptable levels of non-manageability depend on the temperament of research directors and the specifications of the constructs being built. But it will nonetheless be tolerated. The reason such degrees of non-manageability enter in is because synthetic biologists want to engineer organisms in such a way as to take advantage of the capabilities unique to those living systems—capabilities that are likely not altogether susceptible to "the rules of a rational accounting." These capabilities include self-construction, self-conservation, self-regulation, and self-repair. This ambivalence is homologous with the one noted in the first half of this chapter, namely, the tendency to value living systems both for the contingency and their species continuity. To repeat the example introduced above, Keasling's artemisinin project is attractive not only because he was able to design and build functional specificity in the isoprenoid pathway, but also because that designed pathway allows

bioengineers to leverage the power of scalable self-construction: molecules of interest are produced as the engineered yeast naturally makes copies of itself.[238]

Crucially, in the case of the Venter Institute and of the BIOFAB synthetic biologists are aiming at an additional capability of living systems, distinct from and dependant on those that have already been mentioned. They want to leverage the fact that living systems have *polyvalent purposes*. Indeed, the fact that living systems are characterized by such polyvalent purposes is precisely what makes them appear to be so attractive as technology platforms. Canguilhem offers the example of an organ. A single organ can have a plurality of functions, and indeed can even develop new and more refined functionality to compensate for other conditions and deficiencies of the organism. Purpose in a machine, by contrast, is univalent and strictly defined. A single machine can have multiple purposes, of course. And this multiplicity can act together to create flexible and context specific effects. But each purpose is bound by the conditions of its design in a way contrastive to living organisms. Canguilhem: "the living organism acts in accordance with empiricism, whereas the machine, which is the product of calculation, verifies the norms of calculation, that is, the rational norms of identity, consistency, and predictability. Life, by contrast, is experience, that is to say, improvisation, the utilization of occurrences; it is an attempt in all directions."[239] And here in this contrast is the golden ring of synthetic biology: the ability to leverage the polyvalent purposes of life under the sign of rational design and specified functionality. And hence the reason why the strategic attempt to have all of the goods of the organisms and all of the rationality of the machine is often expressed in the use of analogies. Saying that the genome is the "software of life" seems to indicate that it can be programmed and controlled in a fashion similar to software while still retaining the supple flexibility and power of the living organism.

Hence a tension in the brand and project of synthetic biology. On one side there is an attempt to control certain functions through a rigorous and rationalized process—a machinist's response to the heterogeneity and irregularity of living systems. Recall the insistence on the part of Arkin and Endy in their original bio-fabrication proposal to DARPA in 1999: "natural biological circuits" have idiosyncratic mechanisms, rates, reactions, and effects. Hence, "rational design of biological systems by humans," they concluded, has "remained restricted to rather small or hit-or-miss efforts and has often relied on the ability to 'select' for biochemical parts that fulfill some criteria."[240] And yet, on another side is the attempt to harness a power fact of living organisms: the finite set of motifs, structures, and activities, of which the organisms consists, combine and interact in such a way as to produce multiple functions and multiple states. The Venter Institute created a bacterium as a proof of concept. A proof of concept of what? Of the ability to create a series of techniques and processes that inflect the activity of a genome in such a way that a different and better measure of control over the destiny of a living organism is made available to the engineers who synthesized it. That different measure of control is taken to be better in that it allows for the possibility of rationally determining not only the behavior of an organism, but the form, function, and identity of an organism in such a way that it will live in the world to instrumental ends. As JCVI's website puts it: "The ability to routinely write the software of life will usher in a new era in science, and with it, new products and applications such as advanced biofuels, clean water technology, and new vaccines and medicines."[241]

All of which can be repeated in intensified tones with regard to the work of the BIOFAB. The very notion of a standardized part—and even more so the notion of an expression operating unit or expression operating system—suggests the possibility (or at least the hope) of moving

from "rigorously verified" machine-like processes to an open horizon of possibilities. Hence biology as technology platform. The aim and hope is the creation of technologies and processes by way of which a limited set of controls can blossom forth into more or less limitless possibilities—"interoperability," "expression units to make expression systems," "abstraction hierarchies," and so on, which are not only limitless because of an extensible process of addition, but also because living organisms are flexible, adaptable, polyvalent in purpose. The BIOFAB may be aiming to make collections of standardized parts, which are rigorously characterized as to be calculable in combination. But it is aiming to do this in such a way that the subsequent use of these parts will be marked by an under-determination of possibility. Said differently, the BIOFAB parts should be marked by "rigid, univocal, univalent" standards. The functional possibilities opened up by the use of these parts should not.

So what is the status of this attempt to bring the standardizations and simplifications of machines into a technological relation with the polyvalent functionality of living organisms? What is the status of the objects made, and what is the status of the engineer making these objects? These objects clearly don't have the same status as other kinds of machines, however much machine-like functionality is part of the stated aspirations: these objects are not kinetic machines, motors, or even (despite persistent analogies) even computers. Perhaps they are something closer to the "animal-machines," which were a feature and preoccupation of Descartes' imagination. And, if these are animal-machines, then perhaps the problems evoked by the terms monstrous and monstrosity really are more appropriate to the situation than one might suspect or hope. Except that the Venter Institute has actually built neither machines nor organisms. It has combined a collection of technologies which have allowed it to inflect the activities and thereby the status of a living organism in something approximating a machine-like manner. And the BIOFAB for its part (hundreds of person years and tens of millions of dollars behind the Venter Institute) is producing the architecture for a genetic cassette and a collection of elements to drop into that cassette. Neither machines nor organisms are in the works at the BIOFAB either.

Rather, JCVI has, and the BIOFAB is trying to, invent bio-synthetic *mechanisms*. The notion of a mechanism is a crucial third term in Canguilhem's analysis, and is situated between the machine and the organism. The notion of a mechanism is actually understated in Canguilhem's essay. It is, however, the notion which facilitates movement between the other two terms. It is also the term by way of which Canguilhem demonstrates the conceptual worth of trying to explain machines in terms of the organisms rather than explaining things the other way round:

> So long as the construction of the machine is not a function of the machine itself, so long as the totality of an organism is not equivalent to the sum of its parts (parts discovered by analysis once the organism has already been given), it seems legitimate to hold that biological organization must necessarily precede the existence and meaning of mechanical constructions. From the philosophical point of view, it is less important to explain the machine than to understand it. And to understand it is to inscribe it within human history by inscribing human history in life, without however, neglecting the appearance, with man, of a culture irreducible to simple nature.[242]

It is this last point that should catch our attention—culture. Here, in this context, the term refers first and foremost to cultivation, to artificiality, to things human as things artisanal. And at the core of the artisanal activities under consideration is not the machine, per se (although the machine is clearly the point). Rather, the activity under consideration is the construction of the

mechanism. Citing Descartes' claim that because mechanics conforms to physics artificiality is actually natural, Canguilhem insists that contrary to Descartes' conclusion that the tree can therefore be understood on the basis of the watch, the watch rather must be compared to the tree. The mechanisms of the watch, assembled to produce an effect, are after all, "the immediate or derived products of a technical activity," and such technical activity is itself "an effect at first only dreamed or desired." Such dreams are human dreams and such activities are human activities: hence organic before they are mechanic.

MECHANISMS. SOLIDS IN MOTION

Early in his essay Canguilhem offers a definition of a machine as a construct whose essential functions depend on mechanisms. "A mechanism," he continues, "is a configuration of solids in motion such that the motion does not abolish the configuration. The mechanism is thus an assemblage of deformable parts, with periodic restoration of the relations between them."[243] Later he asserts that: mechanisms are "a necessary sequence of operations."[244] All of which clear and persuasive. But it is also significant. Canguilhem goes on to configure these configurations of solids in motion, with the labor of the technical imagination. Having cited numerous examples of the organic being explained by analogy to mechanisms—Aristotle, Baglivi, Borelli, Descartes—he proposes the following: all of these analogies require a moment of forgetfulness. That moment is the interval "between the mechanism's effects and the action of a living being." The action of the living being referred to here is, of course, the action of ingenuity. The explanation of the organic by way of the machine is only possible once "human ingenuity has constructed apparatuses that imitate organic movements." Canguilhem cites the pivot and the projectile but he might have equally well cited the circuit and the program.

The imitation of organic movements is the key here. It is not only the imitation of human movements, but the movements of organs, of processes, of functions, of structures. And of course we should not get hung up on the term "imitation" here either. Canguilhem's language may be etiologically overstated. But the point is right. The construction of mechanisms is the outcome of the desire to engineer an effect. One might consider Venter's "world-tour" in which he gathered thousands of genomes in order to better understand how they might be stripped down to essential components and made to function differently. He was on the lookout for mechanisms, or at least for those places in the genome in which the mechanisms of cell function and survival seemed not to be disrupted by the removal of "unnecessary" DNA.

Mechanisms thus constitute a juncture point between the organism and the machine, and a powerful one at that. They introduce an analogical doubling. First they are the form of the technical imagination brought into being by way of activity. That which is made is like that which is imagined. Second mechanisms exist on both sides of an ontological divide between the organism and the machine. That is to say, if mechanisms are imagined, they are imagined as a kind of production in the artificial of that which is already actual in the natural. Organs, a preferred example for Canguilhem, are marked by functions and those functions by mechanisms. Watches, another preferred example, are marked by functions and those functions by mechanisms.

This analogical doubling—with all the connotation of participation that the notion of analogy entails—is particularly telling for synthetic biology generally, for the work of JCVI in particular, and for the outputs of the BIOFAB eventually. Mechanisms can be made; they are formed out of the technician's imaginative practice. But they are also already given. This means

mechanisms can also be refined, displaced, replaced, leveraged, or redirected. By working on and working over mechanisms JCVI was able to produce effects that were consistent with "the rational norms of identity, consistency, and predictability." These mechanisms, in turn, were able to contribute to inflecting the "experience" of the bacterium in such a way as to preserve and thereby leverage its capacity for "improvisation," and the "utilization of occurrences."[245] The BIOFAB no doubt aims to intensify the first part of this and narrow the parameters for the second. But even in the case of the BIOFAB, with all the emphasis on calculation of function-in-composition, there remains a clear accent on the openness of creative possibility. In this sense, the artifacts perhaps can be said to be on their way to experiments in animal-machines, but without any need to get there.

For all of the obvious differences in scale, funding, strategic significance, scientific legitimacy and the like, it is by virtue of a shared investment in mechanisms that the work of the BIOFAB is directly relevant to the new *Mycoplasma mycoides* bacterium, running on JCVI's synthetic JCVI-syn1.0 genome. It is not inconsequential, of course, that the BIOFAB imagines a bottom-up management of the relations among and between the mechanisms it is trying to fashion. The BIOFAB, after all, does not merely aim to produce parts that function in a calculable way within a given expression cassette. Rather, and more importantly for its imagination of the future, these EOUs themselves should be composable in such a way that their collective function is likewise calculable. The rhetorical register wherein one moves from operating units to operating systems is the register of the machinist. It is a register in which the genetic life of a cell would be rendered according to uniform metrics and qualitative capacities, in which "the effect is dependent on the order of causes." One might think that this imagined possibility is a vision of rationalized life beyond even the techno-bacteria of the Venter Institute's work. And yet JCVI's narrative is of "programming the software of life."

In any event, the susceptibility of a living system to be made to function in a fashion increasingly like the characteristics of a machine is an experimental question with experimental limits. It is certainly not a question that can be meaningfully resolved here. More to the point, the debates about the relative mechanistic possibilities of biological control fail to account for the underlying fact that what the BIOFAB is actually doing is attempting to make and refine the *mechanisms* involved in genetic expression. Attempting, making, refining: key terms that take us to Canguilhem's concluding reversals of the machine and organism. If there is a limit to the extent to which the living organism is reducible to the machine this is because there is a symmetrical irreducibility of "art to science." Turning to Kant's monumental *Critique of Judgment* Canguilhem writes:

> Art, as human skill, is distinguished also from *science* (as *ability* from *knowledge*), as a practical from a theoretical faculty, as technique from theory (as the art of surveying from geometry). For this reason, also, what one *can* do the moment one *knows* what is to be done, hence without anything more than sufficient knowledge of the desired result, is not called art. To art that alone belongs for which the possession of the most complete knowledge does not involve one's having then and there the skill to do it.[246]

As decades of anthropological and sociological studies of the techno-sciences have shown us, the conceptual distinctions between the technical arts and sciences inevitably break down in practice. The contemporary biosciences, to take the example at hand, are driven more by making than understanding regardless of whether or not an experiment is being conducted in a department is called Molecular and Cell Biology or Bioengineering. As noted in chapter two, even the

distinction between foundational and applied within industrial research usually is contrived and a matter of organizational convenience as much as anything else. Canguilhem puts it nicely: "Science and Technique must be considered not as two types of activity, one of which is grafted onto the other, but as two types of activity, each of which borrows from the other sometimes its solutions, sometimes its problems."[247] Nonetheless, Kant's distinction can be taken as analytic light that throws into relief the way in which the ontological side of synthetic biology is necessarily linked to and derived from the practical side: the making of mechanisms capable of instrumentally determining the status of a cell is a practice. And the actuality of that practice is such that for all its aspiration first to the rationalization of techniques (which JCVI is well on the way to doing) and second to the rationalization of living forms (which remains an open and unsettled possibility) synthetic biology is nonetheless an "irrational practice" insofar as artifice is chronologically anterior to rationalization. Which is to say synthetic biology is a lived practice, with all that term carries regarding a form of life and the difficult question of whether or not that form is worth living.

Gibson *et al*. at JCVI have demonstrated that, in terms of the actual practices and procedures of their laboratory facility they can proceed, in an experimentally controlled fashion, from a harvested genome, to digitization of genomic data, to designed DNA, to digital recapitulation, to chemical synthesis, to a functioning cell. In fashion obviously asymmetrical in its profile and perhaps its seriousness, Mutalik, Cambray and the team at the BIOFAB have shown that they can design and test a genetic micro-context and can produce a library of sequences that have a specified function associated with it—on their way to standardized mechanisms. In light of these two programs with the help of Canguilhem's insistent efforts to clarify not only that the machine is not sufficient for explaining the organism, but also that explaining the machine in terms of the organism foregrounds the importance of practice, we are in a position to ask what I take to be a crucial question: have we too readily accepted the longstanding break in the biosciences between the monstrous and monstrosity? Might we need to exercise a more sufficient hesitation? The question, in this case, is not directed to the artifacts of biological engineering ("are these things monsters?") as if the problem was once again the violation of the norms of natural order. Nor is it even the question of the relation between the maker and the artifact, per se—the question of Dr. Frankenstein or the Golem, a question which still has things to teach us as Zoloth and Wolpe have shown.[248] Rather, the question can also be asked of the life of those who are engaged in making and remaking these objects, in relation to *their* form of life. The monstrous and monstrosity, keep in mind, are terms that apply to the ordering and reordering of living beings. In this sense the practitioners of synthetic biology and the institutions and practices they are forming are just as much living artifacts as are the cells they engineer.

The metrics of value and counter-value, as I have already discussed—and is widely evident—turn on instrumentality at the positive pole of value and material danger at the negative. This is why Venter, in his prepared statements about the worth of his institute's new bacterium, has carefully walked a plotted track between the scientifically and politically benign "proof of principle," the economically and politically irresistible "software of life," and the gravely prudential "it can't live outside our labs." These poles of value and disvalue block a consideration of whether or not engaging in the practice of the post-genomics is itself worthwhile. If only the instrumental outcomes of one's work are the determinant of worth, then the vocational and spiritual questions are taken to be gratuitous.

But the whole point of the long exercise of traveling with Canguilhem through these distinctions and of deploying those distinctions in an analysis of synthetic biology, centering first on JCVI and then returning to the embryonic efforts of the BIOFAB's program, was to demonstrate how difficult it is to break the link between the status of the practice itself and the status of the objects being made. Not that there is a kind of moral transference, as has been argued by Kass and others. The point is not just that "we should be worried about these instrumentally driven biologists who will only produce economically viable objects and not ethically viable objects." Such a point might well be worth considering, but it has been stressed by others and does not need to be repeated here.[249] The point I want to draw is, rather, that making mechanisms is an art. And an art implies the need to cultivate artisanal capacities. And artisanal capacities imply the possibility of taking up one stance rather than another to the material world, and in the case of synthetic biology, to living beings as susceptible to being rendered machine-like in their behaviors. And the possibility of taking up one stance rather than another, implies the cultivation of one set of practices rather than another, thus entailing the question of the form of life at play and at stake. The form of life in question in synthetic biology is not only the life of the bacteria in the plate-readers, flasks, and flow-cytometers. It is the life of the bioengineers, and the justifications, rectifications, and ramifications of that life.

My effort here is straightforward: to motivate an inquiry into the question of whether or not the ethical stakes of synthetic biology can be thought through in terms of the form of life characteristic of the practitioners of synthetic biology generally and of the BIOFAB team in particular. It is for this reason that I introduced the question of the monstrous and monstrosity in order to signal the connection those terms imply between the ethical significance of abnormal forms of life and the ethical significance of producing those forms. There is not, I would argue, any single metric by way of which such a question could be answered definitively. There is, however, a task and a challenge. The task is how to parameterize the work of the BIOFAB such that judgments can be made about what form of life is worthwhile, ethically and scientifically, and what form of life is actually a matter of deformation. The challenge is to have the courage to make those judgments and the resourcefulness to make them in such a way that they do not circulate merely as denunciations, but also a points of possible rectification.

In terms of the task of ethical judgment, taking up the terms monstrous and monstrosity in order to think about and evaluate the practices of making mechanisms for the calculable control gene expression requires a recalibration of sorts. As Canguilhem explains, the terms monstrous and monstrosity actually only apply to living organisms, and are terms which, in the end, imply the question of health. That is to say, the monstrous as a matter of the distinction between the normal and the abnormal organism can be taken up as a matter of the play of *organic* norms of health and pathology. Health and pathology have a long-standing place in the history of ethical reasoning and certainly cannot be removed entirely from our analytic field of vision. But in the case of the problem I am trying to push forward, monstrous and monstrosity would not apply simply to aberrations of the normalized and familiar conditions of organic health. Indeed, the predominance of the instrumental as the value of engineered living systems and material danger as its negative value is precisely a situation that I think is blocking serious engagement with a different kind of ethical question. The kind of norm to which the term monstrous will need to be connected if it will prove to be more fruitful for thinking about synthetic biology as a way of life must involve the ethical elements of metrics, means, and practices. These older virtue terms have been taken up and reworked as a matrix for the anthropological analysis of contemporary forms of life.

What we would need to add to Faubion's distinctions is an insistence on a different sort of positionality. The problem at hand for me is not only whether or not I can provide a sufficient diagnosis of life in the BIOFAB—a problem which certainly cannot be taken for granted. And it is certainly not to cast judgments from afar. Rather, the problem consists in posing the question of whether or not the work of the BIOFAB can be indexed to a register of the monstrous or monstrosity in terms of how lives are being formed and deformed, vocationally, scientifically, and spiritually. Which is, after all, what was intended by the term "human practices" as a mode of addressing the post-genomic biosciences from the outset. Such indexing no doubt must take on board the question of experimental outcomes; ramifications are a key component determining the ethical status of an action. This thesis cannot answer the biotechnical and experimental question of whether or not the BIOFAB's parts-based program will be adequate to its stated goals. But I would add that keeping an eye on the successes and limitations of this program and on the extent to which Endy, Arkin or others continue pursuing this avenue of work if it is not actually closing the gap between the imagined future and practices as they are currently designed is itself a key variable that must be weighed on the ethical, that is to say vocational and spiritual, scales.

Let me be clear: the question of the monstrous and monstrosity applies equally to my experiment in human practices. It is crucial that I ask: what kind of life am I forming, and is this life worthwhile? A willingness to become part of an experiment justified in the name of collaboration within a venue in which, for all of the openness of the individuals involved, the bioscientific outcomes will inevitably out-value the anthropological and ethical outcomes means that my work is fraught with the possibility of blockage, marginalization, and frustration. The question then is not only what kind of life is being actualized in the practice of synthetic biology, but what kind of life is being actualized for those adjacent participants, such as me, who care to contribute, however modestly, to the form and ramifications of that life? What kinds of formations or deformations might be required of me?

A MODERN THRESHOLD

In his book *Scientific Life* Steve Shapin traces the fate of a half-century long debate among sociologists and historians of science as to whether or not scientists as a group are ethically special. Shapin explains that for much of its short history sociology of science assumed that scientists were not in fact particularly special, ethically speaking, however much the intellectual virtues of disinterest and integrity were credited by scientists as defining. These same sociologists, however, often assumed and occasionally sought to demonstrate that although individual scientists might not be ethically special, science as a community of experimentation, peer review, and evidence-based reasoning, does enjoys a unique kind of moral rectitude. The claim was that technical practices and the scientific production of knowledge function as mechanisms of ethical vetting whereby the moral standing of any one practitioner—whether greedy, ambitious, generous, honorable, courageous, selfish, and so on—ultimately had little bearing on what kind of knowledge was produced and taken seriously. It is for this reason that methodologically and experimentally rigorous knowledge can be trusted as true, whatever the state of the individual scientist's soul. This view of things—the scientific community as morally vetted—has, however, also fallen out of favor in the sociology of science, Shapin explains. And this is due in no small part due to Shapin's own contributions. Taking a long historical view, Shapin's work has shown how virtues such as trust, loyalty, and charisma, historically bound norms of truth-speaking, and the messy micro-politics of disciplinary formation have all played

their part—whatever the aspirations to disinterested knowledge production. Which is not to say that scientific knowledge is reducible to any of these variables; nor is it to suggest that the aspiration to the disinterested production of experimentally confirmable knowledge isn't regularly realized. It is to say, however, that (as Shapin puts) scientific knowledge is produced by "people with bodies, situated in time, space, culture and society, and struggling for credibility and authority."[250] This may have become a simple truism for science and technology studies, but it bears repeating here because its ramifications for ethical thinking and analysis are crucial. With the exception of the work undertaken as part of the experiment in Human Practices, these mundane but crucial elements of the experience and situation of scientific research have only occasionally been foregrounded in the ethical analysis of synthetic biology. And more importantly, even where they have been foregrounded, no serious attempt has been made by those with power to understand them and engagement them as the basis for an eventual change of habits. Such shortcomings should be counted as much a scientific as an ethical loss.

Michel Foucault offers an insight which is yet again more incisive. In his 1980-81 lectures at the College de France Foucault put forth the proposition that: "the modern age of the history of truth begins when knowledge itself and knowledge alone gives access to the truth. That is to say, it is when the philosopher (or the scientist, or simply someone who seeks the truth) can recognize the truth and have access to it in himself and solely through his activity of knowing, without anything else being demanded of him and without him having to change or alter his being as a subject." [251] The proposition, as Foucault shows, is remarkable only when one understands what stands on either side of this threshold. On the far side of the threshold is the millennia during which antique and then Christian philosophers took it as a matter of course that such as one is, one does not in fact have the right of access to the truth. Such access required transformations of ones being through the cultivation of relations, exercises, experiences, and so on. Speaking of the far side of the modern threshold, Foucault proposes that philosophy can be understood as the art and possibility of dividing up the true and the false. The price to be paid for access to the truth in terms of the transformations to one's life and being Foucault calls spirituality, transformations he elsewhere designates as ethics. The point I want to emphasize is that the modern threshold marks that point at which attention to spirituality, to the arts of working to constitute a particular form of life in order to have access to the truth, effectively falls away.

It falls away in favor of a situation in which the philosopher, or the scientist, or one who simply wants to have access to the truth no longer needs to transform her or his being in order to do so. The accumulation of knowledge is enough. And hence the remarkable characteristic of the near side of the modern threshold. Foucault explains that the production of knowledge on this near side of the modern threshold has certainly required training, mentorship, access to institutions, standards of truth production and the like. Such requirements, however, fall short of the expectation that one needs to transform one's being in order recognize the truth. What one needs, rather is more knowledge. Keenly, Foucault points out that the price to be paid for such a situation is that the knowledge one produces no longer "saves" the one who knows. Foucault's use of salvational language is no doubt jarring on the modern ear. The problem of salvation, of how to achieve a life which is good, *soteria*, constituted the central stakes of the relation of truth and ethics for antique and Christian thinkers, though these stakes were understood and responded to quite differently. Hence, it is no small thing that there was a transition in the history of the relation of thought and ethics of the kind Foucault elucidates. The notion that knowledge as the primary means to the truth excludes the possibility of a transformed life should not be passed by

lightly. Crucially, this notion, Foucault suggests, does not begin with modern experimental science, as one might suspect. Rather, it begins in theology. Specifically, it begins in that moment in which theology takes as its task the possibility of knowing the truth of the divine without recourse to the transformation of the soul of the one who seeks the truth. The problem for theology was pragmatic. In the thirteenth century the church confronted the problem of how to ensure the truth (and thus the salvific force) of preaching in a situation in which the ethical and spiritual status of the priest was in question. Hence the need for a form of truth that no longer depended upon the state of the soul of the truth-speaker. The resonances with our contemporary situation are evident. And the fact that the ethics of knowledge production today (i.e. science) tend to concentrate on the question of the status and consequences of knowledge rather than the knower can be seen as a long-standing state of affairs.

With the notion of the modern threshold of truth, Foucault is marking out a broad distinction. He admits in his lecture that there is no real "moment," and that the difference between modern and antique practices of philosophy, science, and spirituality are inevitably more complicated and there is certainly more to say and to specify. Indeed, Foucault's notion of a modern threshold is offered in the first lecture of what, when transcribed and published, became a 500 page book. Though broad, the distinction is nonetheless relevant. It is relevant because it provides a clear formulation of the fact that in the sciences today the question of ethical self-formation is no longer taken seriously in relation to one's ability to have access to the truth. Knowledge and technique are what matter. But in the case of synthetic biology, and in the case of the BIOFAB particularly, it is clear that question of ethical formation, the question of how one's life is formed, and how one form's one's life is most definitely in play. It is the case that many of us in the BIOFAB, myself included, have experienced the discomfort and irritations of being asked to contribute to a particular vision of synthetic biology by Endy, and have been tested but not always directed by Arkin. This discomfort has produced what I have been describing as a situation of indeterminacy not only at the level of the work to be done—i.e. which protocols should be designed, how they should be designed, and how work prioritized and carried forward. It has also been a situation of indeterminacy in terms of the subject positions each of us is being asked to fill.

To put it in personal terms, when I have been asked by Endy to produce a series of reports that are neither scientifically or philosophically serious, but which serve a purpose within the mandate of the organization, I have occasionally experienced irritation and boredom, or experienced uncertainty with regard to the vocational road ahead: if this work is not going to be taken seriously by my anthropological or philosophical peers, what is the price to be paid for spending my time working on it? There is any number of responses I could have to this situation of discomfort. I could confront the terms of the situation, and thus the discomfort, by refusing to produce work that I don't think is serious enough. I could simply treat my work at the BIOFAB as a job; many thousands of people each day conduct work that they find irritating or less than fulfilling. Or, I could undertake the work of adjusting my stance in relation to synthetic biology and the future of the BIOFAB in such a way that I cultivate a posture of care for and commitment to that future. It has been a premise of this thesis that the latter option is in fact what is being expected of the junior participants in the BIOFAB and in much of synthetic biology more broadly.

The BIOFAB is marked by dynamics similar to other experimental scientific endeavors: questions of virtue, the norms of truth speaking, and the micro-politics of power are

determinative of the kind of program being instituted. The anthropological question, in relation to this first complication, is thus not so much "are scientist more or less ethical than other subjects" but rather "what kinds of changes in subjectivity are actually being required of scientific practitioners in order for them to cultivate one set of habits and disciplines rather than another?" The second complication is the fact that this question has not really been taken up in a systematic fashion by the leaders of the BIOFAB (or other leaders in synthetic biology) except insofar as it can be addressed in terms of work routines, experimental design, methods of analysis, and so on. The ability to pose this question and to take it up in a serious and sustained fashion would require cultivating dispositions toward the relation of knowledge and ethics that are more or less dissonant with the terms of the modern threshold as Foucault described it. Put differently, in order to take seriously the micro-political facts described by anthropologists and historians of science as the premise of both ethical analysis and the formulation of ethical practices, one would have to risk admitting that knowledge production, capacities, and the question of salvation (understood in the broad sense noted above) are matters of central concern in an experimental situation. On one level, such the costs involved in taking such a risk are not at all high. After all, five years ago the "Bio Fab Group" as they called themselves identified the need for new regimes of subjectivation if synthetic biology was going to thrive. On another level, however, the costs may indeed significant. If the question of ethical formation and the practices necessary to such a formation is going to be taken seriously, then the matter of whether or not synthetic biology is a formative or de-formative undertaking would need to be asked as well. That latter question would unsettle the projected futures which currently hold things together.

The themes raised by Canguilhem's "Monstrosity and the Monstrous" require both a patient labor and a refusal to accept (at least on the face of things) that the predominant ethical framings are sufficient. Having taken the time to meditate on these themes, however, I am struck by the untimeliness of his distinctions in relation to such a timely moment in the brief history of synthetic biology.[252] It is a timely moment in that JCVI's recent announcement, and all of the stir it caused, has allowed the Presidential Commission for the Study of Bioethical Issues and others to cast synthetic biology as a matter of pressing economic and political concern, and that the heart of the concern is the promise of instrumental goods and the fearsomeness of possible dangers to environments or human health. While Canguilhem's is an untimely text in that it fails to confirm the significance of the expert talking points. Rather, it introduces a different and possibly more troubling set of distinctions. At the heart of his text is neither the promotion nor denunciation of instrumental gain, prosperity or amelioration. Nor is it the praise of ingenuity and the demystification of the irrational. Rather, at the heart of the text is a recollection of an older moral-theological imaginary that might, if reconstructed, might serve as an irritant, introducing enough dissatisfaction and discomfort to encourage a bit more reflection than might have otherwise seem warranted.

Several experts responding to the Venter Institute's announcement, including all of those testifying before the US Congress, including a bioethicist and all three of the expert biologists the first meeting of the Presidential Commission hearings, took preemptive action against those who might interpret JCVI's work as an act of "playing god." The form of this preemptive action was to assure us: "there is nothing really new here," "it was just a re-assemblage of technological capacities," "they used a host cell and so didn't really create life," and so on. But these experts seemingly had little to worry about. The theological spokespersons seemed to agree. As the *Observator Romano* reported, the Vatican line was strictly pragmatic and tempered: scientists had not created life, but had "substituted one of its engines."[253] No monsters, no monstrosities.

And yet, if we pose a different set of questions, attending to what the Hastings Center referred to misleadingly as "non-consequential harms," we are actually more able to see that this might prove to be a somewhat more unusual moment than might be otherwise indicated. It is already clear that his moment—the publishing of the JCVI paper and the perturbations it caused within the BIOFAB and across synthetic biology—is consequential. In addition to its technical merit, it provided a catalyst for the animation of Congressional hearings and the first meetings of the President's Council on Bioethics. It was arguably a contributing factor to shifts in the valuation discourse connected to synthetic biology, shifts from emphases on the amelioration of health and the environment to an additional emphasis on commercial prosperity. It is also a moment, it seems to me within which the ethical and scientific imagination might possibly be opened and reworked. Crucially, these possible reconfigurations are not only open at the level of experimental and technical design or at the level of funding and regulation. It also offers another occasion to open the question of what it means to spend ones time designing this rather than that experiment or technology, forming these rather than those capacities, taking up this rather than that vocation. JCVI's work—taken both in its specifics as well as an exemplar of a wider potential and orientation in synthetic biology—allows us to "grasp living beings in all their contingency," the artifact, artisan as well as the art.

THE STRICTURES OF AN APPARATUS: TRUTH, POWER AND ETHICS

The JCVI announcement changed very little at the BIOFAB in terms of its daily technical operations. It did inflect the way in which Endy, and to a lesser extent Arkin, framed the stakes and purpose of the BIOFAB's work in the weekly meetings and in more public statements. Emphasis on the need for "whole-genome design and engineering" became a relatively more prominent part of the imagined future, as did suggestions that the BIOFAB's aims and priorities should be taken up at a global scale within multiple facilities with a shared goals and standards as well as a coordinated division of labor. More pertinent to human practices, the JCVI announcement and its ramifications contributed to a recalibration of my position within the BIOFAB and my relation to the growing collection of ethicists and social scientists who had begun to pay attention to synthetic biology. That recalibration consisted of an intensified focus on the ways in which ethics in synthetic biology was actually being limited, and the relation of those limitations to configurations of truth and power. These themes had been foregrounded as part of the human practices experiment at SynBERC from the outset. In the wake of the JCVI announcement, however, I began to experience in a more intense and direct fashion discord among and between the demand for productivity, the aspiration to scientific truth, the right to participate in the governance of the BIOFAB's work, and the frequent incapacity to do so.

On Thursday May 20, the day of the JCVI announcement, Cesar Rodriquez sent an email to the BIOFAB group containing a link to a BBC online report about the Venter Institute's work. Venter had spent the day of the announcement circulating through the major news outlets, BBC among them. The article bore a title similar to others published that day "'Artificial Life' breakthrough announced by scientists." In his conversation with BBC Venter rehearsed the talking points discussed in the previous chapter. Appended to the interview with Venter were sub-headed sections on "Ethical discussions." The ethical discussions were noteworthy only in that their inclusion as become part of the genre of science news reporting and for the fact that, narrowly conceived, they were not about ethics per se but about the relative dangers, material and political of releasing synthetic organisms.

More important than the article was the chain of interactions that Rodriguez's email set in motion. His email was immediately responded to by another member of the BIOFAB team who pointed out with some measure of either surprise or enthusiasm (the ambiguity of email) that the article "Emphasizes the need for ethical thinking in genetic engineering!" The immediate response to this was from Arkin who wrote in a bemused tone: "Ha! Gaymon—want to dare and take a position?" Arkin's comment may have been a throw-away; nonetheless it seemed to me that the JCVI announcement represented something of a minor test: whether or not I could take a contemporary episode in synthetic biology and frame it in such a way as to bring to articulation a more serious set of ethical questions.

Although I did expect my fellow BIOFAB team members to appreciate my formulating an ethical response to current developments in synthetic biology, I did not expect them to respond. Somewhat to my surprise, however, my email was not met with total silence. Arkin immediately sent back a more or less appreciative response—a response that subsequently unfolded into several exchanges. I proposed to Arkin that his framing provided an occasion for re-thinking themes that Canguilhem had identified as the problem of "the monstrous and monstrosity"—the question of what we should make, ethically and biotechnically, of the "same engendering the other'" as Canguilhem put it. Is the making of a monster actually monstrous? I did not use these terms, of course. What I actually said was that by drawing attention to the relation of the maker and the made, Arkin showed that it wasn't all about instrumentalism. In this way he was not too far afield from long-standing debates in natural law: the problem of relations among living beings, their norms, and their forms. The difference here was that questions of biological design and functional composition were being posed without appeal to notions of natural kinds or divine providence.

It is easy to imagine Arkin's response: not hostile, tepidly intrigued, but eventually annoyed. He repeated a familiar polemic syllogism: nature is nature. It can be neither "cooperated with" nor "violated." Hence, by suggesting consonance with debates in natural law, I was opening the gates to irrationalism and forgetting that biologists are uniquely authorized to speak to truth about living beings. The matter was basically settled by an exercise of power: he told me that the BIOFAB should not be offering opinions on these themes. I replied that at least at the level of self-interest and political protection such matters could not be altogether ignored. After all, the BIOFAB will eventually have to deal with the fact that the world was full of people who take these questions seriously and who have more power than we do. If we care about the truth of these matters and think that ethical reasoning should be informed by more accurate scientific explanations of things, then we have an ethical responsibility as scientific practitioners. Arkin granted that there was perhaps a "communications responsibility" that might need to be taken up.

The conversation led neither to action nor to reform. But for my part the exchange was consequential. It exemplified the way in which asymmetries in authority to serve limit and deflect ethical reflection. A blunting experience of the obvious insufficiency of dialogue when understood as improved communication as an index of satisfactory ethical engagement.

Affectively, the exchange with Arkin, with the BIOFAB team looking on, was initially pleasant but ultimately wearying. It was pleasant as an extended exchange on themes central to my interests, both in terms of my domain of responsibility as part of the BIOFAB. It was also pleasant, as a friend put it, a shade sardonically, a "teaching moment." And it was pleasant because Arkin is an energetic and insightful thinker, and most exchanges with him are marked by

a certain intellectual seriousness. It was wearying, however, in that it effectively delimited and blocked the range of my responsibilities, it was not a really a teaching moment in that it did not result in change on his part or mine, and though Arkin is indeed remarkably intelligent, his appeal to the familiar idea that the experimental sciences and reductive materialists have a monopoly on what gets to count as rational was disappointing.

I see few hopeful signs. Claims about the ways in which synthetic biology will affect material dangers are frequently offered under the aegis of ethics, and these are talked about in serious tones. And ethics, as a broad topic, has been included in statements of the "perspectives," that need to be included. To date in synthetic biology, considerations of the former have issued in efforts to bolster existing procedures and mechanisms for biological containment and for calls to improve techniques for the analysis of environmental risk. The latter have resulted in the stated need for better public education, and for the animation of public fora for discussing synthetic biology. That neither safety nor opinion polling exhaust the possible contributions of ethics to the formation of the contemporary life sciences should go without saying. The fact remains, however, that sustained reflection about the kinds of ethical subjects that are being formed in synthetic biology, and the relation of such subject formation to the forms of life being open up or closed down for others remains blocked. Such reflection is permitted up to a point. It is not, however, being allowed to count in the register of truth in such a way that it might contribute directly to the shaping or reshaping of actual organizational, managerial, and scientific practice in synthetic biology. Put differently, ethics is not being allowed to proceed in a *reconstructive* mode, understood in the technical sense that John Dewey gave to that term: engaged thinking which constitutes "the work of developing, of forming, of producing (in the literal sense of that word) the intellectual instrumentalities which will progressively direct inquiry into the deeply and inclusively human—that is to say moral—facts of the present scene and situation."[254]

III. TOWARD RECONSTRUCTION

CHAPTER 7

Articulating Scales: The Apparatus at Work

> *It has to be understood that true discourse is not and cannot be distributed equally in a democracy according to the form of isēgoria [the right to free speech]. Not everyone can tell the truth just because everyone may speak the truth.*
>
> —Michel Foucault[255]

In the previous chapter I explained that the JCVI announcement changed very little at the BIOFAB in terms of its daily technical operations, I also noted that it did have indirect effects on the ways in which the Endy and Arkin framed and justified the BIOFAB's work. [256] JCVI's achievements were figured as exemplary of synthetic biology in a number of settings. In the US a number of events animated under the broad sign of synthetic biology—congressional hearings, meetings of the Presidential Commission for the Study of Bioethical Issues, and the expansion of funding—were actually prompted by the Venter Institute's assembly of their self-titled genome and their stylized announcement. Where for several years synthetic biology had usually been cast either as a playful refactoring of living systems, with iGEM as the exemplar, or as a matter of humanitarian consequence, with Amyris' artemisinin work cited, the rhetoric and promise of prosperity and the dangers of attendant risks were more prominently foregrounded. With the JCVI declaration of "creating life" were coupled with hopes of biofuels and bio-economics to position synthetic biology as a key variable in a more worldly valuation game.

In this regard, the JCVI announcement and its ramifications were directly pertinent to my work in human practices, as I explained in closing the previous chapter. The announcement contributed to a recalibration of my position within the BIOFAB and my relation to the growing collection of ethicists and social scientists who had begun to pay attention to synthetic biology. I proposed that such recalibration consisted of an intensified focus on the ways in which ethics in synthetic biology was actually being limited, and the relation of those limitations to configurations of truth and power. If this recalibration was felt internally to the BIOFAB, it was much more evident in a number of prominent adjacent domains. Principal among these was the Presidential Commission for the Study of Bioethical Issues.

In late May 2010, in direct response to JCVI's work, President Barack Obama announced that his Commission on Bioethics, which had been formed but had not yet been convened, would take synthetic biology as their first topic of concern. Announcing that the standing Commission would be convened, Obama issued the following mandate:

> I therefore request that the Presidential Commission for the Study of Bioethical Issues undertake, as its first order of business, a study of the implications of this scientific milestone, as well as other advances that may lie ahead in this field of research. In its study, the Commission should consider the potential medical, environmental, security, and other benefits of this field of research, as well as any potential health, security or other risks. Further, the Commission should

> develop recommendations about any actions the Federal government should take to ensure that America reaps the benefits of this developing field of science while identifying appropriate ethical boundaries and minimizing identified risks.[257]

The announcement and mandate, partially circumscribing the Commission's work, proved relevant to the Human Practices experiment. First was the way in which the mandate worked to simultaneously expand the range of topics under consideration and the range of participants in the governance of synthetic biology, while ultimately having a contractive effect. The Commission was asked to consider a range of topics that, in terms of disciplinary boundaries, are not often considered to be the proper domain of bioethics: medical, environmental, and security benefits; health, security, and other risks. This expanded range of considerations is testimony to the fact that synthetic biology is reconfiguring previous settlements about the relation between questions of ethics, security, and economics as they ramify across multiple domains. The second is that the mandate effectively determines the metrics of what can be taken to count as good and worthwhile: prosperity and amelioration, where prosperity is a calculation of national economic advantages and amelioration is a ratio of health and harm. The Commission, working with these metrics, is to help protect and normalize: set ethical boundaries and minimize risks.

The Commission's report and recommendations were published six months after the first hearings. At first glance the report and recommendations would seem to take up considerations beyond the metrics of prosperity and amelioration. In fact the report was framed as providing a range of criteria according to which ongoing developments in synthetic biology might be assessed. Among these the notion of *public beneficence* was positioned as critically important in determining how the benefits of synthetic biology should be measured. But the emphasis here was clearly on *public* and not on any critical revision of the terms of *beneficence*. For example, in considering the notion of the public good, the Commissioners write: "Environmentally friendly biofuels and affordable anti-malarial drugs are among the near-term products of synthetic biology already receiving significant attention. These are important current examples of how advances in synthetic biology may deliver widespread benefits that promote social welfare." The metric here is not public beneficence; rather, the metrics remain national security and the growth of industry, which may not be antithetical to public goods, but are hardly animated in the name of some kind of commonweal.

The point here is not that economic prosperity or the amelioration of health are undesirable or should be taken for granted. And an assessment of whether or not synthetic biology is really likely to deliver on such promises and prospects would certainly have been a worthwhile outcome of the Commission's work. The point, rather, is that by assuming that the relevant goods of synthetic biology adhere in the instrumental outcomes of the work, indeed by assuming that there would be positive instrumental outcomes, the role of ethics really only consisted in identifying where such instrumental outcomes were generating harms—harms presumably calibrated to the same set of metrics. This, in turn and not surprisingly, reinforced the technologists' authority with regard to speaking the truth about synthetic biology as well as the non-technologists' position as commentators on the possible negative ramifications. Non-technologists were positioned neither to speak the truth about what counts as synthetic biology, nor were they positioned to raise the question of what counts as good.

This seems an underserved exclusion given that the familiar questions of governance, which the Commission's mandate echoes, remain unanswered. How much should be done to

govern synthetic biology (and thus) how much should not be done? The question implies the problem of how to constitute two ratios. A first of course concerns how much or little power should be exercised and in what ways. The second is less obvious and concerns a ratio of how authority should be distributed in the possible exercise of such power. Said differently, the mandate indirectly introduces again a question that has been in play since the advent of federal bioethical commissions: how much should biotechnicians be governed, how much should they be allowed to govern themselves, and how much should others, non-biologists that is, be allowed to play a direct role in governing biotechnical work?

The Commission tacitly raises these questions by way of the introduction of a watchword central to their report: *prudent vigilance*. The Commission stresses that the public and its representatives be vigilant about risks and harms, standing ready to revise policies that pursue potential benefits with insufficient caution. They likewise stress that "The government should support a continued culture of individual and corporate responsibility and self-regulation by the research community, including institutional monitoring, enhanced watchfulness, and application of the NIH Guidelines for Recombinant DNA Research." This emphasis on self-governance is actually the heart of the concern. They write that "While self-governance is not a sufficient means to mitigate all risks, it is likely an effective way to control many of the risks associated with emerging technologies, including synthetic biology, particularly at this early stage." After all, it goes without saying that "Individual scientists and students typically are the first to notice the laboratory door ajar, the suspicious behavior, or the lack of safety precautions among colleagues."

Despite the rhetorical force of the notion of prudent vigilance, the questions that the Commission never really resolves are who exactly is it that needs to be prudent and vigilant? Is it really anyone other than the biotechnicians themselves? What would the exercise of prudent vigilance actually consist in? And how would we know whether or not whoever it is that is supposed to be exercising prudent vigilance is actually happening? One reason that these questions are left unanswered is the leveling affects created by the Commissions commitment to notions of democratic deliberation. The Commission writes: "Scientists, policy makers, and religious, secular, and civil society groups are encouraged to maintain an ongoing exchange regarding their views on synthetic biology and related emerging technologies, sharing their perspectives with the public and with policy makers. Scientists and policy makers in turn should respectfully take into account all perspectives relevant to synthetic biology."[258] What this actually means and how might it ever happen if not specified and enforced? In a similar vein, and cultivating a tone of fairness, the Commission writes: "Some who provided testimony to the Commission argued that the current system unduly limits scientific advances; others took the opposite view and asserted that the current system works well."[259] Reconciliation of the implication that anyone has the right to participate in the governance of synthetic biology is never actually reconciled with the fact that only certain individuals and institutions will be empowered to do so.

The fact that these questions are not satisfactorily addressed puts in doubt the seriousness of the Commission's claim that they are modeling their work on the famous Belmont Report, the report drafted by the first federal bioethics commission in the 1970s as a guide for work with human subjects of research. Although like the Belmont Report the Commission's report on synthetic biology articulates a series of principles by way of which ethical judgments can be made, the Commission's report fails to emulate the pragmatic emphasis of their predecessor

which connected these principles to specific kinds of actions, and framed those actions in such a way that they could be taken up by a specific kinds of institutional entities. One result was that the Belmont report contributed to the solidification of a cooperative division of labor and power between bioethicist and biomedical and biotechnical researchers. It has been premise of the Human Practices experiment from the outset that such a cooperative division of labor and power is not sufficient to the current situation in synthetic biology, and that a more collaborative relation is called for, consisting of the work of defining problems and actions in common. Such collaboration, from the outset, was designed with an informed view of what might be lost: namely the long-standing effort on the part of bioethicists to ensure a measure of independence from biomedicine and biotechnology with regard to the exercise of power through the institution of a cooperative division of labor. The risk of losing such institutional independence seemed a price worth paying in order to take up a closer relation to the actual micro-practices of research as they unfolded. And given the lessons learned through four years of work in Human Practices at SynBERC it seemed a risk worth taking yet again in with the experiment at the BIOFAB.

A final element concerning the announcement and mandate which animated the commission was the simple fact that the Commission hearings and eventual recommendations constituted only the second significant investment in the ethics of synthetic biology on the part of the US Federal Government, the first being the Human Practices emphasis in SynBERC. Given the Commission's status within the Office of the President, and given the obvious proximity to our efforts, we expected the hearings to have direct ramifications for our efforts. In this light we also had some expectation of being directly involved in the Commission's work, either indirectly as advisors to planning the hearings or directly as invitees to provide expert testimony. In addition to our five-year experience participating in a federally funded center, our expectation of involvement was further warranted by the fact that a number of SynBERC Principal Investigators were being included on the agenda for the first meeting. Endy was among these, invited to give the opening testimony to the hearings, with the explicit task of providing introduction and overview to the field of synthetic biology. Despite reports from Endy that he had encouraged the Commission staff to include testimonies from Rabinow and from me, and despite reports from the staff that Rabinow had actually been on the short list for all three of the hearings, no invitation was extended to include testimony from human practices, and indeed, none of the human practices publications were included in the Commission's background materials. Indeed, no anthropologically informed ethical work was included.

PERFORMING AUTHORITY

The first Commission hearing was held on July 16, 2010. The meeting constituted the first formal engagement with the question of the ethics of synthetic biology on the part of the executive branch of the US government. Although the Commission was formally established near the end of the first year of the Obama administration, it was only actively animated in response to the publication of JCVI's work; two other hearings were scheduled for the fall, and the report was published in December. For all the obvious differences from the situation of ethics in the BIOFAB, the hearings were similarly characterized by the double impasse I began to lay out in the previous chapter: an impasse between the biotechnicians and the artifacts of their work; and an impasse between an invitation to offer an ethical characterization of synthetic biology and the actual ability to connect such characterizations to the life and practice of the

science. This double impasse was actually also noted (albeit in an indirect fashion) by several Commission members. It was not resolved in the course of the hearings or in the report. In this sense, one might say that although circumstances allowed for participants in the hearing to experience and indirectly identified of a serious impasse between truth-speaking, ethics, and the exercise of power, those in a position to do something about such an impasse did not exercise their power in such a way as to affect any meaningful change.

The charter for the Commission's work reflected the wording and tone of several earlier bioethics advisory bodies: President Obama's Office wrote: "The Commission shall advise the President on bioethical issues that may emerge as a consequence of advances in biomedicine and related areas of science and technology. The Commission shall pursue its work with the goal of identifying and promoting policies and practices that ensure scientific research, healthcare delivery, and technological innovation are conducted in an ethically responsible manner." The wording and tone of the Commission's mandate is a clear departure from the previous administration's bioethical council, which had quite deliberately address questions which it considered simultaneously more philosophically fundamental and thereby less politically actionable. Indeed, members of the previous council had declared their distance from policies and other political practices a virtue of their undertaking. Central to the previous council's work were questions about what counts as worthwhile human life, how biotechnology constitutes new capacities to give form to or deform that life, and who, in the light of these considerations should be considered competent to make judgments about the future of biomedicine and biotechnology.[260] I was told by a member of the Presidential Commission staff that the strategic character of the contrast between the apparently straightforward and practical mandate of the Obama administration's Commission and the Bush administration's Council was not lost on those close to what was going on.

Amy Gutmann, the President of University of Pennsylvania was appointed to be the Commission's chair; James Wagner the President of Emory University, was appointed the Commission's vice-chair. In terms of both expertise and style the two were well-paired to carry out the Commission's mandate. Gutmann is an accomplished political scientist and a specialist in democratic theories of deliberation. Clearly practiced in managing and directing proceedings, she exhibits a refined grace and warmth while nonetheless controlling the agenda and the interactions. Wagner is an engineer by training; an expert on food safety and technologies of detection. Wagner displayed the sensibilities and plain-spoken manner of an engineer and the moderated expectations of a long-time participant in regulatory undertakings.

From the outset of the first meeting, Gutmann and Wagner struck a pragmatic tone. Gutmann in particular articulated a desire to move through meetings expeditiously, and intimated a desire to avoid questions and themes judged gratuitous. They stressed the need to move in a direct and straightforward fashion to the formulation of policy recommendations. With very little ceremony, Gutmann moved the inaugural meeting quickly to the invited presenters. Neither she nor Wagner provided a statement of philosophic orientation or political concern, neither provided meta-statements about the specific circumstances or the mandate under which the Commission's work would be carried out—departures from past precedents. All the speakers on the first morning were either biologists or engineers. Two panels of three speakers were assigned the task of setting the facts in order for the Commission, explaining what synthetic biology consists in, generally, and how the recent Venter Institute work should be situated in that general terrain. They were asked to specify how synthetic biology is like and unlike other technical

enterprises. Lastly, they were asked to forecast what the near term horizon of technical possibilities consists in.

Crucially, these speakers were given the opportunity to establish the initial terms of what it is that the Commission should take most seriously about synthetic biology. The titles of the morning sessions "Overview and Context" and "Applications," give something of an indication of the way in which these sessions were structured to provide the materials to which other sessions would directly or indirectly respond. The overview consisted in manifesto-like statements about the power and novelty of synthetic biology. Context referred strictly to technical considerations, taken up with some attention to economic forecast. "Applications" again centered on technical considerations: what synthetic biologists can or cannot make, how what they are making is likely to be used medically and industrially, and whether or not such applications open novel technical challenges in terms of safety and containment.

The structural and procedural effects of these morning sessions were crucial and (at least partially) determinative. The biologists and engineers were assigned the role of telling us the truth about what synthetic biology *is*, and doing so in such a way that the remaining experts might subsequently present salient considerations bearing on "potential medical, environmental, security, and other benefits of this field of research, as well as any potential health, security or other risks." The biologists in this way were positioned on the agenda to enter statements of fact into the record; other presenters were positioned to either respond or comment on these factual states of affairs, or to provide reports on the opinions of representative groups and other pertinent to non-technical activities. It would be too much to say that the structural and procedural effects of the morning sessions over-determined the contributions of the other invited speakers—as I will show. Nonetheless, they did help ensure that "the hearings were conducted in such a fashion that a specific mode of truth-telling was made to be normative."[261] That mode was performative, taken in a two-fold sense indicated by Michel Foucault, namely that "the given elements of a situation are such that when an utterance is made the effect which follows is known and ordered in advance, and that "the subject's *status* is important in a performative utterance [i.e. the subject's status authorizes the legitimacy of the speech act]."[262] The biologists and engineers were positioned to provide an account of the scientific reality in relation to which the other testimonies and comments could be measured as more or less pertinent. This performative determination of things made it unlikely that any explicitly ethical and epistemological directives would be made or authorized which departed from the technician's "overview and context."[263]

The first set of presentations were made by Drew Endy, Bonnie Brassler, a professor of microbiology at Princeton, and Rob Carlson, a physicist-turned-bioengineer and self-employed biotech analyst.[264] Endy's assignment was to provide the framing overview for the meetings. The Venter Institute's work, Endy insisted, was a significant technical achievement comparable to "printing an existing text." It was not yet, he insisted, the demonstration of a capacity to "write a new text." That "bio-integration gap," his talk concluded, was the real challenge and the real horizon of significance.[265] Brassler's assignment was to determine whether or not the work of the Venter Institute was not a "game changer." She argued that JCVI's accomplishment should be taken as a jump in scale and technical efficiency, but as more or less an extension of what biologists had been doing for thirty plus years: synthesizing DNA. She insisted that "they are not creating life."[266] Carlson was asked to map out trends in technological development and economic growth in synthetic biology. Connecting synthetic biology by way of analogy to other

technology domains he offered the familiar and under-nuanced warning that regulation of biotechnology will itself have possible negative and unintended consequences.

The questions that followed the first session exemplified a tone and introduced an agenda that would carry through the rest of the day, if not the meeting. This tone and agenda solidified the authority of technical expertise as the mode of testimony crucial to the Commission's bioethical evaluation of synthetic biology. Harvard Medical School Professor Raju Kucherlapati pressed Brassler to explain and expand the claim that synthetic biology is not qualitatively different than earlier technologies. He asked: "what has changed since the 1970s?"[267] Brassler's answered by emphasizing that although techniques such as PCR amplification have made it much easier to isolate and reproduce targeted DNA sequences, and although tremendous developments in computational technology and their use in genomics have provided biological researchers with much more data than ever before, things were not qualitatively different today either in synthetic biology generally or in the JCVI work specifically.

Kucherlapati's question and Brassler's response took for granted that the significance of the question at hand turned on an assessment of relative changes in technological development. The question of whether or not "anything had changed" since the 1970s was rendered as a matter of relative technological difference. The policy implications of such a framing are clear. If Brassler claims that basically nothing qualitative has changed, but that synthetic biology is essentially an intensification of previous capacities, then existing apparatuses simply need to be augmented. Such a framing not only brackets and externalizes the question of the relevance of the vast non-technical changes in the world since the 1970s—changes that are actually more relevant to determining significance—it simply ignores them. As other presentations in the day would *indirectly* demonstrate—and as has been a central premise of the human practice experiment from the outset—so much has changed with regard to the world within which synthetic biology has developed and operates that the technical question of whether or not quantitative increases in power and capacity amount to qualitative shifts in matters of harm or benefit can actually be dealt with in a more or less perfunctory manner.

Craig Venter was the first speaker in the next session. He began his presentation by delaying his prepared remarks in order to rebut Brassler's claim that nothing had qualitatively changed and that JCVI was not creating new life.[268] Granting that JCVI had synthesized a more or less unrefined (i.e. naturally occurring) genome and planted this genome in an "already existing host cell," he authoritatively declared that the work signified much more than "DNA synthesis at a larger scale." Brassler's sanguine reassurance, he argued, failed to account for the striking fact that after a very small number of population doublings every molecule in the host cell had been replaced by molecules fashioned on "instructions provided by JCVI's synthetic genome." Hence, the organism they had made was actually artificial. Moreover, he went on, JCVI had demonstrated the fact that biology today is at a stage in which researchers are no longer dependent on the sharing and transfer of physical materials. Rather, working anywhere in the world, they can proceed directly "from digital to biological information." The global circulation of capabilities was no longer encumbered by needing to pass materials beyond institutional or national boundaries. Today, all a bioengineer needs is a DNA synthesizer, synthetic chemicals, and a computer with an internet connection. Whether or not Venter cared that his comments put many on the Commission on the defensive was not clear. What was clear, however, was that Venter was ready to intensify the stakes of the question that Kucherlapati had put on the table and thereby the legitimacy of foregrounding technical novelty as the salient

factual and ethical matter at hand. He insisted that things had indeed changed. And the metrics for accounting the significance of that change were by his account altogether technological.

Venter's remarks were followed by two further presentations by biotechnicians, both of whom were competent and unsurprising, and inevitably overshadowed by Venter's provocations. The first was made by Harvard biologist George Church, who rather surprisingly advocated "surveillance" of work in synthetic biology; the second was a detailed assessment of current attempts to build synthetic biology applications by MIT biochemist Kristala Prather. Following these two presentations, the second question and answer session picked up where the first had left off. It was asked again: technically speaking, what is different? And given that difference, what new technical horizons are we likely to cross? A kind of baseline assumption was extended: that the significance of synthetic biology somehow depended on its continuity/discontinuity with previous technologies. And thus the objects in relation to which matters of significance could be judged and courses of action proposed could only really be determined by the technicians.

The biologists in the morning sessions were assigned the role of telling us the truth in answer to the question "what is synthetic biology?" The truth or falsity of the answers given to that question could, in principle, be challenged. (Though, with the exception of Venter's response to Brassler, no one actually offered such challenges). But under the circumstances one could not feasibly challenge whether or not the *kinds* of statements that were being offered by the biologists and engineers *counted* in the register of true and false. The testimonies of the biologists and engineers were entered into the record as precisely that class of truth claims which, however technically subtle, do not require any particular ethical status or personal commitments on the part of those speaking them or receiving them. They may require specialized knowledge to appreciate, formulate, or debate. But they do not require any particular state of the soul or moral commitments in order to be recognized as true. One might be tempted to say (and in fact Guttmann at one point did suggest) that the biologists offered facts as opposed to values and hence their statements about synthetic biology could be counted on as descriptions that subsequently needed to be ethically weighed. Something much more straightforward and problematic was going on. The biologists and engineers were authorized to speak the truth about the present state of affairs and thereby to set the terms and topics of concern.

Of course, everyone in the room was there precisely because the details of synthetic biology, insofar as they concern technical matters do not, in fact, speak for themselves. The Commission, like other bioethics advisory boards before them, is predicated precisely on a kind of assessment of the character of science offered by Max Weber almost a century ago: that whatever else science tells us, it does not tell us what to do.[269] It can, of course, provide clarity about what is actual and what is not. And in the first meeting of the Presidential Commission, it was the biologists and engineers who had been invited to provide this kind of clarity. The biologists, prompted and directed by the question of whether or not the technical artifacts being brought into the world by synthetic biology were especially new or unique, were actually authorized to tell us what significance these technical capacities held for the future.

The first meeting could be cast as a situation in which the biologists and engineers were given the privilege and authority of telling us what synthetic biology is and is not. They may not have been given any specific authority to tell us what to do, *pace* Weber. They could, however, as Gutmann would put it later in the day, provide "knowledge." In this way, she would add, it is up to the others testifying to give us "wisdom." Wisdom, she would remind us, consists in values, and values are criteria of judgment. A certain mechanics of ethical judgment were in

motion: science tells us what is true; ethics tells us how it might be positively or negatively valued. Or, more provocatively, claims offered by biologists and engineers are allowed to count in the register of truth in a way that ethical knowledge is not. Wisdom taken as judgments about the significance of the truth might seem crucial in that it indicates something about how to link truth claims to the formulation and exercise of power. But taken in this sense, wisdom does not need to tell us the truth, per se, but can perform the forensic duty of establishing points of deviation and conformity to norms. This arrangement might be taken as unproblematic (or at least unsurprising) if not for the fact that everyone sitting in the room was there precisely to address the question of how to determine the truth about the significance of synthetic biology, determine which problems count as especially pressing, and in that way open the way to possible solutions.

INSTANCE: KNOWLEDGE, ETHICS, RELIGION

I should be clear: non-biologists and non-engineers were certainly allowed to offer truth claims about states of affairs related to synthetic biology, its possible future ramifications, and its significance. Gutmann carefully facilitated the participation of a range of specialists, from experts on risk analysis, to policy analysts; from regulators, to civil society activists, to theologians. Hearing sessions were held on topics pertaining to "Benefits and Risks," "Ethics," "Federal Oversight," "Knowledge Sharing, Innovation and Translating Research for the Public Good," "Philosophical and Theological Perspectives," and so on. Not all of the expert witnesses for these sessions were biologists or engineers, clearly, and those who testified in these sessions were taken seriously in that they were allowed to present, were questioned, and had their contributions deliberated. The question—the doubt—is whether and how contributions made under the sign of ethics were allowed to count as true and thereby connected or not connected to the Commission's efforts to frame recommendations for the governance of synthetic biology.

Few testimonies actually provided direct ethical assessments of synthetic biology, or the kind of extra-biotechnical accounts of synthetic biology needed to formulate such directives. The better part of the testimonies offered by non-biologists and non-engineers were formulated as parameterizations of the technical state-of-play in synthetic biology relative to legal, regulatory, environmental, or opinion-based considerations. That is to say, these presentations provided considerations that would help the Commission take up the work of positioning synthetic biology in relation to metrics of prosperity and amelioration implied in its mandate. One philosopher and several social scientists offered accounts of how various population groups—groups from certain geographic or national regions, populations of a certain age, of a certain ethnicity, and so on—"perceive" synthetic biology. One civil society activist, one philosopher and one theologian purported to "represent" the views and concerns of certain constituencies. And several legal and regulatory experts as well as several senior government bureaucrats reported on the current state of affairs in US and non-US evaluation and regulation of biotechnology. Most of these first-order presentations purported to offer substantive truth-claims on matters adjacent and seemingly relevant to synthetic biology. They did not, however, consist in truth claims pertaining directly to the ethical status of synthetic biology or of synthetic biologists. Few even provided specific empirical claims about synthetic biology; most provided accounts of activities or lessons learned in analogous domains. Indeed, one philosopher frankly admitted what many others had papered over: that with regard to synthetic biology as a specific case of biotechnology: "I don't really have a specific recommendation at this point."[270] The Commissioners were offered a series of general sociological, civil, or legal variables that might be used to account for what synthetic

biology *implies*, how is likely to be *perceived* by various affected parties, or whether or not current *technical expertise* and regulation is likely to be sufficient for assessing and accounting synthetic biology's economic, environmental, or political impact.

In this light, it is perhaps not surprising that the remaining sessions on the first day of the Commission hearings frequently defaulted to an extension of the question posed in the morning concerning the relative difference of synthetic biology to past practices in bioengineering. This time the question framed those relative differences with an eye to questions of environmental impact and bioethical issues: are these technologies sufficiently distinctive to warrant new considerations of impact and do they actually raise new issues? Several of the afternoon presentations were not remarkable. These took it as a matter of course that their task was to determine whether or not synthetic biology, narrowly exemplified by the Venter Institute's work, really introduced anything new which might require different capabilities in evaluation, strategies for regulation, or programs of public education. This means that these same presentations neither sought to provide a better understanding of synthetic biology nor to directly provide ethical evaluations.

By contrast, three of the presentations were worth remarking on precisely in their deviation from the predominant orientation and in the failure of such deviation to produce any significant unexpected ramifications. The first of these three is worth remarking on for what it provoked, the second for what it failed to provoke, and the third for what it began to expose. The first was the presentation made by Jim Thomas, the Program Manager for the Action Group on Erosion, Technology and Concentration, or the ETC Group. ETC Group stylizes itself as a kind of clearing house organization for civil society activists concerned with the geopolitics of bioengineering, with particular concern for justice, land use and agricultural development. Thomas' presentation pressed, in vehement tones, the problematic relation between synthetic biology, the so-called "biomass" economy, and the politics of land use.[271] Thomas argued that if synthetic biologists continue deliver products such as biofuels whose underlying feedstock is biomass, then subsistence farmers worldwide will be pushed off even the marginal farmland that they now currently occupy by commercial and state actors interested in using that land for the production of such feedstocks. As such, he stressed, in the name of global justice there should be a moratorium on synthetic biology. Work should not proceed unless and until land use politics "especially in Africa and South America" are sorted out. Thomas refused to index the technical promise of synthetic biology to a ratio of risks and benefits pertaining to either economic growth or environmental amelioration.

In a fashion quite dissimilar to interactions in the morning's sessions, Thomas was pressed to justify himself and his right to make unequivocal claims about the economic character of synthetic biology and its geopolitical ramifications. He was asked why he did not think that the environmental benefits of biofuels could be balanced with questions of food production—"doesn't this enter into the calculus?" He was asked to justify his right to speak on behalf of some seemingly non-specific group—"the global poor?"—and was chastised by one member "I care about the poor too." Finally, the Chair concluded: "it seems to me that there are actually no feasible scenarios in which you would endorse this work going forward." In this regard Thomas could not actually help them fulfill their mandate, and therefore he indirectly challenged its sufficiency. No one actually responded to his central and seemingly self-evident claim that synthetic biology is likely to ramify in such a way that land use and food production will be impacted, and that such impacts would likely exacerbate existing injustices. And the

Commission's report effectively repudiated Thomas' central claims, stating: "these applications of synthetic biology are still young, the impact of biofuels production on land use remains unknown."[272]

If Jim Thomas' presentation is worth noting in that it provoked the commissioners to defend (however tacitly) the sufficiency of their mandate and their metrics, the presentation by Nancy King, a Professor in the Department of Social Sciences and Health Policy at Wake Forest's School of Medicine is worth noting for what it did not provoke.[273] King's presentation was the first to suggest that the modes of reasoning characterized by the Commission's mandate and the framing were characterized by several critical limitations. King acknowledge that her presentation was somewhat removed from the specific substance of synthetic biology. It was, however, a step closer to posing the question of the sufficiency of different modes of reasoning in conceiving synthetic biology as a problem for ethical consideration. King outlined several tactical lessons learned in dealing with what she took to be analogous technologies. Among those lessons were two that presented particular conceptual challenges to the hearing's direction and emphasis. First, King argued that the Commission, despite the wording of its mandate, should consider the possible *harms* of synthetic biology rather than its possible *risks*. Risks, she pointed out, are harms which have been made calculable. Moreover, such calculations are typically produced in relation to disciplines of risk-analysis whose objects and concerns have multiple data-points—a situation that does not seem to apply in the case of synthetic biology. She insisted that the more general question of harms was what was really at stake. The challenge that the Commission faced was to think about the kinds of harms that might be most pressing. The additional advantage of such a framing was that it did not over-determine the kinds of harms which could be taken seriously, i.e. it would allow the Commission to take seriously only those harms which might not be subject to familiar regimes of calculation.

King's second tactical lesson for the Commission was that pertinent ethical variables were often context specific, as was the significance of those variables. Knowing which contextual variables needed to be considered was therefore a key ethical responsibility. Given the focus throughout the day on the relative *technical differences* bearing on the significance of synthetic biology, King's emphasis on *contextual differences* struck something of a dissonant note. During the question and answer session following her presentation King was not asked elaborate on what contextual conditions might be most relevant to synthetic biology. Whether or not King could have answered such a request remains unknown. Later in the day, during the time allotted for public questions, I asked that any of the invited experts respond to King's challenge. Neither she nor any of the other bioethicists or social scientists responded.

The third presentation worth noting was made by Gregory Kaebnick, the editor of the *Hastings Center Report*. Where Thomas' presentation provoked immediate responses which indicated the limits of the Commission's mandate and suggested that Thomas' recommendations could not, in the end, be seriously considered and King's conceptual clarifications and modal suggestions failed to open up an alternative range of ethical problems, Kaebnick's presentation exposed an impasse.[274] This impasse consisted of the critical tensions between the invitation, implied in the fact of the Commission's existence, that ethical truth claims should play a role in governing synthetic biology, and the inability of the Commission to find a means of actually facilitating that role. Indeed, when Kaebnick's presentation exposed this impasse, it was quickly covered over.

Kaebnick's presentation took up the question of whether or not synthetic biology raises any new bioethical issues. In this regard Kaebnick's presentation recapitulated a series of publications and presentations developed as part of a larger Hastings Center project on synthetic biology. And indeed, Kaebnick narrative style was that of a reporter, speaking in the name of the Hasting study and not in the name of the ethics of synthetic biology per se. Stylizing himself in this way, Kaebnick proposed that the Hastings study had been predicated on a distinction between ethical issues of an "intrinsic nature" and ethical issues of a "consequential nature." Admitting that the distinction was not absolute Kaebnick nonetheless continued as if it was. Ethical issues of an intrinsic nature, he explained (perhaps unnecessarily), are those which are taken to be problematic regardless of the consequences. He proposed as an example arguments against embryonic stem cell research predicated on the moral status of the developing blastocyst, or arguments suggesting that recombinant DNA technologies are a violation of the order of nature. On the consequential side of the ledger Kaebnick cited environmental impact as an example. Kaebnick's framing was received as "helpful." Its central distinction between intrinsic and consequential as well as its treatment of "issues" as more or less timeless philosophic questions presented a categorical schema of the task and stakes of bioethics that no one on the Commission seemed initially uncomfortable with.

In explaining his use of the term "intrinsic," Kaebnick suggested that this category included those activities which would be taken as violating something sacred. He proposed that these "intrinsic" issues are usually only raised by "religions," that they were more or less "religious" in character. Issues of a consequential nature are presumably secular, though Kaebnick did not say this. He did imply, however, that consequentialist issues can count as problems for everyone, where intrinsic issues require some special set of commitments regarding the status of the objects being manipulated. Having arrayed what he thought were the key questions provoked by synthetic biology, Kaebnick concluded by saying that "as of right now" our study determined that there are essentially no ethical issues of an intrinsic nature that we need to worry about with synthetic biology. There are consequential issues, particularly concerning environmental safety and security, which will need to be attended to in due and prudent course.

Kaebnick's presentation raised three questions. The first was whether or not there are actually any examples of intrinsic issues in bioethics other than the two that Kaebnick introduced, and thus whether these are actually not categorical but specific. If so, it might subsequently be determined that the distinction between "intrinsic" and "consequential" may be insufficient as a primary ethical framing for synthetic biology. Hence a second question concerns what kinds of other ethical problems might actually fall outside of or across the distinction between intrinsic and consequential. The question of the ethical character and dispositional status of those involved in synthetic biology, for example (a question raised throughout this thesis), would seem to belie the sufficiency of this distinction. A third concerns the fact that what was counted as "issues" in Kaebnick's presentation seemed to be limited philosophical questions of long-standing, questions that might be posed in distinction from any particular situation or setting. That the notion of issues might be treated in this way is not particularly unusual in bioethics or other areas of ethical reasoning. But work conducted by the Hastings Center scholars often purports to foreground matters of historical specificity and context. Indeed, in at least one of the Hasting Center's publications on synthetic biology the question of context is explicitly raised, albeit only to ask whether or not issues of long standing are mooted or intensified.

Of these three questions, only the first was raised by the Commission members, and then only indirectly. The question was put to Kaebnick as to whether he could clarify what he meant by the term religion and why he connected religion to intrinsic rather than to consequential issues. Commission member John Arras, a professor of philosophy at the University of Virginia, raised the matter, asking Kaebnick directly to explain what the term religion might include and how, in that light, religious considerations might be included in the Commission's deliberation. After all, he suggested, given first amendment considerations, it isn't clear how the commissioners should incorporate matters of the sort Kaebnick was pointing to with his designation of "intrinsic." Kaebnick was obviously caught off guard by the question (admitting afterwards that he had not expected his use of the term religion to be taken account of and considered it to have been something of an incidental aside). And he deferred answering, suggesting that the connection of intrinsic and religion had been something of a convenience for those involved in the Hastings project and was basically an artifact of the particular examples he had offered.

As to the broader question of how religion might be included, he did not answer. Kaebnick was subsequently asked by Commission member Anita Allen, a Professor of Law and Professor of Philosophy at the University of Pennsylvania Law School, to justify his association of the terms intrinsic and religion. "I was surprised by that connection," she said. "Justice is central to my religious tradition and that would seem to fit in your consequential category."[275] Kaebnick did not respond.

However, Allen Buchanan, the other invited bioethicist speaking in the same session as Kaebnick, did propose a response. Religion and religious views, he suggested, should only be allowed to contribute on the same grounds that anyone else can contribute: it has to offer reasoned arguments for its position. It cannot, therefore, appeal to its premises, many of which won't be shared in a public setting. Buchanan was, of course, rehearsing a well-worn view, a view predicated less on a kind of legal argument pertaining to church and state, and more on a kind of tacit notion that, unlike religion, secular discourse can proceed without relying on a history of presumptions about the nature of the world or history or what counts as true or good. The obvious fact that such a view of things would essentially eliminate most of the substantive content of most religious traditions was not lost on Commission member Daniel Sulmasy, a physician and Franciscan Friar from the University of Chicago. How might such a trade-off between participation in public deliberations and substantive contributions be mitigated, he asked Buchanan. At this point in the exchange Gutmann closed the discussion and proposed to shift to questions from the audience. The question of synthetic biology, ethics, and religion and how to bring these three into a relationship that the Commission members might find productive was not returned to at that meeting.

THE DEMOCRATIC RECTANGLE

In his 1982-83 lectures at the Collège de France, Michel Foucault proposed that in order to analyze the relation of the truth-speaker to the exercise of power and to ethics it is helpful to distinguish between having the juridical *right* to speak in a situation where the exercise of power is at stake and the *capacity* to speak in such a way as to directly influence the exercise of power. Examining Greek (especially Athenian) democracy, the first was a matter of *isēgoria*: all citizens had an equally distributed right to speak in the agora; the second was a matter of *parrēsia*: only

some citizens were actually capable of speaking the truth and even fewer capable of speaking it in such a way as to thereby achieve a measure of authority. To repeat the epigraph above: "It has to be understood that true discourse is not and cannot be distributed equally in a democracy according to the form of *isēgoria*. Not everyone can tell the truth just because everyone may speak the truth."[276]

In democratic settings, this distinction between the *right* and the *capacity* to speak the truth authoritatively entails a second distinction: matters concerning politics (*politeia*) should be distinguished from matters concerning the exercise of power (*dunasteia*). In these Greek city-states *politeia*, politics, concerned constitutional and juridical matters and hence provided a framework within which the governance of the city would be marked by the equal rights of citizens to speak the truth. As a political problem, understood in this register, speaking the truth is only a question of the rights of citizenship. Does one have the right to speak the truth in the consequential setting of government as a member of those fellows who are also formally and juridically allowed to participate in governance? In the Commission hearings all of the invited participants had the equal right to speak the truth as a contribution to the work and task of framing recommendations for the bioethical governance of synthetic biology.

The second part of the distinction, *dunasteia*, refers to ruling or to being able to rule. It is thus a term crucial to politics but clearly not identical with it. It is a capacity term, referring to the actual exercise of power, often in matters having to do with strategies and techniques, and in the case of democracy, authority and persuasion. As a problem of the exercise of *power*, Foucault helpfully clarifies, truth-speaking is not only or even primarily a question of rights. Rather, it is a question of capacity, of *dunasteia*, that must be cultivated and attended to: the capacity of the citizen to exercise the right to speak in such a way that authority and the exercise of power are realized. The ability to successfully link *politeia* and *dunasteia* required the cultivated skills and disciplined virtues of the speaker: the ability to know the truth, to have the courage to speak it, and to have a love of the city sufficient to compelling them to speak up in the truth even in potentially costly situations. It also required appropriate circumstances: the status of the individual speaker's family, the speaker's military accomplishments, the stakes of the matter at hand, the relative ability of one's opponents in the agora, and most importantly, the ability of fellow citizens to listen. In the situation of the Commission hearings not all of the speakers were capable of speaking the truth in such a way that their contributions had an equal relation to authority and the exercise of power. And this inequality was only partially a matter of skill and courage.

In light of this distinction, Foucault proposes to examine a series of factors whose ratios, connections, and disconnections contributed to the deterioration of the relationship between truth, ethics and the exercise of power in Greek democracy. Among its many ramifications, this deterioration formed part of a shift in the venues of truth-speaking and ethics from the democratic *agora*, to the court of the prince, a displacement of truth-speaking in the citizen's efforts to exercise power to the philosopher's task of giving truthful advice to the prince. The crucial historical differences notwithstanding, Foucault's examination of this shift offers a certain analytic light relevant to the problem of ethics, truth, and power in the situation of bioethics and synthetic biology. Most relevant is the fashion in which Foucault proceeds in imagining the relations among politics, power, truth, and ethics as a kind of rectangle of relations. Like all schemas, Foucault's democratic rectangle comes at the cost of attentiveness to historically nuanced and specific forms and formulations. Nonetheless, it offers the analytic

advantage of breaking down complex relations into distinctive elements, which can then be aligned and tested in relation to one another. Foucault suggests that the elements of this rectangle (politics, power, truth, and ethics) must be given a certain interconnected form in situations concerning the exercise of power, situations in which the *right* to speak the truth is effectively actualized as *authoritative* in a democratic situation. Put briefly, the elements must be configured in such a way that truth remains in an active and effective relation to power.

At the first corner of this analytic rectangle Foucault places *isēgoria* as the formal condition for the possibility of connections among these relations: the presumption of some basic formal equality among those participating in the exercise of power. Hence, the *right* to speak the truth. In the second corner Foucault places what he calls the *de facto* condition of a good relation of truth and power, namely that among those who have the right to speak the truth there are those who exercise that right in a superior fashion. Which is to say, there are those who speak the truth with authority. In the third corner Foucault places what he calls the "truth condition." In order to have a good relation among the elements of the rectangle, the discourse offered by those with authority has to be a true discourse. It has to consist of an attempt on the speaker's part to bind himself publically to what he believes to be the truth (in the Greek city-state, of course, it was only men who were allowed to participate in these political games of truth and power). And lastly, in the fourth corner Foucault places what he refers to as the moral element. [277] The ability to link the right to speak the truth to actual discourses of truth and possibly thereby to achieve an ascendency to authorized truth speaking. The ability to speak the truth requires the willingness to confront those who also which to exercise power. This ability requires the cultivation of ethical capacities, especially prudence and courage.

At the first meeting of the Presidential Commission everyone who testified had the right to speak the truth. Some who testified were able to speak with authority—authority in the sense that their testimonies played a formative role in the proceedings, deliberations, and in the Commission's formal report. Most who testified purported to speak truthfully, at least in the simple sense that they did not appear to be willfully lying. The presentations by the biologists and engineers were framed as distinctively truthful, in simple statements concerning what synthetic biology is. Yet it is worth noting how frequently these presentations relied on analogy; no participating biologists related mundane details of day-to-day work, their actual results, their experimental failures, or the relation of synthetic biology to the development of their careers and research programs. Equally important is how frequently these presentations treated analogies as though they were identities: "genomes are software the writes hardware." In this regard, these presentations were characterized by "half-truths and half-lies"[278]: the testimonies offered were almost never honest about the fact that capacities and understandings are far less advanced and settled than one might think given their authorized status within the hearings—accept where making the case that there is urgent work to be funded and taken up. More importantly, these presentations almost never set current technological programs within the institutional and political settings that animate them and position them as uniquely worthwhile—would biofuels be funded at current levels if not for the Bush-era wars during which energy was strongly linked to questions of national security. The key point here is that the truthfulness of what the biologists were saying in their presentations could be taken for granted given the performative ethos of the setting within which the presentations were offered. And hence, the truth content of the biologists was almost never challenged by the members of the Commission, although the claims being made by the various technical witnesses clearly did not provide a consistent and homogeneous account of synthetic biology.

And, hence, in this regard, the fourth element of Foucault's analysis, the ethical element only entered into the proceedings in a circumscribed manner. Most of what was presented did not demand the cultivation of the ethical capacity to speak the truth courageously. Of course, given the high profile of the hearings many presenters were no doubt nervous about whether or not they would successfully carry out their performance; the courage to perform per se, however, does not concern the ethical element in the sense that Foucault was proposing. The ethical element, rather, came into play in terms of whether or not presenters spoke in a fashion coherent with the metrics of the Commission's mandate, and in a fashion which more or less left the task of defining synthetic biology to those competent to address technical considerations, biological, economic, and legal. And even in these technical cases surprisingly little was actually said about synthetic biology with reference to concrete specifics. Said differently, few of the presenters offered testimonies which would be difficult for the Commission to accept as part of their analysis and recommendations. There were no "irruptions of the true discourse" that might "opens the situation and makes possible effects and makes possible effects which are precisely not known," to quote Foucault. And even where such testimony was offered that might possibly have unsettled the proceedings (e.g. definitive accounts of synthetic biology and its significance at odds with the conclusions of the biologists and engineers; or the elaboration of ethical metrics that are not covered by prosperity, amelioration, and risk; or directive statements about what synthetic biologists should be made to do or not to do), such testimonies were predominantly offered as reports on *other people's opinions* or as *generalized admonitions* about the good or safe practice of biotechnology and thus admonitions not yet entailing anything specific that might require a change of habits on the part of synthetic biologists.

Hence, and in this light, places where presentations fell outside of, cut across, or otherwise put in critical question the Commission's mandate, the state of play in synthetic biology as defined by a narrow focus on technical considerations, or a tacit commitment to scientific self-rule were unusual, striking, and ultimately inconsequential. Sustained presentations of this kind might have posed a problem for the Commission: how to extend authority to those presenters whose right to speak was being exercised in such a way as to present the stakes and significance of synthetic biology as a matter not only of the environmental, political, or economic status of the objects made as well as their use and circulation, but of the ethical status of both artificers, their habits, dispositions and practices, and only thereby an examination of the ramifications of synthetic biology's artifacts? Truth-claims which may have required, demanded, or even foregrounded the cultivation of the moral element of the democratic rectangle on the part of the speakers were ultimately covered over by the dynamics of politesse and their reduction to deliberative opinions: "Welcome this morning. We look forward to your comments. Well, thank you. It's a pleasure to be here. I'd like to thank Dr. Gutmann and the whole Commission and also—also thank your staff which I think have done a great job in terms of supporting everyone who has been involved?"[279]

Two presentations stand out as relatively more ethically directive in tone and substance. The first was given on the final day of the first hearings by Paul Wolpe, the Director of Emory University's prominent and well-funded Ethics Center, and a past president of the American Society for Bioethics and Humanities.[280] Wolpe's testimony was unusual in that it foregrounded the ethical salience of the relation between the ethical character of the engineer and the ethical status of the engineered artifact. Given the short summary of his presentation I provided in the previous chapter, I will only repeat a few basic points. Wolpe's comments were offered in response to the assignment that he provide "religious perspectives." He admitted that his

qualifications with regard to synthetic biology consisted in "having spent a few weeks reading the literature" and having spoken "to people from a variety of faith traditions." He had very little to say in direct response to this literature or to report from his conversations, other than to assure the committee that things were still too new, and that none of the "high placed" religious leaders he spoke to had any *a priori* concerns. Wolpe spent the bulk of his testimony providing comparative analysis of the spiritual lessons learned from the Frankenstein and Golem stories. The crucial point that he stressed was the need to consider the ethical stance of the *maker* of novel life forms in relation to the ramifications of having *made* those life forms. Wolpe proposed the need for synthetic biologists to cultivate dispositions and practices of humility, care, and prudence He concluded prospectively, suggesting that synthetic biology be oriented less by the avoidance of evil and more by a positive vision that can function to delimit and focus energies and resources.

The second testimony that is worth mentioning in light of the analytic element of the democratic triangle was given by Sondra Wheeler, a Professor of Christian Ethics at Wesley Theological Seminary.[281] Wheeler's presentation was given at the second meeting, and she singled out similar themes as Wolpe. What is worth attending to in Wheeler's presentation is that she stressed ethical metrics that were not obviously reducible to the risk-benefit terms of the Commission's mandate. Wheeler spoke in a session dedicated to "Theological and Philosophical Perspectives," and was assigned the task of telling the Commission what a "Christian perspective" on synthetic biology might consist in. Despite the title of the session her conclusions, like Wolpe's, were not, strictly speaking, perspectival, but rather included several strong assertions about the appropriate ethical dispositions for undertaking the production of artificial biological systems. In her testimony wheeler explained that questions concerning the creation of life were central not only to Christian theology, but to long-standing considerations of ethical practice and the formation of the spiritual life. The theological proposition that God created, she informed the Commission, is often put forward as a means of stressing divine power and eminence, and therefore a qualitative difference in status, roles and capabilities. Such emphasis covers over the salient fact that themes of creation in Christian theology equally stress matters of divine responsibility for the care and sustenance of creation. It follows, she suggested, that "the vast and growing human powers are at once a divine gift and a sort of test," a test whose results can be indexed to such metrics. Poignantly, it is a test most often failed. She offered the wry observation that "the human propensity for evil is the only Christian doctrine for which the empirical evidence is overwhelming."

Wheeler foregrounded the question of how humans generally, and bioengineers in particular, should structure and cultivate their relations and habits so as to tend to questions of human flourishing: "If human flourishing is social and relational, the nature of human evil is deeply corrosive, destructive of the connections between us in favor of the pursuit of individual or group advantage at others' expense." She then posed a question: in what fashion should engineers take up the power offered by synthetic biology? A satisfactory answer to that question, she argued, must be less a matter of rule-making and regulation—though these cannot be taken for granted—and more "the inculcation and sustenance of certain attitudes, habits of mind, and dispositions." "In short," she asserted, "for our rules to work will require the intentional formation of character, as an indispensable part of scientific education." Concluding by offering general guidelines for such a formation Wheeler called for ethical pedagogies which couple technical optimism and prudence, attention to affect as well as intellect, humility as well as ambition, and the fostering of self-distrust in relation to self-confidence.

Wheeler was not asked to clarify or expand; Wolpe was asked two questions about how religious objections could feasibly be taken on board given the non-religious setting of the Commission's work. More significantly, neither was asked to say anything about specific about synthetic biology and about how ethical pedagogy and the cultivation of dispositions such as humility, care, prudence, or self-distrust might be formed in relation to the specific situations of synthetic biology. No doubt at least some of the Commissioners agreed with Wolpe and Wheeler that a sufficient program for formation of synthetic biology would include just such an ethical pedagogy. It would have been reasonable to ask what such pedagogy consists in with regard to specific developments in synthetic biology as well as how such pedagogy might be actually be undertaken and made mandatory. Works in the and anthropology history of science have demonstrated what both Wolpe's and Wheeler's presentations seemed to take for granted: that the habits, dispositions, and capabilities of those engaged in the life sciences today are realized in significant part through more or less informal and tacit regimes of moral education.[282] These regimes are no doubt always partially individual, and hence to the extent that they are reflected on require a form of *phronesis*, practical wisdom. The question should have been: where and how exactly are synthetic biologists being formed today, what are their career trajectories, what capacities are they cultivating, which are they giving up, and what exactly are they able to do and to make as a result of these pedagogical formations—questions which have proven centrally important to work at the BIOFAB.

The experiment in Human Practices, as I explained in the prologue, was formulated in part as an effort to foreground and conduct inquiry into these formative situations that demand practical wisdom and the cultivation of ethical capacities sufficient to the demands and challenges of synthetic biology as it is actually being assembled, branded, and elaborated. The challenge from the outset has been to give these situations a conceptual form as problems of ethical pedagogy that would open up the possibility of formulating possible solutions. The experiment has been rife with difficulties and blockage. Not least of which is that those with access to power (even where sympathetic, as seems to have been the case with the Presidential Commission) have not yet exercised power in such a way that such ethical pedagogy—at once a matter of character and disposition, of the organizational forms and the biotechnical artifacts that they do and do not actualize, and therefore the vocational stakes and ramifications of synthetic biology—could be designed, put into practice, and experimented with in a sustained and rectifiable manner.

Only one question was asked of Wolpe and Wheeler that might have opened up the problem of how to link the need for ethical pedagogies with the specifics of synthetic biology and thereby to the possibility of formulating a program of implementation. Wolpe was asked to provide examples of the kinds of near-term "positive visions" he had in mind when speaking of the need to orient synthetic biology. His response was to say that synthetic biology was too new and that he was not qualified to speak to these things. He then offered an analogy: as in medicine where institutions such as the NIH decide priorities for health research, so too in synthetic biology funders and regulators should think about what positive vision of the future might be formulated. In sum, despite the effort on Wolpe's and Wheeler's part to foreground the problem of the ethical formation of synthetic biologists, neither was asked or offered to speak to how such formation should be organizationally instantiated, connected with the actualities of synthetic biology, and hence interfaced with the micro-political realities of settled habits, reward structures, and power relations. In this sense, despite foregrounding ethics, neither spoke in a reconstructive mode—i.e. neither offered insights that might have addressed the specific

situation at hand in such a way as to locate what they were proposing in the concrete actualities of the practice of synthetic biology today.

Neither Wolpe's nor Wheeler's recommendations were included in the Commission's reports in anything like a direct, substantive, or prescriptive fashion. Which is not to say that they were excluded. Both were directly cited. And Wheeler's testimony was quoted in a key passage concerning religious perspectives. But that quote, as with the direct citations, were framed as the kinds of statements the Commission and others might reasonably agree with. The quote from Wheeler, for example, did not include her formal recommendations, but only her theological point of departure. Neither Wolpe's nor Wheeler's testimonies were explicitly connected to recommendations for governance and action.

It no doubt could be argued that these two testimonies did play a substantive role in the Commission's deliberations, albeit in an indirect fashion. As explained above, the notion of "prudent vigilance" was presented as a central theme of the Commission's report.[283] This notion was presented differently in different sections, but basically was put forward as a call for the development of standing capacities for ongoing monitoring and reflection on the Commission's key domains of bioethical concern—public beneficence, responsible stewardship, and so on. The emphasis placed on the cultivation of dispositions adequate to the ethical practice of science is certainly consistent with the Commission's guiding notion. And it is particularly consistent in view of the fact the report makes frequent reference to the need for biologists and engineers to pursue their work in a fashion consistent with this emphasis. But the report rarely specifies anyone other than the technicians who might be responsible for adopting a stance of prudence and vigilance. In its recommendations it frequently mentions agencies and offices of the federal government who need to think further about particular issues (e.g. intellectual property, environmental safety, funding priorities), but it almost never goes so far as to specify who other than biologists and engineers should be prudent and vigilant, and what, if any, powers to intervene in scientific practice such a prudent and vigilant observer might be allowed.

The closest the Commission report comes to a substantive response to the ethicist's testimonies is in a section called "Creating a culture of responsible stewardship," and in the recommendations portion of that section under the heading "Ethics Education." Having noted again that it is the biologists and engineers who will be in a position most capable of implementing any recommendations pertaining to responsibility, and oriented toward their section on "intellectual freedom" in which the Commission endorses a minimization of mechanisms for governance, the section on "Ethics Education" acknowledges the need for ethics curriculum to be built into technical training. In this light, they recommend that "the Executive Office of the President, in consultation with the National Academy of Sciences, the National Academy of Engineering, the scientific community, and the public, should convene a panel to consider appropriate and meaningful training requirements and models." Such a recommendation is certainly consistent with Wolpe's and Wheeler's proposals for the cultivation of certain ethical dispositions on the part of biotechnicians and the adoption of certain ethical stances in the pursuit of biotechnical work. In fact this section might be said to follow from the thrust of their testimonies. It bears noting, however, that nowhere in this section do the specifics of the two testimonies come into play. It is not proposed that the Office of the President, the NAS, the NAE, or anyone else create ethics programs for the cultivation of humility or appropriate affect or self-distrust. It is not even proposed that the Office of the President, the NAS, the NAE, or anyone else think through what such ethical dispositions might mean under the specific

circumstances created by the development of synthetic biology. And it certainly does not make any recommendations about how such ethics education would be put into practice and enforced. In short, even at this point of relative connection to the testimonies of the ethicists, the truth-claims made in those testimonies are not actually put into even a recommended relation to the exercise of power.

It might be supposed that it was outside the purview of the Commission to make strong recommendations about which specific ethical disposition should be cultivated, which ethical pedagogies should be mandated, and who should be responsible for enforcing such a mandate. Except that the Commission's mandate explicitly called for policy recommendations, recommendations the Commission seemed hesitant to make in a concrete and directive fashion even with regard to topics such as environmental safety, the freedom of scientific research, and the need to foster governance structures predicated on a preeminent concern for innovation. Indeed, it is a striking feature of the report that its strongest ethical language, such as emphasis on a principle of public beneficence or responsible stewardship, assumes, as more or less a matter of course, that innovations in synthetic biology will provide a means of fulfilling an ethical vision of the near future, as long as risks can be mitigated.

One place in which one might have expected the recommendations made by Wolpe and Wheeler or other self-identified ethicists to be incorporated in a more substantive and evident fashion is in the section entitled "Weighing Moral Objections." Wheeler was especially clear in her presentation that the capabilities put into play by developments in synthetic biology should be understood as a kind of ethical test, a test whose failure is marked by the evils of exploitation and domination. Indeed it is in view of such possible failures that Wheeler recommends humility, prudence, attention to affect and so on. This section, however, functions as something of a *cordon sanitaire* against those who articulate "intrinsic objections" to synthetic biology. It functions this way in an indirect but effective manner. In the first place it connects the fact that "intrinsic objections" have been raised in relation to other developments in biotechnology to the political fights over stem cell research and cloning. It thereby ignores the possibility that one might have intrinsic objections having to do with the stance and status of researchers and not only the metaphysical character of certain objects of biological intervention. In this way the report introduces the rather obvious and loaded comment that these objections have "led to direct policy consequences in other areas of biomedical science and technology."[284] It offered no judgment one way or another as to whether or not such consequences might be worthwhile, justified, or illegitimate.

In a curious but effective manner, the report also seals off any serious consideration of ethical objections by actually admitting the worth of conversations about such objections, but also assiduously avoiding any statement about the conditions under which enforceable ethical requirements (let alone ethical practices) might be made to follow from such conversations. The report reads: "These varied concerns [i.e. ethical objections] are quite valuable, however, in calling attention to fundamental, challenging questions regarding how to best understand interactions among humans, technology, and nature beyond the limited context of synthetic biology. To what extent and in what valuable ways are the many different kinds of life on earth more than the sum of their standardized and non-standardized biological parts? Such discussions and the related attention they direct toward potential objections to synthetic biology will surely continue as the field matures, as well they should."[285] Conversations about objections to synthetic biology are worthwhile because they direct attention. Having had their attention

directed, however, the Commissioners assert that synthetic biology does not introduce "unique concerns that are so novel or serious that special restrictions are warranted at this time." The question, again, is whether or not synthetic biology is new enough to warrant any new action. The question is certainly not whether or not the world is such that synthetic biology warrants action, nor whether or not the existing apparatuses are sufficient. The Commissioners tell us, however, that they are not closed to the possibility that ethical objections might lead to action. And indeed they offer Recommendation 10 "Ongoing Evaluation of Objections," in which they write: "Discussions of moral objections to synthetic biology should be revisited periodically as research in the field advances in novel directions."[286] Discussion is the key term here and is framed as though it offered more than it actually does. Specifically who it is that should be having these discussions and what the point of these discussions might be in terms of any attempt to intervene in the practices of synthetic biology is left to the side. Unlike other recommendations, there is no attempt to identify real venues, real agencies, real actors with access to real power who might play a role in such periodic discussions.

Serious objections to synthetic biology actually have been raised; and the Commission actually offers examples. But in offering these examples, the Commission introduces a shift in its narrative style. The objections cited are directly attributed to specific authors and attributed in such a way as to simply bracket the question of whether or not the objections are substantive and true. Objections, rather, are things raised by specific individuals or institutions and not necessarily a matter of grave and shared concern. In other sections, on topics such as intellectual property, the Commission is similarly non-committal, and seems to take as a virtue the presentation of multiple sides of an issue as if all sides were equally warranted. Not even this perfunctory attempt to weigh the merits of the matter is offered here. Ethical objections are treated as the kinds of things that various constituencies raise. They are not treated as the kinds of things that are susceptible to reasonable consideration, or the kinds of things that the Commission should have to take a position on. The Commission's stylization of ethical objections is curious on some level. Minimally one would think that they could at least have agreed with Wolpe that the cultivation of care is needed or with Wheeler that affect plays as important a role as intellect. Such agreement would likely not have been coupled to enforceable recommendations in any case. In short, the ethical stakes of the relation of the right to speak to capacity to speak in a manner that results in the actual exercise power turns on the ability to speak truthfully and thus on the ethical labor of forming oneself in such a way as to be able to speak truthfully. The Commission effectively encumbered this link between truth, power, and ethics by making ethical objections a matter of opinion, *doxa* not *logos* as it were.

The Greek city-state is obviously not an advisory board. The situation in bioethics and the scene at the first meeting is unlike the situation and scenes that form the substance of Foucault's analysis. Among the salient differences is the fact that the Commission members are not really in a position to link the right to speak the truth with the capacity to exercise power. Bioethics remains advisory, after all: the Commission has an advisory role to the president; the invited experts have only an advisory role to the Commission. In this regard, what Foucault has to say about the relation of truth, power, and ethics in a non-democratic situation—as philosophical advisors to the prince—may be more pertinent.

Nonetheless, it seems to me that the elements of Foucault's analysis, and the problem of how these elements are brought into relation, proportioned, and given form are worth attending to. Of particular importance, I would argue, is Foucault's diagnosis of the conditions under

which relations among truth, ethics, and power become ill-proportioned and ill-formed. To this end Foucault examines the ways in which, in Greek city-states, deteriorations of the third corner of the democratic rectangle—true discourse—ramified in such a way as to eventually compromise the others and contribute to the deterioration of democratic rule. Despite the preservation of the formal right to freely speak the truth and despite the fact that certain individuals continue to exercise that right in such a way as to achieve authority, this right and this exercise become detached from the effort to speak truthfully. The result is those who actually exercise power are those who appeal to flattery in order to achieve the ends of power and glory. Foucault cites the famous passage on the failures of democracy in Plato's *Republic* as exemplary of concern for the corrosive effects of flattery. The democratic situation, Foucault points out, contains the seeds of its own undoing: the right to speak the truth is the formal condition wherein those capable of knowing the truth and speaking the truth can exercise authority. But it is also the formal conditions needed for the ascendency of those who are not willing to undertake the moral cultivation required for such truth-speaking, and who, in any event, seek to rule by simply telling the people what they want to hear .

The relation of truth, power, and ethics in the Presidential Commission—and perhaps equally in other settings in which there are attempts to bring ethics into a single frame with technology in order to govern the possible ramifications of technological development—is suffering a different impediment and different corrosive. The main problem with these elements and their relations and proportions is not that those speaking with authority have turned to flattery and are no longer committed to true discourse—although such commitment can certainly not be taken for granted. The problem, rather, is that truth speaking is compromised by the constant need to promise the goods of health, wealth, and security, by the needs of communication to ever wider audiences, and by the flattening of ethical directives by the dictates of opinion and deliberation. In the case of the hearings, as I've pointed out, many of the technical presentations relied heavily on analogy to guide their assessments. Moreover, too many of the expert witness actually knew very little about synthetic biology specifically, and so introduced talking points about biology, technology, regulations, opinion polling, or bioethics in rather more general (and therefore less accurate) terms. The principle impediment and the principle corrosive, in this regard, was not flattery. It was, rather, the fact that only certain kinds of testimonies actually got to count among those which were taken up and taken up seriously in the Commissioner's recommendations. Using the terms of Foucault's analysis, only certain kinds of truth discourses got to count in the *de facto* exercise of power. This means that despite being authorized to speak the truth, some invited witnesses were not actually in a position to do so in a way that would effectively connect with the exercise of power. These were testimonies that stayed true to the performative specifications of the situation. The price to be paid for being able to say something beyond those specifications requires the disciplined labor of cultivating the capacities for sustained and engaged inquiry, a labor that was simply not asked of those who were invited to testify. This was true not only of the technicians asked to speak about the relative technical distinctiveness of synthetic biology. It was also, and more disappointingly true of those whose task it was to foreground the ethically relevant details of the situation at hand. To borrow Jim Faubion's useful term, those whose task it was to situate synthetic biology within an "ethical field" of relations remained both unauthorized and yet capable of speaking in a mode that might have disrupted the terms of that blocked situation.[287]

CHAPTER 8

Problematizing Modern Problems: Ethics and Science

> *In reality,* logos *is complete only if it can lead to* ergon *and organize it according to the necessary principles of rationality.*
>
> —Michel Foucault[288]

In chapter 4 I explained that when asked what he thought about having an embedded ethicist as part of the BIOFAB, Endy responded: "Bennett is not an *embedded* ethicist; he is a *member* of the BIOFAB." From the outset Endy made it clear that he had supported my participation in the BIOFAB with the expectation that the facility's goals and mandate would be taken as my own, even if I also intended to make the BIOFAB's work and my contributions to it an object of anthropological inquiry.

In a gesture of full membership, shortly after inviting me to take a position as the lead of Human Practices at the BIOFAB, Endy also invited me to participate in a closed-door meeting sponsored by the National Institutes of Health and the National Cancer Research Center. The meeting was held in Washington, D.C. in early April. The purpose of the meeting was to determine whether or not these two institutions should invest in synthetic biology. I was the most junior participant and one of only two participants from the human and social sciences. I was also the last to present on a 10 hour, one-day agenda which included many of the principle US biologists associated with the notion of synthetic biology: including Endy, Adam Arkin, George Church, Ari Patrinos, and Craig Venter, among others. Prior to arriving at the meeting I had been coached on the appropriate genre of presentation. "Offer plausible answers to difficult questions. No one wants to hear about blockages and problems. Synthetic biology is an opportunity." My impulse actually had been to foreground the critical limitations and difficult lessons learned in the years of working with SynBERC: the price to be paid in terms of power and protection entailed in shifting from a cooperative to a collaborative mode of engagement independence; the persistent ambivalence in the definition of synthetic biology which were continuing to intensify the politics of career adjustment; the need to establish mechanisms whereby embedded ethicists my work both within and without technological settings, and so on. I attempted to frame criticisms as opportunities and thereby split the rhetorical difference. My presentation went fine. Surprisingly, given the time of day, I was even asked several questions and told I was "understandable."

During the reception which followed I had an exchange with SynBERC PI Wendell Lim, which was quite remarkable, and worth considering. Speaking in a casual manner Lim asked: "how does it feel to be SynBERC's trophy wife?" Two facts blunted the impact of his question. First is that I am on basically friendly terms with Lim. At SynBERC and other synthetic biology events he is willing to chat, he says the door of his lab is open, and, at least over drinks, he is philosophically inclined. Second and more importantly, is that Lim asked the question as though he weren't saying anything offensive—as one member of the club to another.

The day following the Washington meeting I sat for my oral examinations in preparation for this thesis. In the wake of the meeting, the stress and the stakes of the examination were both increased. Participation in the meeting had been stultifying: the affect of simultaneously being invited to participate in a situation of possible consequence, but only on the tacit condition of remaining a minority participant. That stultification became a theme of the orals. All of the committee members posed the same question, in one form or another: what is work did I need to do on myself either to carry the experiment forward, but carry it forward knowing that the formal stakes of the engagement could no longer be framed in terms of contributing to the formation of the facility or the bioengineer, or, if such a remaining in the experimental position continued to be too stultifying, then what work would I need to do to exit the situation, and end the experiment?

A number of days later I attended a public lecture at UC Berkeley by anthropologist of religion Webb Keene. During the question and answer session Keene made the remark that in the modern world religion completes ethics.[289] Keene is one of a cadre of contemporary anthropologists in the tradition of work that seeks to show the extent to which modern notions of distinct spheres of value (e.g. the public and the private, the secular and the religious, the economic and the political) and modern notions of the individual subject are actually predicated on and thereby connected to prior formations and conceptions, which included a predominance of thing religious, particularly. Given this particular legacy Keene's comment had a double effect. In the first place it drew attention to the fact that ethics has often been figured as private, personal, volitionist, resolutely a matter of values. As an extension and completion of religion, therefore, however internally coherent it may be, ethics always involves either something of an extra-rational component of belief and or personal commitment. Even where ethics turns on such seemingly de-personalized goods as rights, health, or prosperity its legitimate place in the world lies with the individual. In this way and in this spirit religion and ethics can be coupled and framed as though they have no proper place among things public, matters factual, and secularized. The second effect of Keene's comment turned as much on the delivery and context of Keene's comment as on its content. Keene spoke broadly and seemingly off-handedly, as if to remind everyone that such notions of religion and ethics are, of course, recognizably modern and liberal. They are therefore culturally peculiar and even parochial, in the sense of historically local—whatever their now-global instantiations and ramifications.

Perhaps part of the reason Keene could speak off-handedly, was that his work and the work of several other anthropologists in the audience had shown that in fact, in actual practice, even in those places thought to be most obviously modern and liberal, things are always much more complicated. It struck me listening to Keene that however historically particular these notions about religion and ethics may be, and however specific and distinguishable their institutional forms and practices, they are not for that reason any less real, the force of their ramifications any less puissant, and the institutional and existential difficulties they produce any less challenging. Domains and values designated by the categorical terms like religion, science, and politics, have in fact been distinguished and externalized relative to one another as something like "spheres" of value. The trouble today is that having been distinguished and institutionalized they are currently in the process of being reassembled. Which means that these distinctions and their conceptual and practical legacies are not going away; and it means that sites of possible reassemblage do not necessarily involve any significant changes in norms and forms of truth speaking or in the exercise of power. It is evident nonetheless that the character of previously settled relations are being reconstituted in response to different problems and as such

are likely to operate in the world with an adjusted logic and significance. The question is: what to do if one plays a participatory role, however minor, in these unsettled spaces? Perhaps the most one can hope for is that such re-assemblage creates the space, resources, time, and institutional protection for modest experimentation with what Rabinow and Dreyfus termed "marginal practices."[290]

THE ETHICAL FIELD AND BIOETHICS

In the last chapter I began to work through elements of an impasse between the right to participate in the hearings, the ability to speak the truth with authority, and the uncertain place of ethics in this relation of truth and power. I identified Paul Wolpe's and Sandra Wheeler's presentations as being perhaps closest to troubling the performative settlement of the hearings, a situation in which the biologists and engineers were empowered to tell us the truth about synthetic biology and the others were invited to comment on how things human and environmental might be effected by such developments. Wolpe and Wheeler offered clearly stated ethical directives. The shortcoming of their presentations is that they said almost nothing about synthetic biology, and even less about the specifics of the contemporary assemblages into which synthetic biology is being brought into existence. To this extent, their admonitions to humility, care, prudence, or flourishing were left unconnected to anything specific enough to have required a change of behavior on the part the bioengineers. Perhaps this was not their job. After all, it is the Commissioner's task to make recommendations. It was the ethicists' assignment to provide perspectives. It was not lost on some of the Commissioners that both Wolpe and Wheeler offered their testimonies under the sign of *religious* perspectives; in this respect perhaps it comes as no surprise that the substance of their comments (however general and non-specific to synthetic biology) did not appear in the Commission's final report. Although formalized connections between religion and ethics are a recurrent feature of US bioethics, how to include such connections in the governance of the life sciences has never been satisfactorily settled.

The problem of ethics, truth, and the exercise of power—or, more exactly, the inclusion of those designated as responsible for speaking in the name of ethics and truth in the exercise of power—is not unique to bioethics. James Faubion has argued that serious contemporary thinking about ethics continues to labor and even falter under the constraints of the assumption that ethics is less a matter of truth or even practice and more a matter of beliefs and commitments.[291] A primary, if basic, task of thinking is thus to get clear about what ethics might consist of beyond these constraints, designing possible courses of action, and, where possible putting such designs into practice. For those moving toward such an end, Faubion regrets that there is little consolation in "modern philosophy," which is likely to prove "less an aid than a further hindrance." As a clarification Faubion explains that, "On the one hand, Immanuel Kant and his diverse successors have insisted upon the subordination of the 'good' to the 'right,' of the consequential to the deontological. On the other hand, utilitarians and the majority of their conventionalist and subjectivist confreres have objectified the good, but only at the cost of reducing it to what one or another person (or community, or society, or civilization) believes it to be."[292]

This double limitation—a failure of ethical theories of the good on one side and the reduction of ethics to the desires of particular constituencies—has left professional philosophers generally wary of committing substantive proposals to the cause of bioethics and the governance of the life sciences. That's the diagnosis put forward by Albert Jonsen in his history of the short

life of bioethics.[293] Jonsen proposes that in the late 1960s a small cadre of elite scientists and doctors had become vocal about what I earlier cast as the Weberian limitations of the technical sciences: that whatever else the sciences can do, they cannot tell us what we should do. Jonsen's history foregrounds the role of technological innovations as the principal contributing to the creation of situations (well studied by human scientists and philosophers of science) in which direct appeal to the details of the technology itself was clearly insufficient for guiding scientific practice. Jonsen suggests that such innovations intensify a kind of realism on the part of biomedical researchers and physicians about the limits of their capacities to sort out the situations in which they find themselves. These scientists, and subsequently certain political figures such as Senators Mondale and Kennedy, begin to invite non-technical scholars (i.e. theologians, philosophers, and lawyers) to help identify and think through the most significant problems. Jonson further suggests that in the course of undertakings which followed it was primarily the theologians and not the philosophers who were willing to offer directive assessments of the ethical status of scientific practice. The habits of the theologians suited them to making normative claims about the world. The philosophers in this telling were more suited to formulating conceptual clarifications and vetting forms of argumentation.

Jonsen's *telling* of the history is, in places, anthropologically uncomplicated; the events he describes, however, are perhaps more fraught then his narration of them might suggest. Jonsen does not directly take up such questions as what has changed by the 1960s so that researchers who had been working on human subjects studies for 30 years were suddenly more sensitive to the ethical stakes of their undertaking. And his account of this division of labor between theologians and philosophers is centers on the differences between select figures and does not emphasize that several of the leading bioethicists were students of philosophers such as Hans Jonas, Hannah Arendt, and Leo Strauss. Although his history indicates a persistent friction and even hostility to the notion that non-biologists and non-doctors should be allowed to influence the actual exercise of power in the governance of the biomedical and biotechnical sciences, he does not comment on the fact that this friction and hostility is basically resolved by ensuring that bioethics remains in an advisory relation to government. He does not foreground the fact that those theologians and philosophers participating in the early formulation of bioethics were personally and institutionally connected to both the elite researchers and politicians who ultimately agreed to leverage their connections to animate the meetings within which bioethics became formalized. He mentions, but does not foreground, the fact that the micro-politics of the early meetings of these boards were sometimes fraught with tension over who was authorized to define agendas, legitimate modes of reasoning, styles of argumentation, the priority of expertise and so on. And, crucially, he mentions but does not comment on the fact that the theologians and professional ethicists who were involved never actually got to participate in a manner that was straightforwardly connected to the substance of their traditions of thought. Rather, theological propositions were mediated by way of principles which presumably could be supported by those who were non-religious. Or, as Jonsen puts it, theological *commitments* were given putatively non-theological articulation. Bioethicists, whether trained as theologians, philosophers, or otherwise, were not expected to speak the truth about science, per se. Rather, they were expected to articulate principles and limits that could be made an operational feature of institutional mechanisms, institutions which in turn were invested with the authority to limit or reorient biomedical and biotechnical research in certain respects and under certain conditions, and usually in connection with funding.

The point is that the interfaces created between biology, ethics, and the human sciences produced through the invention and institutionalization of bioethics, and through the now long-standing attempts to formulate bioethical problems as a key aspect of the governance of the biomedical and biotechnical sciences, have, from the outset, been limited by, and suffered the contradictions of, an unsettling of the modern political imaginary. It has been unsettled insofar as ethics might otherwise be taken to be characterized by an essential difference from science, whose essence, in turn is not to be confused with politics. And if ethics and science are considered to be essentially distinct from politics then the insistence that theologians, philosophers, anthropologist, and other might contribute to governing the life sciences can only be taken as an unsettling state of affairs. Of course, as I've already noted, the reality of these domains is much more complicated, and whether or not anyone holds to such essential delineations is more or less beside the point. Nonetheless, it is the case that the expectation that ethics should play a role in the governance of the life sciences has proven institutionally and procedurally fraught. One solution to reconciling these formal tensions has been to simply institutionalize bioethics as a matter distinct from, if in a cooperative division of labor with the daily practice of biomedical and biotechnical science, such as one finds with Institutional Advisory Boards. Another solution, animated as part of the Human Genome Project's ELSI program, is to place ethics and the human sciences outside and downstream of biomedical and biotechnical practices, per se, and thereby simply remove them institutionally and temporally from the question of governing the work as it unfolded. Another is to create deliberative bodies in which representatives of various constituencies can ostensibly participate in the democratic governance of science.

The strengths, tensions, and critical limitations of these various modes have received considerable analysis.[294] Strengths include the fact that where ethics and biology have been figured as institutionally distinct, a certain autonomy and division of the exercise of power is permitted. Ethics here has the possibility of exercising power through specified and punctuated audit procedures. Biologists retain a large measure of self-governance. Tensions arise when ethics is taken to include more than the jurisdictional audits, but also applies to the form of life—its ends, its substance, its capacities—that the sciences embody and make possible. In this case, a division of labor and power predicated on a cooperative relation begins to beg the question of whether and how ethics is really in play. The critical limitations show themselves in proceedings like those of the Presidential Commission in which it is asserted that the hope of a more ethical biology does indeed turn on the adjustment and cultivation of certain habits and dispositions. But in which there is no specification or enforcement of ethical pedagogies worthy of the name, i.e. pedagogies requiring specified metrics of good and bad practice, regimes of exercise form capacities in relation to those metrics, and second-order reflection about organizational form, existing trained incapacities, dominant career rewards and patters as well as possible vocational openings of an ethically determined sort.

The Human Practices experiment was partially proposed and designed in light of these prior efforts and a diagnosis of their strengths and limitations.[295] A central feature of these designs was an insistence on the need to shift from a cooperative to a collaborative mode of interaction in which problems and division of labor could be defined in common. Such a mode would require a change in habits on the part of both the biotechnicians and the human scientists involved. It would also require a willingness on the part of the human scientists to make ourselves vulnerable to the inevitable asymmetries in power, and asymmetry to which we might have otherwise shielded ourselves from if we had remained in a more classically anthropological

position of observational adjacency or bioethical position of advisors.[296] Such positionalities, however, would have been contrary to the terms and stakes of the experiment as the Human Practices group understood them.

Among the organizational encumbrances to successfully putting our designs for Human Practices into practice with SynBERC three stand out. The first was that SynBERC was simply too fragmented an organization, with Principal Investigators who simply did not receive enough funding from the Center to make significant adjustments to their research portfolios. The second, which follows from the first, despite its clearly formulated organizational mission, project aims, and center-wide research foci, SynBERC has never really functioned as an integrated research program. In other words, the principal participants in SynBERC really did not care to align their research and scientific ambitions with the SynBERC's stated aims, and SynBERC really never had enough power to make them do so. The third is that there were none of the opportunities for sustained interaction of the sort that might have resulted in a kind of mutual curiosity. Despite the fact that we spent energies on a weekly basis to understand the work being conducted in the SynBERC labs, we were rarely if ever asked about our research. Such a lack of reciprocity was in part a result of a lack of physical adjacency, and it was also a result of the trained dispositions of the bioengineers. The work we did was not interesting to them, that is, it was not interesting except for when we foregrounded these institutional blockages and shortcomings as key elements of our diagnostic and evaluative work. In any event, these encumbrances, which have been explained at length elsewhere, meant that the Berkeley Human Practices group, which had formulated its program on the observation and interaction with Center-wide research developments as they unfolded, never really had a stable object or venue with which to collaborate.

Comparatively speaking, the BIOFAB seemed to offer a remediated setting for conducting Human Practices work. It was a locally instituted undertaking, with limited goals, and a tight organizational structure. Moreover, there was a stated willingness on the part of the directors and the lead engineers to include Human Practices—or at least to include me as a representative of Human Practices—as a regular an integrated part of the organizations daily affairs. From the outset, the ethical task—a question that persisted in a central fashion throughout my involvement in the development of the BIOFAB program—concerned designing ways in which the inclusion of Human Practices might contribute to the formation of the practices, relations, and capacities needed to carry out the work of the facility in a manner that might be judged scientifically and ethically worthwhile.

At the risk of being too schematic, and falsely presenting the Human Practices experiment at the BIOFAB as carried out in a systematically planned fashion, rather than a mode that was experimental, restless, and recursive, three parameters of my endeavor can be identified as particularly crucial. The first, which has been emphasized from the outset by the Berkeley Human Practices group, is that a key starting point for thinking about ethical formation is the notion of *flourishing*.[297] Initially, the Berkeley group introduced the term as a more or less adequate translation of the Aristotelian ethical term *eudaemonia* and as a critical outside to the predominance of notions of health, wealth, and security as the ethical metrics used to justify and fund the life sciences today. A strength of this term, in our view, is that traditionally it remained under-defined and therefore called for the exercise of a practical wisdom, taken in the sense of having the capacity to effectively diagnose and respond to the situation within which we have been positioned and of which our work has formed a part. In this regard the term flourishing

seemed well suited to the inquiry-based mode of our undertaking. But as the Berkeley Human Practices group has explained elsewhere, its deficit was that that, traditionally, the philosophical work dealing with the notion "too far removed from the lived realities whose discordancies trouble us today."[298] For this reason, and in view of the lessons learned from our experiences and experiment as part of SynBERC and the BIOFAB the Berkeley group has begun to give more careful attention to the nuances of this term, and what it demands of the situation in which we have found ourselves.[299]

A second parameter in the design of my experiment concerned the place of technique and technologies in ethical formation. Assembling and arraying the conceptual aids needed to conduct an anthropology of ethics James Faubion has pointed to a key conceptual shift in understanding the careful labor entailed in ethical self-formation. The shift involves the acquisition of virtues such as flourishing. Citing Aristotle, Faubion points out that teaching and pedagogy have often been centrally emphasized, taking as examples the acquisition and cultivation of the dispositions needed to ply an "art" or a "craft."[300] And yet Aristotle (and others in this tradition) often distinguish between "practices" as the object of ethics defined by a kind of immanent (i.e. not instrumental) worth, and notions of "creating" or "making," which imply an activity whose worth lies in its outcomes—"whose end is distinct from it." In this view technological activities can be distinguished from ethical practices. The conceptual shift that Faubion points out entails a kind of reversal, a foregrounding of activities of making and creating not as analogies, but as crucial elements of ethical formation. Identifying this shift in the work of Michel Foucault (albeit in a lineage of consonant thinkers), Faubion writes that technical enterprises, enterprises that aim at brining ethical practices into existence "which Foucault refers to as 'practices of the self' or 'techniques of the self' or 'technologies of the self" are resolutely technical enterprises. That is to say, they are enterprises whose "end is distinct from it" insofar as they are oriented toward the generation of specific ethical capacities, ways of being, the cultivation of certain modes and forms of subjectivity. Crucially, such "technologies of the self" are never a question of isolation and individualism, however much they require an exercise of discipline and freedom on the part of the subject who wishes to become a more ethical being. "An ethics completely unmoored from public criteria of validity would simply be no ethics at all."[301] For the experiment in Human Practices (and this is not unique) all of this redounds to the fact that techniques of making and creating with regard to the cultivation of ethical capacities are integrally connected to situations of authority, direction, and power. The problem of whether or not the growth of ethical capacities can flourish depends in significant part on the posture one is able to take in relation to the exercise of authority; a fact that has been clear from the outset at the BIOFAB.

A third parameter reasonably follows from the first two: it is one thing to recognize in the anthropology of ethics that the question of virtue and the cultivation of dispositions is one of technology, techniques of the self, *bios technika*, as it were. It is quite another thing to take the possibility and stakes of such formation as one's own, and to identify the space of inquiry as precisely that domain in which such practices of formation are animated and put to the test. In the case of the BIOFAB, then, a question I have tried to pose, more or less coherently from the outset, is this: in what ways and to what extent are these biotechnical endeavors, predicated as they are on the notion and possibility of making biology more engineerable, and to that end making biologists more like the figure of the engineer technology, spaces of virtue? What dispositions and habits are the biologists and engineers expected to invent and embody? How have the biologists and engineers responded to the expectations, what postures of acceptance and

resistance have they taken up? To what extent will the discordant notions of what it means to become a synthetic biology become a skin that eventually becomes an essence? And as important as any of this, I have asked all the way through, and am asking now in a more directed and serious manner, in what ways is our work with those who are cultivating technologies, work whose is to bring ameliorated health and economic prosperity, also a space in which a certain cultivation of virtue is possible? In what ways can an experiment calibrated to the instrumental ends of prosperity and amelioration also be made a space of possible flourishing? I would submit that the answer to any aspect of these ethical questions begins with the simple exercise of determining what's actually going on in synthetic biology and in our relation to it. It is only in taking up the work of inquiry, and in passing through the micro-practices of life in these research programs that I—we—will be able to intervene. And the form of that intervention, as the Human Practices experience and experiment has shown, is precisely the ability to conceptually capitulate and reconstruct the problem and situation at hand in such a way that possible solutions, possible ways forward can be opened up. And, with additional efforts, possibly be taken.

Writing their 2005 manifesto, the self-described "bio fab group" insisted that the possibility of synthetic biology as a field and as a collection of institutionally supported practices turned, in large part, on the possibility of convincing those with funding and institutional know-how to seek the long-promised health, wealth, and security of the genomic sciences through the fostering of intuitions modeled on the double analogy of chip fabrication and computer programming. A key to animating this possibility, it further suggested, is the reworking of the dispositions and intellectual habits of young practitioners in such a way that those habits and dispositions would be calibrated to an engineer's feel for the relation between engineering and biology. In this light, the call for an ethical pedagogy does not only come from the side of ethics and the human sciences. The question, then, is whether or how such pedagogies will be foregrounded, who will be authorized to determine the specific metrics and techniques by which they are animated, and who will have the institutional possibility of carrying them forward? I propose that those concerned with the breakdowns and difficulties connected to the modern problem of ethics and science should attend to the malaise which marks the prospects for the inclusion of ethics in the governance of the life sciences today. A malaise in that despite all of the efforts given to formulating and reformulating the role of ethics in relation to the governance of the life sciences "a general feeling of worry or discontent of no diagnostic significance" persists.

Few strong ethical directives are offered by the Presidential Commission in part because responsibility for ethical pedagogy is more or less left up to the biologists, engineers, and their organizations. Although others are invited to discuss objections and participate in democratic deliberations, and although the public is attended to as an object of science education, no one other than the biologists are actually positioned to have an active hand in the formulation of the actual habits and dispositions of research. There is a certain logic in this. As the Commission states it, the biologists and engineers are actually the one's doing the work. As such, they need to take a primary role in developing a stance of "responsible stewardship" relative to the pursuit of synthetic biology. What such a stance would consist in is not really specified with any detail relative to the actual organization and practice of synthetic biology. Nor is it clear what assurances the Commission would put into place to determine whether or not such self-pedagogy was proceeding or what metrics they would use to determine whether or not such pedagogies were producing anything like the outcomes (i.e. the responsibility) hoped for and expected.

A better way of formulating this justification for self-governance might have been to acknowledge that any ethical pedagogies worthy of the name will need to involve what Faubion has highlighted as the practices of *autopoiesis*—of self-making.[302] In order for biologists and engineers to actively cultivate specified dispositions and habits under the always somewhat specific conditions of everyday life, they will need to take up the task as a matter of work on the self. There are, of course, examples of ethical traditions that require a lesser degree of self-formation. These traditions are those in which the aim is to get one's life to conform to a rule. Such a task no doubt requires diligence and self-direction on the part of the individual practitioner. But such diligence is directed in light of the sense that the norms and forms of ethical life have already been determined and that it is only embodiment of those norms and forms that is required. In the case of the contemporary life sciences, however, these norms and forms of responsible practice are actually not settled. As such, a kind of flexibility and capacity for self-invention would seem to be called for. Although, it bears noting that for those involved in the BIOFAB the capacity for self-invention is limited and troubled by the discordant mode and stylizations of synthetic biotechnology which were described in the early chapters of my thesis: namely, that the future is articulated in terms that effectively function as an under-specified rule to which one is being asked to conform oneself and one's work.

Acknowledging that self-formation is a crucial part of any contemporary ethical program worthy of the name, the argument made by the Commissioners that the biologists and engineers need to be allowed the facility of self-governance in matters of ethics is, nonetheless, over stated and under-thought. The notion that the person who does the work of ethical consequence is the only one responsible for such consequence is a historically prosaic proposition. In the great traditions of ethical reflection and practice, ethical formation was pursued as part of a wider community in which self-formation was always dependent on one's relation to others, including friends, mentors, and guides. Such dependence is obviously the case in the contemporary life sciences in which mentorship and patronage are the proverbial names of the game. Moreover, and more to the point of this thesis, in the case of the Human Practices experiment, those of us charged with paying careful attention to questions of ethics have been included as part of the enterprise from the start. The problem throughout, as has been carefully chronicled elsewhere, has not been access. The problem has been that any demands that the biologist and engineers tend carefully to questions of disposition and habits other than those that advance either their research or the reception of their research have been either ignored or attacked by those senior participants who might otherwise be able to affect the implementation of the kinds of programmatic efforts needed to attain to such attention.

TRUTH-SPEAKING: FROM RIGHTS TO CAPACITIES

The problem is what to do. Ethics has been invited to form a part of the constitution of worthwhile scientific practice in synthetic biology, but have not been given the power to participate in any significant manner—not even in matters of technical criticism pertaining to safety and licensing, though roles of opinion polling and informal education remain available. One response to this problem is to simply accept and thereby reinforce the practice that bioethics has been given, and works to maintain: an advisory stance relative to biotechnical and biomedical practice. In the case of the Presidential Commission, after all, the point of animating discussions of synthetic biology is not actually to govern. The Commission "identifies issues" and "recommends any legal, regulatory, or policy actions" it deems appropriate. The Commission, to use an outdated but appropriate vocabulary, is not the prince; it is only the

counselor to the prince. Moreover, and more pertinent for this analysis, even within the Commission those experts who are asked to testify are only testifying in an advisory capacity. Given this formal disconnection from the actual exercise of power, ethics can assume it has the right, and perhaps even the freedom, to speak. Ethicists can speak in a representative mode "as a Roman Catholic I don't support stem cell research" (in which case the testimony can be logged onto the books not as true or false, per se, but rather what a certain group of citizens likely thinks), or, in the mode of a social scientific reporter on what "those others think." In the case of either mode, again, the Commission can deliberate about how to weigh the "interests" or "commitments" of that group of citizens. This is all very serious, to be sure; it focuses attention and opens up conversation as the Commission points out. The question of whether or not what one individual or group believes is ethically sound and a matter of truth and falsity, however, is not taken seriously. Said differently, one response would be to simply give up the second and third corners of Foucault's democratic rectangle—authority and truth. Bioethics can speak freely, but they cannot rule. Or, bioethics can participate in ruling but they cannot offer true discourse, only representative opinion.

Another response would be to follow the recommendation offered to the Commission by both Buchanan and Wolpe, and commit ethics and ethicists to the task of formulating any substantive and detailed contributions into statements of general principle—a putatively neutral and public discursive mode. Such a response has been tried out as the solution to the limitations and impasses of ethics and the governance of the life sciences in other bioethical Commissions, notably the Clinton administration's National Bioethics Advisory Commission (NBAC). The NBAC was noteworthy in its efforts to surpass other executive bioethical advisory committee in formalizing and foregrounding the participation of religious ethicists. The success of their approach turned on a commitment to inclusion and participation as preeminent virtues. The price to be paid for their approach was that, in the end, the religious testimonies only counted in the register of true and false insofar as they were stripped of any of their particularities and reformulated as secular principles. The possibility and worth of such an exercise turns on the notion that the secular modes of reasoning escape the particularities and mico-politics of historical particularity. Challenges to such a notion were not advanced at either the Clinton Commission hearings or the hearings on synthetic biology. One reason for this is that the use of general principles offers the virtue of being more or less acceptable to the biology establishment. After all, such principles are only onerous if they are connected to specific courses of action and empowered institutions. This response leaves bioethicists free to speak, say what they think is true, and even participate in the apparatuses of governance. The crucial sacrifice, however, is the ethical element. The use of general principles, the introduction of generalized moral norms, when not directly connected to either actual practices or institutions, relieves bioethics from having to make *specified* demands in the register of changing habits, dispositions, rewards, or punishments.

A third response is simply to stand with those who insist that ethics today, for better or for worse, is a "subjective" matter. As such, it shouldn't trouble us too much that the testimonies offered by biologists, engineers, and other technical experts at the Commission hearings are more likely to be entered into the record as a matter of fact, whereas testimonies presenting either non-technical accounts of synthetic biology or assertions about worthwhile ethical practice are more likely to be entered as either a representative opinion, or, as a "rule of thumb" for further deliberation. Whatever else, testimonies that directly tell us what we should do must be handled with caution. Unless, of course, these testimonies pertain either directly to questions of rights that have been violated, economic transactions that can be quantified, or medical and

environmental harms that can be calculated. Such a response, not overly troubled by the formalization (legal as well as habitual) of the separation of value spheres, can proceed in a relatively careful and thoughtful manner. After all, if the constitution of value spheres in anything like its current configurations is likely to remain in place, however troubled and even unsettled, then the challenge is how to move among and between these spheres and how to rectify and negotiate the terms of the differences among and between them.[303] Such a position, like the second part of the first, would require compromising, or at least adjusting and tempering, a commitment to true discourse. The job of ethics would not be to speak the truth, but to facilitate and negotiate participatory discussion.

A more truthful response than any of these requires taking seriously the rather obvious point that science is not a disembodied set of technical propositions.[304] It is, rather, a field of practices. As such it is historical, with all such historicity entails in terms of social conditions and the exercise of power. This is not to say that the sciences are not about the production of true knowledge. Rather, it is simply to insist that the production of that knowledge and the recognition of that knowledge as true are only possible because of the establishment of a prior set of norms concerning the possibility of distinguishing the true from the false and for accepting those distinctions as normative. The challenge, as Rabinow wrote in 1988, is to take up the work of identifying the historical conditions within which these practices of dividing up the true and the false were established. In this way there is some possibility of identifying where change is both possible and desirable—a historical ontology of ourselves, as it has been called.[305] Or, as it has been put about religion: it is one thing to study what it is that believers actually believe; it is another thing to study those relations of coercion, domination, exercise and care by way of which such beliefs are actually brought into the world and made believable.[306] The question is thus not one of denying truth. The question, rather, bears on which practices and forms of life are necessary for truth to be formulated and what practices and forms of life are necessary for it to be formulated differently.

All of this is, in anthropological and social scientific settings, might simply be taken for granted. The question is thus not whether or not such studies of the relations among and between science, ethics, and power are possible. The question is how are these relations are given the form they are currently assuming today? The case can be made that the relation between biological artifacts and biological practice is mutually entailing and determinative. In what ways that mutuality is significant, and how it applies within specific situations, remain pressing questions. The problem I pose in this chapter, however, is how might these relations be given a form that is adequate to their actuality? Put differently, how and whether is it that the actuality of the relations of truth, ethics, and power—an actuality marked in my experience at the BIOFAB by breakdown and impasse—can be reconstructed.

But, of course, this fourth response, a response that would entail thinking about biology as a human practice, and only then and thereby taking up the question of how synthetic biology might be distinctive, is precisely what has been positioned (though not yet ruled) out of court.

TRUTH AND SERIOUSNESS

During the round table at the close of the first day of the Commission meeting Gutmann invited comments and questions from the attending public. I took the opportunity to point out that the question raised in the morning session—is synthetic biology distinct from prior modes of bioengineering?—had been addressed in terms of technical continuities and discontinuities, and only in this light had other questions been posed pertaining to the sufficiency of existing

regulations and norms of ethical practice. I encouraged the Commission to take seriously Nancy King's emphasis on ethical significance as a partial function of context. Taking her point seriously, I proposed, requires attending to the possibility that answering the *technical* question of what is *distinctive* may not be sufficient to addressing the *ethical* matter of what is *significant*. Such a stance encouraged us to take account of the world into which synthetic biology is being articulated and how that world is distinctive today. In short, the question is not just "is synthetic biology like recombinant DNA technologies of the 1970s," the question is also "what else has changed since the 1970s that contributes to the significance of synthetic biology today?" I concluded by asking the two invited ethicists, Kaebnick and Buchanan take up my question.

Gutmann seemed impatient with the extended framing of my question. Nonetheless she prompted Kaebnick and Buchanan to respond. Kaebnick said that nothing immediately came to mind, and that the issues being raised by synthetic biology, as his Center had published, were more or less the same as they had been for synthesis and recombinant DNA technologies. Buchanan, seemingly annoyed at the question, responded in abrupt and authoritative tones that basically nothing had changed. Gutmann moved to the next question.

Several minutes later, during discussion of a different question, Endy told Gutmann he thought we should return to the question that I had asked. He suggested that the question was self-evidently important. To Kaebnick and Buchanan he proposed that in thinking about the ethical stakes of synthetic biology in distinction to recombinant DNA technologies of the 1970s, one would minimally need to account for the internet, with all it entails in terms of the circulation of materials and knowledge. "What about the prospect of non-institutional biology?" he asked. The fostering of biology in different venues would seem to change the ethical calculus—as the Commission would acknowledge in its report. Endy might have continued multiplying examples: that the US and the world were currently suffering the fruits of decades of deregulation, exemplified by the implosion of the financial sector and the BP oil spill; the fact that in a post-9/11 environment biofuels can be framed and justified not only as an economic and ecological question, but as a matter of national security; that as a social fact synthetic biology was being assembled, branded, expanded and valued in a fashion distinct from prior techniques per se. The attempt to return to the empirically relevant facts of the present situation was ignored.

Any of these variables might have served to foreground the additional fact that the programs and practices of biotechnology today are being assembled differently than they were even a decade ago. This, in turn, would have reminded everyone present that however impressive the artifacts of JCVI's work may be, the form and kinetics of that work with all they imply in terms of reworking biological and moral imaginations and thereby facilitating new technical and organizational capacities were simply not being taken up and advanced as matters worthy of ethical reflection. As a result, the broad outlines of an ethical pedagogy being directly put forward by Wolpe and Wheeler, and indirectly by others, could easily be received as general, if worthwhile, aphorisms and not as concrete demands or proposals for the transformation of real practices. That is to say, they could be received for what they were: points of discussion and opinion, to which most in the room easily assented without needing to be burdened with the obligation of treating them as matters of truth and falsity and thereby having to recommend or not recommend them to those in power.

The principle limitation exposed by the Commissioners' struggle with questions about religion were significant in that they exposed the fact that the Commission was not capable of serving as a venue in which serious ethical questions could be linked in a direct and effective

fashion with matters of truth and power. Ethics, in brief, could not really be taken seriously and thereby seriously taken up. The term *serious* has been given technical purchase by Paul Rabinow as a pair to the term *truth*.[307] Scientists, Rabinow argues, have become unsettled by the fact that although they still concern themselves with truth, they do not concern themselves with the ethical and political practices that make such truth possible, nor with the ethical and political ramifications of these forms. They are not, as it were, capable of being ethically and politically serious while still being themselves. This lack of seriousness was both acknowledged and covered over first in my exchanges with Arkin and then in the deliberations of the Presidential Commission. Thus my assertion that the questions posed about how to bring religion into a conversation about the ethical governance of synthetic biology, and the impasse and discomfort produced by those questions not only expose a significant contradiction, but are thereby deeply serious. The contradiction between the fact that bioethics assumes that scientists cannot, per se, govern themselves, and the fact that when it comes to governing the sciences only the truth claims offered by the biologists and other technicians can really be taken seriously.

This contradiction, I propose, serves as a primary blockage to designing and putting into practice a form and mode of scientific and ethical collaboration worthy of the name—precisely the kind of collaboration that synthetic biology seems to require. Structurally speaking, the politics and governance of science as exemplified by the Commission meeting is naïve about the question of power. Science no less than ethics is a practice. The form and mode of that practice would seem to be a principle consideration. But such a consideration would require us to think seriously about the ways in which science and scientists are being formed and are forming themselves. And since the question "what is synthetic biology" has already bracketed the relation of the biologist as the producer of artifacts and knowledge from those artifacts and that knowledge and the forms and modes of their circulation, such a consideration hardly seems to be in the works, at least in official settings.

The Presidential Commission hearings, no doubt like most discursive endeavors, privileged certain modes of dividing up the true and the false. This privileging shows itself not only in who has the right to speak but, more importantly, in which speech acts actually become connected to the actual exercise of power. And despite the fact that, as a genre of political exercise, bioethical commissions presume to treat the biotechnical and biomedical sciences as thought they were not supposed to exercise of power without a certain measure of oversight, it is not clear that this Commission was able to make good on that presumption. The question throughout the hearings, a question reflected in the report, was whether or not synthetic biology needs to be subjected to either more or less governance. This question was made to turn on the extent to which synthetic biology is like or unlike prior biotechnical undertakings. What the biologists said about their own work was made to count in the Commission's recommendations in a uniquely privileged fashion. And the fact that non-technical experts, who were invited to help think about the governing of synthetic biology, were effectively not allowed to connect their extra-technical truth claims to the exercise of power (even if only in the form of the report's recommendations) is telling.

The fact of an asymmetry in authority between the biologists and non-biologists or between the technicians and non-technicians is hardly surprising. Bioethics has been in a minority position to the biotechnical and biomedical sciences from the outset. And despite changes in the governance of the life sciences over the last thirty years, the effort on the part of scientists and regulators alike to preserve as much self-governance as possible persists. Reasoned

arguments given for this commitment to the self-governance of the technical sciences. Among such arguments the Commissioners offer the desire to maximize possible instrumental benefits, the value of intellectual freedom, and the fact that, in the end, it is the biologists who will carry out the work. The Commission sounds notes of ambivalence. Their emphasis on vigilant prudence is both a recommendation concerning the stance that biologists should take up relative to their own work and the stance that should be adopted by regulators. They emphasize the need for further bioethical discussion, the worth of democratic deliberation, and the legitimacy of moral objections. However, they foreground themes of responsibility and self-education on the part of technicians and bioscientific organizations. The result is that the report, perhaps not surprisingly, recapitulates the asymmetries in authority that were performed in the hearings: respect, politeness, and deference to the status of those involved, if not for the seriousness of the testimonies themselves; an eagerness to agree with testimonies calling for moral rectitude and prudence, yet little effort either to make difficult ethical judgments or to offer recommendations that might seriously impinge upon the funding and commercial flexibility of the synthetic biologists, let alone their habits and dispositions.

This asymmetry in authority is homologous with the position of the Commission itself. It is, as I have previously noted, only an advisory board; it does not make policy or exercise power of any direct sort. When I pointed out to a senior bioengineer that the Presidential Commission's report lacked any serious judgments either about the character, worth, or dangers of synthetic biology, but at best only provided a framework whereby others might be able to make judgments, the response was: "maybe that's not really their job." In this respect, maybe it would be more appropriate to analyze the work and proceedings of the Presidential Commission according to Foucault's analysis of the relation between the philosophic advisor and the prince rather than his analysis of the democratic rectangle. In that situation the problem is no longer the question of how to link *politeia* to *dunesteia*. The advisor, after all, does not necessarily have the right to speak freely or to presume to ascend to authority and the real exercise of power. In this regard, truth and ethics can easily be disarticulated from power. Power is a concern of the prince, and truth and ethics a concern of the philosopher. To this extent the advisor only really need speak the truth in a fashion consistent with the status of the advisor. As advisor, the philosopher is expected only to tell the prince what he needs to know in order to rule effectively. The advisor does not need to tell the prince what metrics he should use. Rather, the advisor should only tell the prince how to best parameterize and thereby actualize the metrics the prince has selected. Or, put differently, when the President gives the Commission a mandate to tell him what the costs and benefits of synthetic biology are relative to prosperity and amelioration, the Commission can only really be expected to carry out that mandate.

The trouble enters in when the philosopher begins to worry about the prince's soul, or the salvation of the city, or simply that the functions connected to the status and position of the advisor are in conflict with what the philosopher knows to be true. Foucault provides an account of Plato's interactions with Dionysius the Younger. Plato has been invited by Dion the brother-in-law and advisor to Dionysius, to come to Sicily to provide council to the prince on how to rule. During the course of his interactions with the tyrant, Plato tells Dionysius that because he does not rule according to just laws, he lives an ignoble life Foucault points out that Plato's frank-spokeness actually has nothing to do with this role as a visiting councilor, per se. In that position, Plato could have carried out his responsibilities in any number of ways. Taking the role of the teacher he might have tried to explain to Dionysius how he might proceed as a tyrant in a more effective manner. Or, he might have used the arts of rhetoric to try and persuade Dionysius

to act differently, employing a range of techniques. Plato, however, exercised *parrēsia*. He made a frank-spoken enunciation, and in doing publically bound himself to a truth whose ramifications he couldn't control. He bound himself to the truth not by appealing to the authority and status of a famed philosopher or by speaking in a fashion consistent with his status as a counselor. Rather, he bound himself to the truth as an individual who believes what he is saying and must say it because he believes it.

The configuration of ethics, truth, and power remains critical in the philosopher's relation to the prince. But the variables change. The task is not to exercise the free right to speak the truth in such a way that one ascends to authority among fellow citizens. Rather, exercising the courage to face the consequences of telling the truth to the prince, one offers a true discourse in the spirit and hope of integrity before the truth. Such frank-speech, Foucault suggests, was always a dangerous affair—whether for the citizen or the advisor. It was dangerous because it opened up different and unexpected possibilities. Indeed, frank-speech can be classified as frank-speech precisely because the effects which follow are not known and ordered in advance. More to the point, these unknown effects which are opened up are dangerous precisely because they create a situation in which those in power must confront the fact that they may not be on the side of the truth in quite the way they had hoped or expected. Such a confrontation is likely to provoke either indifference or hostility. The philosophic advisor, of course, can always simple stick to the status of the advisor and to speak in modes consistent with that status. The declarative, the pedagogical, the rhetorical, the demonstrative, are always there as means by which one can simply do one's job.

The situation of the BIOFAB is not advisory. Endy and Arkin are the directors and the other members of the BIOFAB are employees. And it holds insofar as ethical *parrēsia*, however informed by anthropological inquiry, is ruled out of bounds. Once out of bounds it can only be reasserted in a fashion that is bound to bring about indifference, annoyance, or hostility. To date the challenge and the task of the ethicist is not altogether different from those who were asked to testify to the Commission: there is an opening to speak to the truth and to speak it in an effort to help govern the activities of the BIOFAB. On several occasions Endy told me he wanted me to make decisions for the BIOFAB, to tell them what to do. He had in mind things having to do with the circulation of the BIOFAB's materials—matters of licensing, matters of safety, and legal responsibility. I was not asked to help make decisions regarding ethical pedagogy. The question of what kinds of biologists the members of the BIOFAB should become in order to fulfill aspirations for the future of synthetic biology is another matter altogether.

The wrinkle in all of this, as I stressed in chapter 6, is that the empirical question of what the biologists are making cannot be disentangled from the equally empirical question of what it is the biologists are really doing. And these practices form part of a wider ethical field. This social fact may be unremarkable and well rehearsed. The contingency of context and practice are no longer really in question. However, the social fact of the practice of science and the presentations of that practice are nonetheless crucial in the actual governance of the conduct of biology today. Moreover, it is a social fact that lies at the heart of an asymmetry between the right that many have been given to speak the truth about the significance of biological research today and the fact that only a few of those who speak the truth actually get to exercise power. Said differently, of those who are permitted to speak the truth, only a few are allowed to connect those truth claims in any direct fashion to the exercise of power.

Two moments in my exchange with Arkin about the ethical ramifications of the JCVI work are worth considering in this light. A first is Arkin's introduction of the tautology "nature is nature." However true such a tautology may appear to be, within the context of our exchange it bears keeping in mind that his reason for raising it is that complaints against the Venter work (or any other work in bioengineering for that matter) that are predicated on the notion of a violation are out of bounds. Whatever biologists show us to be the case about the character of living beings, their elements, or their milieu is simply statement of fact. One might then have problems with how that work is circulated, whose lives are affected by it, and what ramifications, positive or negative might unfold. But one cannot, per se, critique the work itself on the basis that something sacred has been transgressed. That is to say, one cannot speak in the name of nature against what biologists are doing. Moreover, biologists are granted a kind of rolling authorization. That is to say, whenever biologists demonstrate something to be the case about living systems, either discovering something about their character or showing their susceptibility to new forms of controlled intervention, they renew their rights to speak the truth. The fact that these new claims might in fact show the limitation or errors of past claims is not foregrounded.

On another level, what could be problematic about Arkin, a bioengineer insisting on the counter-metaphysical integrity of biological practice? After all, if I thought there was something fundamentally sacrileges about biological engineering I would certainly not have spent as much time as I have working in close adjacency to biological engineering. I do not hold that there is a pre-given order to nature that biologists are violating. Indeed, one of the powerful and captivating aspects of biological engineering is precisely the experimental demonstrations of the re-composability and functional flexibility of living beings and their contexts. The problematic element in Arkin's tautology is the fact that in insisting on the self-identity of nature and therefore on the impossibility of criticizing interventions in nature in the name of some other order-of-things (except, as Arkin pointed out, by appeal to the super-natural) Arkin is reinforcing the authority of biologists to set the boundaries on who can articulate criticisms of their work. Criticisms of the practice of biology can effectively be blocked in the name of a monopoly on the capacity to speak the truth about nature. Or, if not blocked, then limited. They are limited in that they rule out of the bounds of reasoned discourse questions other than those of the positive and negative outcomes connected to the circulation of work (e.g. environmental impact, or distribution of benefits, etc.). In other words, if nature is nature, and if this nature is determined by biological research and interventions and if therefore it is illegitimate to criticize interventions on any "intrinsic" basis, then there is nothing left to do but to let biologists speak the truth about the living world, and for non-biologists either to comment on what the "implications" of these truths might consist in or to communicate about them. The one thing non-biologists are not in a position to do is to tell biologists the truth about what it is that they are doing.

This throws into relief a second asymmetry, which is really just the other side of the first. Any non-biologists who make claims about the practices of biological research and technology apart from claims about implications pertaining to questions of security, property, and health (and even this cannot be taken for granted) can only allowed to advance these claims in the name of one's values, the values one represents, or in the name of the values of those one has studied. This is another way of saying that it is not as if other topics and criticism can't be raised. Rather, it is that they cannot be raised in the name of a truth "that we can all take seriously." In the case of my exchange with Arkin his specific point was simply to underscore that those who make natural law claims about the order of nature and possible violations of that order are necessarily irrational. It bears noting that Arkin, having spent formative years of his intellectual and

vocational development with very bright and very learned philosophers and "religionists," as they are sometimes caricatured, is magnanimous about such irrationality. It is not, he insists, problematic per se. And it is not, he insists, necessarily untrue or unimportant. It is, however, outside the bounds of the rational. Allowed inside the bounds of the rational, of course, are those who speak as technical experts. That scientific discourse itself is characterized by multiple veridictional modes is not accounted for. Nor is the fact that such multiple modes are themselves often irreconcilable, or at least incomparable. What was not possible in my exchanges with Arkin, either for reasons of argumentative deficiency on my part, or because of the asymmetry in power built into a putatively open exchange, was the proposition that truth claims put forward in a mode other than what Arkin would allow as "scientific" could in fact be rational and therefore be brought into a legitimate relation with the exercise of power. Such a refusal and such a blockage is an old move in the exercise of power, but it is not for that reason any less significant. Particularly in a situation in which the non-biologist is ostensibly participating in the name of helping to ensure a more secure and more ethical future.

RAMIFICATIONS: THE REALITY TEST OF HUMAN PRACTICES

In examining relations among truth speaking, power, and ethics in Greek political life, Foucault proposed to track a shift in the site and circumstances of truth speaking from the democratic *agora* to what he names as the *ecclesia*, the gathering of the prince's court. He characterizes the terms of this shift and the salient changes in the relation of truth and the exercise of power through a reading of series of texts by Plato, or at least texts attributed to Plato. The problem he selects, the problem for Plato that converges with the themes Foucault wants to analyze is: "the real role of philosophers […] in Greek political life, at least to the way in which they thought about this possible intervention, and of how they wanted to be recognized as playing the role of those who state the truth in the field of Greek politics."[308] Put in a way that captures the stakes of the problem with a bit more urgency Foucault writes: "For Plato, it is clear that to be no more than the philosopher who is the author of *The Republic*, that is to say, who says what the ideal city should be, is to be no more than logos. Now the philosopher cannot be merely *logos* with regard to politics. To be more than just "hollow words," he must take part in and put his hand directly to action (*ergon*)."[309] Foucault outlines a strategy or guide for answering the question: how is it that thought resists becoming "mere verbiage," how can it made to be an active task, and in what does such a task consist?

It is worth quoting Foucault at some length here:

> I think we have here an injunction that is absolutely important and which corresponds somewhat…to the first Platonic dialogues, concerning philosophy having to be not merely *mathēsis* but also *askēsis*. If it is true that philosophy is not merely the apprenticeship of a knowledge but should also be a mode of life, a way of being, a practical relationship to oneself through which one elaborates oneself and works on oneself, if it is true that philosophy therefore should be *askēsis* (ascesis), then when the philosopher has to tackle not only the problem of himself but also that of the city, he cannot be satisfied with being merely logos, with being merely the person who tells the truth, but he must be the person who takes part, who puts his hand to *ergon*.[310]

The question he addresses constitute a problem that Foucault names as the *reality test* of philosophy, the test of its relation to reality, to action, to philosophical action. "When [Plato] worries about being only *logos*, when instead of being merely *logos*, he wants to try his hand at the task itself (at the *ergon*), it seems to me that Plato raises the question that could be called the

question of philosophy's reality."[311] Or, to use terms closer to how the Berkeley Human Practices group has framed their experiment, terms which I think are consonant with the problem Foucault is trying to pick out and analyze: what is the reality test of inquiry and thinking?[312] How does one "put one's hand to ergon?"

In some basic respect this is a question that has animated the experiment in Human Practices from the outset, first in SynBERC and then in the BIOFAB. In the case of the passages in Plato which Foucault examines, the first answer seems quite straightforward. The shift from philosophy cast as a catalogue of particular items of knowledge, the formulae of knowledge, to a practice that involves not only one's self-formation, but one's relation to the formation and conduct of others requires becoming: "the real counselor of a real politician in the field of the political decisions he really has to take." But what does it mean to be a counselor of a real politician? Here the seemingly straightforward answer to the question of the task of thinking becomes more complicated. The task—and hence the test of philosophy's reality—is not whether or not it provides "useful and effective advice on the decisions to be taken," though perhaps such useful advice might be offered.[313] Nor is the task to persuade the real politician to accept the truth that the philosopher is speaking, for, Foucault explains, following Plato that persuasion "is no more than the instrument by which the person who wants to exercise power can only repeat exactly what the crowd, leaders, or Prince wants. Rhetoric is a means of persuading people of what they are already persuaded."[314] Nor is it even for philosophy to know the truth: "It is true that for a long time some have thought, and some still think today, that philosophy's reality is sustained by the fact that it can tell the truth, and that it can tell the truth about science in particular."[315] The reality, "the test by which and through which philosophical truth speaking will demonstrate its reality" is none of these—its political effectiveness, its persuasion, its informative substance. The test is, rather, quite simply "the fact that it addresses itself, can address itself, and has the courage to address itself to whoever it is who exercises power."[316]

Of course the everyday work of Human Practices and the substantive contributions of this experiment turn on more than whether or not philosophy has been addressed to those who exercise power. The experiment has been calibrated, from the outset, to the task and work of inquiry: of tracking what is actually unfolding in the development of synthetic biology both in terms of what it is bringing into the world and how synthetic biologists must stylize and cultivate their capacities in order to bring such objects into the world. But what Foucault's examination of Plato's test of philosophy's reality reminds us of is a question of a slightly different order than the question of how inquiry should be conducted day in and day out. The question is: how do you test whether or not all of this other work that one is engaged in—examining, diagnosing, conducting inquiry, attempting to make determinations and provide some direction—can become more than discourse but also and actually part of the constitution of oneself and others? The first answer that can be given is whether or not the work that one is doing, the thinking that one is engaged in, is addressed to those who exercise power. The work that must be done on oneself in the conduct of scientific inquiry and the work that must be done on oneself to address the truth of the matter to those who exercise power. Both require a certain work and therefore must be earned, as it were, and both must be tested.

There is a further question, which is actually more pressing. In what way does the test of the reality of thought not only *where*, but also *when*, and under *which* circumstances to put one's hand to the task of thinking? Foucault points out that Plato actually renounces participation in the politics of Athens. The reasons for this are complicated but amount to the fact that "the

population of Athens has acquired such bad customs over such a long time that it is no longer possible to reform it…the reason he gave for having renounced participation in a any political activity at Athens was that he had not found any slight improvement, any break in the bad situation of Athens. At no time had he thought that there was something like a *kairos*, an opportunity." And what was the substance of these bad customs, this lack of an opportunity? No one in Athens was willing to listen. And so Foucault shows that the test of the reality of philosophy has a first and crucial parameter in answer to the question: how do you know when to try and speak the truth and when it is time to stop? "For philosophical discourse really to be able to find its reality, to be real as philosophical veridiction and not just empty verbiage, the first condition—which may seem paradoxical—concerns those to whom it is addressed. For philosophy not to be pure and simple discourse but actual reality, it should not be addressed to all and sundry but only to those who wish to listen to it."[317]

The test of listening entails another question and another parameter: how do you recognize those who will listen to you? The way in which you know someone is willing to listen to you is that they recognize or are willing to accept that the essential thing about philosophy is that its significance does not reside in what Plato refers to as *mathemata*…particular items of knowledge…the formulae of knowledge…learning a formula which is given by the teacher, heard by the disciple, and learned by heart…"[318] Its essence, rather, lies in the fact that it is pragmatic, that it consists in *pragmata*: "concerns, activities, difficulties, exercises, and all the forms of practices in which one must train oneself, to which one must apply oneself, for which one must take great pains, and which really give one a lot of trouble….[they] are activities, everything with which one is occupied and to which one applies oneself." [319] Said more plainly and straightforwardly, the significance of thinking in relation to the exercise of power, and therefore the test of the reality of philosophy in a situation where discourse needs to find its task, its activity, is that it must be listened to by those who understand that it requires active work and is not simply reducible to a series of statements—indeed by those who are willing to take up such long and difficult work.

LOYALTY AND EXIST

From early winter 2010 to the annual SynBERC and BIOFAB site review in early spring 2011, a number of episodes took place at the BIOFAB that would converge and contribute to a kind of reality test of the Human Practices undertaking. Among these are several that might be designated as less directly influential, but nonetheless relevant. The experimental team had finally begun to finish up its pilot project. Despite the fact that the initial work and modeling had been completed by May 2010, the team had encountered a number of difficulties in producing clean and reliable reproductions of their initial results. These difficulties only served to underscore the initial points that Arkin had stressed about context dependence: the difficulties turned on the handling of materials, the selection of colonies, the ability to get different reporter genes to function in a reliably parallel fashion, and ongoing questions about the use of optical readings of cell populations as a best way to measure and score the small catalogue of parts. Despite the difficulties, the results seemed to be consistently reproducible. And though an 80% success rate in predicting combinations would be insufficient to the grand goals of "programming DNA at scale," these results were now thought to be trustworthy and therefore could provide a basis for the kinds of refinements and scaling of libraries that needed to be done in the C.dog project. And indeed, this work too was well underway.

Mutalik and Cambray had made significant progress on building sets of promoter and terminator parts characterized within Mutalik's C.dog architecture. There was some question, however, as to how much of this work would be completed by the 2011 SynBERC site review. When it would be possible to begin drafting manuscripts for papers, and when the online data services would be complete enough to begin displaying the results of these experiments as catalogued products with a regularized scoring system. A key sticking point, which I described briefly in chapter 5 was what to do about the fact that two of the designated "parts" in the C.dog architecture "5'UTRs" and "CDSs" did not seem to be susceptible to modularization. This presented a micro-biological as well as design-strategy problem. Several possible ways forward were put on the table. All risked compromising a clean message about modularization and interoperable parts libraries. Taken together these delays and their seeming near-term resolution put Endy into high gear working to determine how the story of the first year of the BIOFAB's work would be framed and "celebrated."

More directly relevant for Human Practices was the fact that during much of the fall I spent a good deal of time producing text for what would become this thesis. This meant that although my daily interactions with the BIOFAB team did not change much (I continued to attend the weekly meetings and to actually interact with Mutalik, Cambray, and others in a much more directed fashion as I began to write about what they had been doing during this first year of work), Endy and Arkin nonetheless allotted me the freedom to background expected deliverables in order to foreground the thesis work. In Endy's words: "Gaymon be selfish. You're better off to everyone with the thesis done." The practical difficulty was that the thesis work had slowed down my efforts to complete the Human Practices reports that Endy and I had agreed I would produce. Work on the thesis, however, was not the only reason for the slowdown, and in fact was equipping me to be much more capable of producing the short descriptive and "plain-language" accounts that Endy favored. A more proximate cause of the slowdown was simply that the drafts of the reports that I had written had not been read. I completed the first report by the end of February 2010. I gave it to Endy and Arkin before posting on the BIOFAB website and emailing it to the SynBERC PIs with requests for comment. Endy provided some general feedback, which emphasized "accessibility" and the need to curb what might be taken as an excessively critical "tone." Arkin did not provide detailed feedback, but seemed pleased and told me he had already circulated it to others in his lab. The only person in the BIOFAB who read it closely was Mutalik. This was in part a function of the fact that he was assisting me in finding articles that spoke to the biotechnical claims made in the report. It was also a function of the fact that he was trying to work through the unease he was encountering in the BIOFAB meetings about the scope and feasibility of the facility's undertaking and his relationship to it. Mutalik encouraged me to publish the report, especially since he had begun circulating it to colleagues in India. No other members of the BIOFAB team read the report, as far as I could ascertain, despite Endy reminding them that a minimal goal of the reports was to provide a pedagogical resource to the team.

I completed a more or less final and revised draft of the first report by the end of March. That month and the month that followed was eaten in terms of time, concentration, and energy by the attacks on the Berkeley Human Practices team. The attack required response, both direct and indirect. The direct responses included providing short answers to the accusations leveled against Rabinow and our work. The indirect responses include beginning the long and important task of depersonalizing the attack, analyzing it, and finding a way to convert the experience into experimental lessons learned in such a way that a new phase of experimentation (whether in

SynBERC, BIOFAB, or elsewhere) could be taken up in a reconstructed manner. Another disruption that consumed time and morale was the invitation to Rabinow from the SynBERC administration to assist in identifying a new leader for SynBERC Human Practices, and then their refusal to permit him to participate in any of the official selection interviews and meetings. Rabinow actually proposed a list of three names. One was rejected as too intelligent and critically minded, and therefore not capable of the kind of communications work that Human Practices would need to begin foregrounding in place of research; one was rejected as too close to the security establishment and hence invited high-level scrutiny, which seemed to be a means of borrowing trouble. A third person in Rabinow's list of recommended replacements was Drew Endy. Although Endy was not equipped to design and facilitate the kind of research program that the Berkeley group had been pushing as its core agenda from the outset, he had been closely related to the circles of power in the US government and in the funding community concerning matters of ownership, biosecurity, and ethics. He was one of the few SynBERC PIs that had taken time to interact with the Human Practices team with some regularity. And in accepting this position he could provide a better structural link between Human Practices efforts at the BIOFAB and SynBERC. All of this was supposed to be settled within 60 days according to the NSF injunction. Endy finally accepted the position of the director of what he began calling "T4" in early September.

One affect of these swirling dynamics is that my time for working on the Human Practices reports was seriously disrupted, and the worth of taking such time seriously put in question. If the work of the Berkeley Human Practice group had been attacked, what would the response to my reports be? The pressure of Endy's suggestions to make these "accessible" and "basic" were intensified. Nonetheless, by the end of April I had finished a second report on the relation of BIOFAB to the iGEM competition and by the middle of June I had completed a draft of what I felt should be a more substantive undertaking. It was never clear to me whether Arkin read either of these drafts. It was clear that Endy had looked through them enough to ask me not to circulate the first yet; its tone needed to be adjusted so as to not risk driving a wedge between the BIOFAB and iGEM. With regard to the second report, which focused on the question of what it meant for the BIOFAB to be producing an open technology platform, Endy's response was equally categorical: it was simply too conceptually complicated to do the first-order work of declaring to the world that the BIOFAB wanted to give its work away. Technically minded readers would not have the patience to work through such details as the conceptual distinctions between things like Amyris' *platform technology* and iGEM's *technology platform*, regardless of the salience of this difference for the circulation and valuation of the BIOFAB's work. Asked not to share either of these two reports until Endy got back to me with more substantive details, I decided to put them on hold and begin concentrating on a longer and more systematic analysis of the BIOFAB's programmatic efforts, which would eventually become the basis for this thesis.

In mid-December the Presidential Commission on the Study of Bioethical Issues finished and submitted their final report on synthetic biology. The report had the effect of assuring almost everyone involved in SynBERC and the BIOFAB that synthetic biology would continue to see increases in funding as well as the inclusion of experiments like Human Practices for the near term. Synthetic biology and Human Practices would seem to be in a materially better position as a result of the report. Moreover, the combination of Endy's prominence as a spokesperson for synthetic biology, the director of the BIOFAB and the scientific director for SynBERC with his new position as the leader of Human Practices, he would seem to be ideally positioned to leverage the resources and visibility likely to follow from the Commission's work. Several

factors complicated this situation, however. The first was that although Endy had been appointed the lead of Human Practices in early September, by December when the report came out, and even January when the annual report writing and review would get underway he had not yet formulated a research program for Human Practices as mandated by his appointment. The one concrete step he had taken was to hire a post-doc out of MIT, Megan Palmer as an Associate Director. On one level Palmer seemed a strategically sound choice. Much of the SynBERC community had been annoyed by the fact that Human Practices did not seem to "speak its language," and did refused to orient its work toward what some bioengineers perceived as its real concerns—better communications and better public relations. Palmer was a trained bioengineer who had grown restless with technical work, and, inspired by a number of extra-curricular discussion groups on "social issues" at MIT and work on informal science education as a volunteer in a science museum, decided to try her hand at Human Practices. As a first act of orientation and engagement Palmer went on a "listening tour" in order to collect opinions about Human Practices and to construct a table of possible topics for consideration as the core agenda for Human Practices. In this light, and on a more serious level, the choice of Palmer was altogether dissonant with the substantive needs of the situation. The integrated position of Human Practices within SynBERC had always been at risk of compromising its legitimacy as a critical observer among the bioethics and science studies communities; the hiring of a bioengineer to direct its work on safety, security, ownership and ethics had intensified this risk. And to hire yet another bioengineer as co-director only reinforced a lack of sufficient seriousness.

A second complication followed from the first. As the leader of Human Practices Endy of course did not need to have his own research agenda—did not need (yet) to have a program in Human Practices under his direction. He could, rather, rely on the work being done by the other Human Practices participants in order to fill out the substance needed to report on year-to-date activities. This consisted of work being produced by the Oye group at MIT and the Rabinow led team at UC Berkeley. In a less direct fashion it also included the integration of Human Practices in the BIOFAB. In the weeks leading up to the completion of the annual report (which would include sections on SynBERC Human Practices as well as the BIOFAB) and in preparation for the annual site review, which would be held in March, Endy proposed a series of meetings first with the Rabinow group and then, once Palmer had returned from a month long vacation, meetings with the Rabinow group and Palmer. The purpose of these meetings was, frankly, hard negotiations about where the substantive research program of the Rabinow group and the BIOFAB would fit within a reworked schema that Endy could present to the National Science Foundation. Endy was convinced that the principal problem for Human Practices in relation to the NSF ERC reviewers was that it needed better packaging. It needed to frame its high-level and critical research projects in a fashion that could be understood and therefore accepted, funded, and protected for another year.

This, however, is where the second complication began to emerge for Endy. In addition to its SynBERC funded work on preparedness and ethics, the Rabinow group had been actively working on a non-SynBERC funded experiment with the production of online "studios"—productions that aimed to give an initial form to project materials and to present them in such a fashion that they could be critiqued and reworked. The group had been working on three that would provide a significant supplement and illuminate our funded Human Practices portfolio. These three would be finished by the time of the site review. The three studios dealt with topics likely to be disfavored by many within SynBERC. The first was a case of ethics examining the

relation of the SynBERC Industrial Advisory Board; the second was an examination of the critical limitations of the Presidential Commission on the Study of Bioethical Issues; the third was an elaboration of ethical directives that we took to be central establishing a critical relation to our work with synthetic biology. And although we did not plan to present the studios at the review—the work did not belong to SynBERC, after all—we made it clear to Endy that an honest and critical approach to these and similar themes was likely to characterize our work in the time to come. Endy articulated a willing to provide a space of minimal protection for work of this critical sort, and even offered his take on the themes we had outlined. He proposed introducing a four-fold schema as the structure for future "T4" work in SynBERC. The first would be the production of an educational module on lab safety and security for synthetic biology. This, he insisted, could be produced by the education group in the Center, and could basically take these "basics" off our back. A second element of the schema would involve work on ownership, sharing and innovation. This would be where Endy would put the bulk of his efforts. A third element would be entitled "mind the gaps" and could be presented as including topics such as ethics or preparedness that SynBERC researchers were uniquely positioned to advance given their close adjacency to the technical work. Endy stated plainly that "mind the gaps" would provide a space and justification and therefore likely protection for our work. The fourth element centered on community building and outreach. Its primary aim would be to get technicians to take Human Practices more seriously. Rabinow responded by reminding Endy that nothing formally and structurally had been done to ensure the protection of the work of the Berkeley group, which had been so viciously attacked at the previous review. He stated plainly that such protections would need to be in place in order for work to proceed. If they were, everyone in the Berkeley group agreed that "mind the gaps," however colloquial a framing, nonetheless provided a sufficiently accurate category for the inclusion of the work the group was interested in pursuing.

At the conclusion of a third meeting outlining these categories and interfacing them with the Berkeley and BIOFAB Human Practices priorities, Endy caught me and asked for a minute of my time. It was January, the report was due in a month, and the site review would follow in March. Endy expressed concern that the reports were not done yet and that, as such the legacy of my contributions to the BIOFAB might not be recognized. More specifically, he said he was worried about how to justify my inclusion to the funders if he didn't have the reports in hand. I assured him that I was working to have three core reports completed by the time of the review. I also reminded him that one reason the report production had stalled was that he had asked me not to circulate them until he gave me feedback. Endy agreed that he needed to get back to me, but that I needed to remind him to do so once I had given the drafts to him. A short time later I proposed to Endy that the most significant contributions I had made during the course of the year were in fact not the reports. The most significant contributions were my participations in the daily formation of the BIOFAB's program, particularly in my efforts to raise up to an explicit level a number of questions that I thought were producing irresolution on the part of the BIOFAB experimental team. These included perceived differences between Endy and Arkin on matters of biological rigor, design, measurement and the target audience of the BIOFAB's work. It also, and more importantly, included the question of the extent to which Endy's style and expectations about "good synthetic biology" were having a formative effect on the development of the lead practitioners. Endy agreed that the team leads still had not "synched up" with his view of things, and that this continued to trouble him, and in his view, had slowed the BIOFAB's

efforts. He then reminded me of the importance of getting the reports done, packaged, and put online. Then we could talk about strategies for circulating them.

Two weeks later the SynBERC annual report, including a report on the BIOFAB, was circulated to the "all-synberc" mailing list. Although I knew that the report needed to be filed by the third week in February I was a bit surprised to see it in its completed form. It had been the practice for the first five years of the Center that each section of the report would be principally composed by the Thrust or Test-Bed leader, but it would include the input and review of all of the Principal Investigators in that Thrust. Given that Rabinow had been removed as the director of the Human Practices thrust, everyone on the Berkeley team was looking forward to having relatively less work to do. To not have been consulted at all in the composition of the report and to not have been given the opportunity to review the sections that described our work, however, was disconcerting. In any event the sections of the report which described the Berkeley work were more or less accurate, and had clearly been based on descriptions we had written of our own projects. They were somewhat out of date, they were more or less back-grounded relative to other activities, and they had been framed according to the four-fold elements that Endy had recently proposed. All of which was irritating but seemed ultimately inconsequential.

Two aspects of the report were more consequential, however. The first was that Endy had changed the name of the Thrust 4 research component. Rather than "Human Practices" the name was now "synthetic biology practices"—the "practices thrust." As the new leader of the research thrust Endy was no doubt perfectly within his intuitionally assigned rights to change the name. The name "Human Practices," however, whatever its rhetorical pluses and minuses had been the designation for all of the work that we had been conducting, and for the overall orientation and distinctiveness of our undertaking for five years. To change the name had the indirect effect of partially erasing, or at least of retiring that legacy. Which may have been frustrating but acceptable if the Berkeley Human Practices group, including the BIOFAB, had been told that it was going to happen. To read the change for the first time in the report was startling. The second aspect concerned Human Practices in the BIOFAB directly. Although I was listed as a BIOFAB participant nowhere in the BIOFAB's report was my work mentioned or reviewed, positively or negatively. Endy no doubt had reasons for both omissions. With regard to the first I can only guess that he probably thought it easier just to make a summary decision and not to communicate it. When I called Endy out on this, he simply admitted that he should have handled it differently. When I brought up the second Endy simply explained that he did not think Human Practices would be continuing in the coming year (by that point I had accepted a position to help found the Center for Biological Futures at Fred Hutchinson in Seattle), and that it would be easier to explain not replacing me if he simply did not mention my work at all.

By the annual site review at the end of March, I had completed the three reports that Endy and I had agreed would be the basis of my contracted contribution to the BIOFAB's work. My insistence that there were actually more important aspects of my participation was not brought up again. As the new director or the "Practices Thrust," it was Endy's responsibility to provide the presentation at both the 2011 SynBERC retreat and site review. Two days prior to the retreat Endy asked the Berkeley Human Practices group whether or not we wanted to present on our work. We declined insisting that given the events of the previous year's review it was best that Endy stand up and define the new agenda. Endy's presentation was more or less what we had anticipated from having read the report. He provided a list of funded projects, which included several in the Rabinow group. He then provided an overview of his four-fold schema,

mentioning few specifics particularly with regard to his designation "mind the gaps." Endy's presentation was followed by a presentation by Palmer. She explained that she had conducted a "listening tour" in order to give investigators who were working on the technical problems to have a direct hand in defining the agenda for Thrust four. She noted that a special focus moving forward would be on getting the "younger researchers" excited. She clarified that what she meant by this was that Human Practices would especially target everyone besides the Principal Investigators. She explained that better communication, community building, and having fun would be the watchwords. The Berkeley Human Practices group stood in the back and listened. During the question and answer session Endy was asked by a member of the Scientific Advisory Board to describe more of what was going on in this category called "mind the gaps"—whether this included types of project other than those covered in the other areas like safety or ownership, and if so what might those be? Endy replied, "Nothing comes to mind."

A PROLOGUE TO THE NEAR FUTURE

Existential Tests: An Exit Toward Reconstruction

The test (the probatio*), unlike abstinence, can and must become a general attitude in life, and not just a sort of trading exercise whose limits one fixes at a certain moment.*
—Michel Foucault[320]

I conclude this thesis with a short prologue to the near future. Such a prologue, I propose, consists of the work of reconstructing significant elements of the experiences and experiments in Human Practices so as to render them in a form which is useful for thinking through the stakes of the endeavor as well as reorienting to a new phase of inquiry. In this mode, I recapitulate three episodes from my experiment, arraying them in relation to three concepts. These initial reconstructive efforts can be cast as *existential tests*, as I will briefly show.[321]

STATUS: WHAT IS OUR STANCE?

The inclusion of Human Practices as a component of SynBERC was mandated as a requirement of funding. Jay Keasling *et al*. who proposed the Center were perfectly willing to accept this requirement and invited Paul Rabinow at Berkeley to design and co-lead the experiment. Rabinow, in turn, invited me to and then Anthony Stavrianakis to help think through a form of post-ELSI ethics, and we took the proverbial plunge together.

What we proposed was to design ontological and ethical inquiry: how are the SynBERC researchers bringing things into the world (their careers, modes of expertise, institutions, biological objects)? How are they naming these things, distributing, and modifying them? We foregrounded analysis of the micro-politics of organizational form, with normative questions of ethics as the crucial variable. In this way, from the outset, we concerned ourselves with *status*, taken just in the simple sense of monitoring the state-of-play in a developing situation. Given the promise of formal equality within the center, however, we also concerned ourselves with *status* in the sense of rank and position. We were not naïve about asymmetries in authority, and we have taken these asymmetries as both objects of analysis and sites of intervention. Lastly, and less obviously, we devoted sustained attention to questions of *status* understood in the etymological sense of the term, *starē* or *standing*: the way in which synthetic biology has been proposed and fashioned as a way of life, with all this implies in terms of affect, habits, dispositions, and aspirations—not least of which our own.[322]

TEST OF OBJECTS: WHAT IS BEING MADE?

During the first year of the BIOFAB's operations synthetic biology began to come into its own in the US: Congressional hearings, meetings of the President's Bioethics Commission, a sharp increase in government funding and venture capital. All of these events were energized, at least in part, either by the promise the synthetic biology could catalyze the so-called bio-economy through the production of biofuels and other industrial chemicals of interest, or by the Venter Institute's announcement of the assembly of their self-titled JCVI-syn1.0 genome.

Through some combination of these two, synthetic biology was framed more as a question of prosperity and less about playfulness or amelioration.

Reactions to JCVI's work within the BIOFAB resonated with emphases and affects expressed elsewhere, but to quite specific effect. Drew Endy's public responses were an amalgam of professional competition and Keynesian optimism: "This is only a technological augmentation; but this is a proof-of concept of what now needs to be done." He proposed analogies to the printing press and the programmer: it's one thing to print a book, another thing to write one; one thing to compile code, another to write it. All this is familiar.

The BIOFAB's other co-director, Adam Arkin, responded less publicly, but in an anthropologically more interesting fashion. Arkin frankly admitted to playing it both ways. On one side, he told colleagues that the near-term technical value of JCVI's work was lower than other less heralded efforts, such as the Church Lab's MAGE technology. On another side, and with regard to the long-term, he expressed what we have all heard in one form or another: namely that the significance of JCVIs work lies in the notion and prospect of *phylogenic discontinuity* and its ramifications for both the biological and moral imagination. Arkin detailed the ontological consequences of leveraging a repertoire of existing cellular mechanisms: genomic minimization, *in vivo* assembly, genomic transfer, cellular reconstruction. Six to twelve population doublings and all the molecules of the host cell have been replaced by the synthetic DNA. The effect is the further unsettling of genetic continuity as either a design constraint or an index of identity.

Crucially, Arkin left aside the predominant analogies to machines and programming as well as polemics over creating life. (This is, after all, a man who regularly says "Parts? I want to understand the physical constants of genetic expression!") Rather than analogies, Arkin stressed what Canguilhem specified as the role of *mechanisms*: ensembles of articulated actions and effects that serve as a conceptual and material juncture point between the organic and the artificial, and thereby between the engineer and the engineered.

Over the course of several exchanges I proposed to Arkin that his framing provided an occasion for re-thinking themes that Canguilhem had identified as the problem of "the monstrous and monstrosity"—the question of what we should make, ethically and biotechnically, of the "same engendering the other'" as Canguilhem put it. Is the making of a monster actually monstrous? I did not use these terms, of course. What I actually said was that by drawing attention to the relation of the maker and the made, Arkin showed that it wasn't all about instrumentalism. In this way he was not too far afield from long-standing debates in *natural law*: the problem of relations among living beings, their norms, and their forms. The difference here was that questions of biological design and functional composition were being posed without appeal to notions of natural kinds or divine providence.

Arkin's response was not hostile. Rather, he was tepidly intrigued, but eventually annoyed. He repeated a familiar polemic syllogism: nature is nature. It can be neither "cooperated with" nor "violated." Hence, by suggesting consonance with debates in natural law, I was opening the gates to irrationalism and forgetting that biologists are uniquely authorized to speak to truth about living beings. The matter was basically settled by an exercise of power: he told me that the BIOFAB should not be offering opinions on these themes.

It strikes me that Arkin miscalculated. The conceptual interconnection of problems, taken as a test and method of determining what's actually being made, is exactly what's at stake and

what needs to be pursued. Introducing a shift in analytic registers, I would propose that synthetic biology is marked *precisely* by the need for what Foucault, summarizing Marcus Aurelius, referred to as "tests of the object." The term *test* here is a more or less adequate translation of the Greek *elegkhein*, which means an *examination* as well as a *trial* or *refutation*.[323] Aurelius' tests of the object were constituted by a series of disciplined exercises whose aim was to achieve analytic clarity about things of the world and to establish the measure of their worth. They were predicated on a problem characteristic of other spiritual exercises of the antique world: how does one go about the task of clearly seeing the flux of objects encountered (or made) in the course of life, without resorting to the seductions of logically necessary relations?

As one possible solution, Aurelius prescribed a kind of regulated movement between seeing objects as a part of a larger whole (BIOAFB, SynBERC, biofuels, valuations games), decomposing it into its constitutive elements (genetic expression, transcription functions, start sites, base pairs), and rehearsing their names (parts, chassis, human practices). The *task* was to grasp the object in its variability, instability and inevitable decay. The *aim* was to free oneself from the constraints of prior opinion and to delimit the frameworks that structure experience. The ethical worth of the test—the "enlargement of the soul" as Aurelius puts it—required a further step. Disciplined analysis needed to be connected to systematic valuation. This phase tested the value of the object across the multiple relations that constitute it. What is its use in the cosmos? What is its use for things human, in the polis or the household?

Through analysis and evaluation tests of the object opened the possibility of taking up a more proper, that is to say, more virtuous posture toward things of the world. To quote Foucault: "Thanks to this [test] we will be able to define what virtue the subject needs with regard to these things." Given that the worth of the artifacts of synthetic biology and our relation to them are *unlikely* to be determined by the harmonics of a cosmos, the nature of the polis, or the respite of providentially given names, how do we determine which tests of the object are worthwhile and where should carry them out? What is a synthetic genome? Is it a function, an object, a relation? How are parts libraries actually used? Is work in *E. coli* valuable, or only work in fermentable yeast? Which petro-chemical feed-stocks might be replaced by biomass? And who has the right to say?[324]

TEST OF DEPORTMENT: WHAT IS A SYNTHETIC BIOLOGIST?

The BIOFAB's original proposal and mandate was to "create thousands of new BioBrick parts" capable of "controlling replication, transcription, and translation." Endy's catchphrase was that the BIOFAB would "take the central dogma off the table as a research question for bioengineering." This broad framing—tantamount to a proposal to solve the core issue in genetics for the past 50 years—actually has no *direct* effect on the constitution of the BIOAB's program.

It has, however, had an *indirect* effect on the BIOFAB biologists and their unease about the eventual significance and seriousness of their work. After all, no one actually knows what a standardized biological part should or will be. Endy has countered this unease with assertive and brusque confidence. When work plans are presented he will say: "Why are we talking about this? Tell me what the outcomes are going to be? Don't be hypothesis driven!" His rebuffs are one part self-stylization and one part confidence in the salience of his vision. Endy's manifesto, as you know, turns on notions of standardization, decoupling, abstraction hierarchies, and an ethos of sharing. It substance, strictly speaking, is not a plan. Rather, it combines cases of prior

engineering successes with the proposition that biologists need to learn to *deport* themselves in a way consistent with those successes.

The challenge, of course, is how to literalize Endy's *figural* rendering of the future of synthetic biology as an embodied stance and practice, thereby making it manageable. The shortcoming of prior work in synthetic biology, Endy would emphasize in the early going, did not turn on its biological feasibility as some critics have suggest, but rather on lack of opportunity and facility. A parts-based approach needs to be *professionalized*. This meant, most simply, paying a technical team to get work done in a routinized fashion. It also meant supporting bioengineers willing to take up a certain stance toward their work, one predicated on the ability to simply get-things-done and to treat something-as-better-than-nothing. Professionalization thus entailed a certain price to be paid. Endy has expected members of the BIOFAB to cultivate a disposition toward synthetic biology consistent with the terms of his manifesto and mediated by an emphasis on production.

If Endy's manifesto has had energizing effects for funders and for the field of synthetic biology more broadly—and it obviously has—it has sometimes had stultifying affects on the BIOFAB biologists responsible for carrying out the work. A few weeks after work began—and well before operational protocols had been settled—BIOFAB members were asked to present their work at the SynBERC annual retreat. For those who remained uneasy about the framing or technical feasibility of the stated BIOFAB's goals, the SynBERC retreat presented the uncomfortable task of justifying one's scientific place in the world. More seriously, it entailed the risk of not being taken seriously by one's friends and colleagues, or worse, by oneself.

Switching registers again, it seems to me, in this light, that the work of the BIOFAB and parts-based synthetic biology more generally can usefully be thought about as what I would call a *test of deportment*. *Deportment* should be distinguished from *attitude*. It is a bodily term denoting "bearing," "posture," or "stance." In several letters Marcus Aurelius exhorts his correspondents to orient their tests of objects to the problem of virtue.[325] It is not enough to test the value of an object in relation to nature, the city, or providence. It must also be tested in relation to oneself. And thereby one must also test oneself in relation to the object.

Aurelius proposes that in distinction from tests of objects, tests of deportment begin with a focus on the discontinuity and fragmentation that marks life, body and soul. One exemplary exercise concentrates on the fragility of the isolated breath. One breath must be made to follow another, and another, toward a horizon of possible duration. The object of such an exercise is to unflinchingly attend to the reality and problems of irresolution and instability that affect life. The purpose is to inoculate oneself against the stultifying affects of such fragmentation. Concentration on discontinuity, Aurelius proposes, opens the possibility of finding stability and resolution through the cultivation of virtue. And in being freed from stultification and irresolution through virtue, one might be able to comport oneself more appropriately and more resolutely.

The senior biologists on the BIOFAB team have not yet sufficiently confronted their sense of irresolution about Endy's insistent style and orientation to production. This has left them in a mildly purgatorial state. They are not quite willing to risk being changed, and not quite willing to walk away. It bears noting that as experimental work began to progress in a more serious fashion and data generated the irresolution has begun to dissipate. No one has changed

their minds about the work of course. Rather, they've gotten to work and *work* is beginning to change them.

In this light I have put a number of questions to the members of the BIOFAB, questions they really need to be posing to themselves: Why this irresolution? What might be done, if anything, to move toward a more satisfying position? Should we continue to black-box sequences in analyses? Should we go on describing work as an "expression operating systems"? In short: What does it mean to actively take up the position of a synthetic biologist? What do you have to give up? Is it worth it scientifically and also vocationally? And how will you know whether to move on or see this through?[326]

TEST OF CAPACITY: HOW SHOULD WE FORM OURSELVES?

The relevance of such questions for my own work has certainly not escaped me.

At the SynBERC site review Endy was asked what he thought about having an embedded ethicist around. Endy retorted: "Bennett is *not* an *embedded* ethicist; he is a *member* of the BIOFAB." Endy has made it clear: he wants me to contribute to the facility's goals and mandate even as I make it a critical object of study.

In this spirit-of-full-membership, Endy invited me to participate in a closed-door meeting sponsored by the NIH and the NCRC in Washington. The meeting was to determine whether or not these two institutions should invest in synthetic biology. I was the most junior participant and one of only two social scientists. I was also the last to present on a 10 hour, one-day agenda which included many of the principle US biologists associated with the notion of synthetic biology: Endy, George Church, Dan Gibson, Craig Venter and a number of others.

The presentation went fine. Surprisingly, given the time of day, I was even asked several questions and told I was "understandable." More interesting was the wine-reception which followed. During the reception I had an exchange with SynBERC PI Wendell Lim, which was quite remarkable, and worth thinking about. Speaking in a casual manner Lim asked: "how does it feel to be SynBERC's *trophy wife*?" As I explained in the final chapter of the thesis, two facts blunted the impact of his otherwise startling question. First is that I basically get along with Lim. The second is that he asked the question as though he wasn't saying anything offensive—as one member of the club to another.

Given this exchange it has been crucial to ask: What can the human sciences contribute to synthetic biology? Taken in light of Lim's blunt question, one sardonic response might be: we offer symbolic capital. A more appropriate response would be *thumic:* turn the question back and ask, "What does synthetic biology offer to the human sciences?"

A third response is more difficult: to provide strategies for living with an apparent dilemma, and to foster the capacities needed to do so well. The dilemma, of course, is this: in our work many of us have tried to show *how* the production of scientific knowledge and institutions, as well as the *figurations* on which they depend, crucially entail matters of habit, character, disposition, credibility and the micro-politics of everyday life. But if the implications of Lim's question are taken seriously, at least for some cases, these are the factors most likely to encumber our ability to contribute to this thing called "synthetic biology." Which means analysis and interventions at the level of habits and dispositions are very much in order, despite our knowing that such domains are precisely where we may be *least assured* of making a difference.

A question then is: what is the worth of participating when crucial aspects of *our* scientific analysis, our figurations, cannot be foregrounded and dealt with in any direct and consequential manner *within* these bioscientific settings? How do we determine the worth of our efforts when it produces indifference and even hostility? And when do we know that it is time to exit?

There is a third and final class of tests that bears consideration. This class of tests the Stoics referred to as *probatio*—the root of the English word probation. They are tests aimed at knowing what you are capable of: the measure of what you can take, what you can do and whether you can see it through.[327]

Two aspects of these *tests of capacity* are pertinent. First—and here I'm following Foucault's reading—is that they are tests of the self on the self. They are not a test of objects or of one's deportment toward an object or situation. These are, rather, tests you carry out on yourself in order to locate just where you are in terms of the development of capacities, how far you've come, where you need to go. These tests are typified by a kind of contract: "I will make a certain measure of progress within a certain period of time and will measure myself and ensure my growth bit by bit." "How regularly do I critique the biologists I work with? How often to I find myself holding back? How often is my advice listened to or acted on? Who takes it seriously when I define problems or propose analyses? How often am I asked to justify myself, tacitly or directly? Do I know when to exit, change course, or carry things through?"

A second aspect is more difficult but more crucial: The Stoics asked: how can tests of capacity be made into a form of life? How can the measure and cultivation of capacities become a general disposition? Seneca offers an analogy to the divine life. The divine, he explains, relates to humans in a mode of *pedagogical vigilance*. This pedagogical vigilance is marked by both strictness and by care. The divine makes human life into a continual test as a form of care. Pedagogical vigilance, according to Seneca, entails a paradox and an outcome. The paradox is that the divine tests most vigorously those who are good; the wicked are given over to pleasure and sloth. The outcome is that by being tested the good may become increasingly fit, capable, and prepared. An obvious question follows: prepared for what? It's significant that Seneca does not thematize the question of *fixed* ends. Instead, the *work* of becoming prepared, knowing what it *takes*, what *forms* it consists in: these are his primary concerns. One reason for this emphasis is that neither life's events nor the form of life appropriate to those events can be known in advance. Being capable of a life worth living, of enduring difficulty, requires being ready to respond, having one's capacities ready-at-hand.

The fact that Wendell Lim or other senior figures in synthetic biology may not be persuaded of the *equal* worth of the social sciences and *the fact* that they are *unlikely* to change their habits or dispositions in response to our work, *should not* be taken as the index of the worth of our contributions. A *vigilant* commitment to *pedagogy* requires a different practice: binding ourselves to the work and worth of observation, analysis, assessment, and the critique of scientific and vocational practices, as well as speaking frankly about the implications of these assessments, even where there is little hope of reform. (And need I add: for ourselves as well as others).[328]

DIRECTIVES: WHAT SHOULD WE DO?

As an aid to conducting our experiment, the Berkeley Human Practices group has been developing a repertoire of what we are calling *directives*.[329] Directives are points of orientation,

indications, and guides. They are brief, schematic, and somewhat maxim-like. They indicate what to do and carry a certain authority. But whatever authority they carry derives from *experience* and not from *power* or *station*. Consonant with Seneca's directives for testing capacities, the aim of these directives is to prepare ourselves to face unknown futures, and hopefully thereby to test ourselves, scientifically, ethically, vocationally.

In March 1982, in the last session of his twelve week lecture course at the *Collège de France*, Michel Foucault summed up and pointed forward.[330] He reminded his auditors of a key premise: that the antique philosophical imperative to know-thyself had become an overriding preoccupation in the history of thinking in the West and was privileged as the guiding thread for problems of the subject and reflexivity. A principle aim of the course had been to show that in its earliest formulations this imperative had actually been taken up in the context and service of another imperative: to care for the self. To care for oneself, Foucault explained, meant primarily to give attention to whether or not one was an ethical subject of the truth, and, if not, what might be done.

Care of the self implied a task and a challenge. The task was to realize and actualize a form of life consistent with the truth. The challenge consisted in learning, developing, and practicing appropriate *techne tou bios*, arts of living: the cultivation of exercises, habits, relations, practices and experiences of a formative sort. Hence the need for a permanent and strong connection between self-knowledge and self-care. And hence the objective of Foucault's course: to examine the modes and forms of reflexivity as well as the history of the practices on which they are based in order to discern and specify the dynamics by way of which certain forms of life, certain ways of being a subject, were made possible: thought though, worked on, embodied.

Crucial among these modes and forms of self-knowledge were those pertaining to the future.[331] How should one imagine the future; how should one face it? How should one test oneself in relation to it so as to determine whether or not one was capable? And if one found oneself to be less than fully capable, how to determine which exercises one might undertake in order to become more capable? The future can be disruptive and unsettling, bringing irresolution, restlessness, and hesitation. It can cause fragmentation and inaction—the affliction of *stultitia*. The task was thus to prepare oneself for the future in such a way overcome *stultitia* and better equip oneself for right action.

Polar sets of strategies consisted in either denying the reality of the future—meditating on its nothingness—or in accepting the fatefulness of the future—seeking to free oneself from it by recognizing one's inability to change the minds of the gods or the vicissitudes of fate. In distinction from these was the Stoic exercise of the *praemeditatio malorum*—the premeditation of evils. This set of disciplined practices focused on the future as unknowable, but real and not entirely fateful. The work consisted in imagining a range of possible future difficulties and to meditate on the appropriate responses in terms of both affect and action. The purpose and aim was to make those possible futures present in such a way as to test oneself against them. Such testing offered a two-fold aide. First it prepared one, in a disciplined fashion, to have the right passions and truths ready at hand. Second it illuminated the actual non-reality of what one was imagining and therefore sealing off its stultifying affects.

The range of disciplined practices designed by the Stoics in the work of *praemeditatio malorum* may no longer be relevant. After all, as Rabinow has stressed, echoing Foucault, much

of antique thought was “a profound error.” “It was a profound error because it was committed to mastery of the self either a means of the preparation to rule or to endure fate’s slings and arrows.”[332] For those working at the BIOFAB the challenge and opportunity was never been to rule or to endure fate. It did, however, involve the need to face up to an unknown future in such a way as to ward off the affliction of *stultitia* so as to become ethical subjects of the truth. Or, at least to take up a stance toward one’s work that could be found scientifically serious and ethically worthwhile.

BIBLIOGRAPHY

Abelson, Harold, *et al.* "Amorphous Computing." Technical Report on Logic, Programming, and DNA. Available at: http://hdl.handle.net/1721.1/5929, 1999.

Anderson, J. C., Clarke, E. J., Arkin, A. P. & Voigt, C. A. Environmentally controlled invasion of cancer cells by engineered bacteria. *Journal of Molecular Biology* 355, 619–627, 2006.

Anderson JC, Dueber JE, Leguia M, Wu GC, Goler JA, Arkin AP, Keasling JD. (2010). BglBricks: A flexible standard for biological part assembly. *Journal of Biological Engineering* Jan 20 4(1):1.

Andrianantoandro, Basu, Karig, and Weiss. "Synthetic biology: new engineering rules for an emerging discipline." *Nature Molecular Systems Biology* v.2: E1-14, 2006.

Anthropological Research on the Contemporary. http://anthropos-lab.net/

Arkin, AP. "Setting the standard in synthetic biology." *Nature Biotechnology* 26(8): 771-774, 2008.

Baker, Church, Collins, Endy, Jacobson, Keasling, Modrich, Smolke and Weiss. "Engineering Life: Building a Fab for Biology." *Scientific American* June: 44 – 51, 2006.

Barben, Daniel, Erik Fisher, Cynthia Selin, and David Guston. "Anticipatory Governance of Nanotechnology: Foresight, Engagement, and Integration." In Hackett *et al.* eds. *The Handbook of Science and Technology Studies, 3rd ed*. Cambridge: MIT Press, 2007.

Bedau Mark, Parke, Emily, eds. *The Ethics of Protocells: Moral and Social Implications of Creating Life in the Laboratory*. Cambridge: MIT Press, 2008.

Benner, Steven A. and A. Michael Sismour. "Synthetic Biology." *Nature Reviews Genetics* 6, 533-543 (July 2005).

Bennett, Gaymon, Anthony Stavrianakis, and Paul Rabinow. "From Synthetic Biology to Bio-Hacking: Are We Prepared," *Nature Biotechnology* December 2009, Volume 27 No 12, 1109 – 1111, 2009.

Berg, Paul. "Asilomar and DNA."Online at http://nobelprize.org/nobel_prizes/chemistry/articles/berg/index.html.

BioBricks Foundation. http://biobricks.org/.

BioBrick Standard. http://openwetware.org/wiki/Biobrick_standard.

BIOS Centre for the Study of Bioscience, Biomedicine, Biotechnology, and Society. http://www2.lse.ac.uk/BIOS/home.aspx.

Bios-Technika. http://bios-technika.net/.

Boldt and Muller. Of Newtons and heretics. *Nature Biotechnology* 27, 321 – 322, 2009.

Boltanski, Luc and Laurent Thevenot. *On Justification: Economies of Worth*, trans. Katherine Portor. Princeton and Oxford: Princeton University Press, 2006.

Brenner, Sydney. "The end of the beginning." *Science* 287:2173-74, 2000.

Bugl *et al*. "DNA Synthesis and biological security." *Nature Biotechnology* 25, 627-629, 2007.

Burke, Kenneth. *Permanence and Change*. Indianapolis: Bobbs-Merrill, 1965.

Campos, Luis. "That Was the Synthetic Biology That Was." In *Synthetic Biology: The Technoscience and Its Societal Consequences.* Markus Schmidt *et al.*, eds. Springer Academic Publishing, 2009.

Canton, Labno, and Endy. Refinement and standardization of synthetic biological parts and devices." *Nature Biotechnology* 26(8): 787-793, 2008.

The Center for Bioethics and Medical Humanities, University of South Carolina. http://www.ipspr.sc.edu/cbmh/default.asp.

The Center for Nanotechnology and Society, Arizona State University. http://cns.asu.edu/.

Church, George. "Let us go forth and safely multiply." *Nature* 438: 423, 2005.

Church Lab, Harvard University. http://arep.med.harvard.edu/.

Cook-Deegan, Robert. *The Gene Wars: How Science, Politics and the Human Genome Project*. New York: Norton, 1995.

Daston, Lorraine and Peter Galison. *Objectivity*. Cambridge: MIT Press, 2007.

Dewey, John. *Liberalism and Social Action*. New York: G. P. Putnam's Sons, 1935.

Dewey, John. *Reconstruction in Philosophy*, enlarged edition. Boston: Beacon Press, 1957.

Ellington, Andrew D. "Man versus Machine versus Ribozyme," *PLoS Biology* May; 6(5): e132, 2008.

Endy, Drew. "Foundations for engineering biology." *Nature* 438(7067): 449-453, 2005.

Evans, John. *Playing God?: Human Genetic Engineering and the Rationalization of Public Bioethical Debate*. Chicago: Chicago University Press, 2001.

Faubion, James D. "Toward an Anthropology of Ethics: Foucault and the Pedagogies of Autopoiesis." *Representations* 74, Spring 83-104, 2001.

Faubion, James D. *The Shadows and Lights of Waco: Millennialism Today* Princeton: Princeton University Press, 2001.

Fisher, Erik *et al.* "Midstream Modulation of Technology: Governance From Within." *Bulletin of Science, Technology & Society* 26(6): 485-496, 2006.

Flahaut, François. *La méchanceté*. Paris: La Découverte. (English translation by Liz Heron, *Malice*, London: Verso Books, 2003, 1998.

Forster and Church. Towards synthesis of a minimal cell. *Molecular Systems Biology* 2:45, 2006.

Foucault, Michel. "What is Enlightenment?" In *The Foucault Reader*. Paul Rabinow, editor. New York: Pantheon Books, 1984.

Foucault, Michel. *L'Herméneutique du sujet, Cours au Collège de France, 1981-82.* 'Hautes Études,' Paris: Éditions de l'École des Hautes Etudes, Éditions Gallimard, Éditions du Seuil, 2001.

Foucault, Michel. *Sécurité, Territoire, Population: Cours au Collège de France, 1977-78*, Paris: Hautes Etudes, Seuil/Gallimard, 2004.

Foucault, Michel, Paul Veyne, and François Weil. *Des travaux*. In Michel Foucault, *Dits et Ecrits, T. IV*, 1983.

Gabaldon *et al*. The Core of a Minimal Gene Set: Insights from Natural Reduced Genomes. In Rasmussen, Steen *et al*. eds. *Protocells: Bridging Nonliving and Living Matter*. Cambridge: MIT Press, 2008.

Ganguli-Mitra, A., Schmidt, M., Torgersen, H., Deplazes, A. & Biller-Andorno, *Nature Biotechnology* 27, 321-322, 2009.

Galison, Peter. *How Experiments End*. Chicago: University of Chicago Press, 1987.

Garfinkel, M, Endy D, Epstein G, Freidman R. "Synthetic Genomics: Options for Governance." *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 4: 359-62, 2007.

Gibbons, Michael. "Science's new social contract with society." *Nature* 402, C81, 1999.

Gibson, D. *et al.* "One-step assembly in yeast of 25 overlapping DNA fragments to form a complete synthetic Mycoplasma genitalium genome." *Proceedings of the National Academy of Sciences USA* 105(51): 20404-9, 2008.

Guston, David. *Between Politics and Science: Assuring the Integrity and Productivity of Research*. New York: Cambridge University Press, 2000.

Hacking, Ian. *Historical Ontology*. Cambridge: Harvard University Press, 2004.

Hacking, Ian. "Inaugural lecture: Chair of Philosophy and History of Scientific Concepts at the Collège de France, 16 January 2001." *Economy and Society*, 31: 1, 1 — 14, 2002.

The Hastings Center. http://www.thehastingscenter.org/.

Hirschmann, Albert O. *Exit, Voice, and Loyalty: Responses to Decline in Firms, Organizations and States*. Harvard University Press, 1970.

International Association Synthetic Biology. http://www.ia-sb.eu/go/synthetic-biology/.

Jasanoff, Sheila. *Designs on Nature: Science and Democracy in Europe and the United States*. Princeton: Princeton University Press, 2005.

J. Craig Venter Institute (JCVI). http://www.jcvi.org/.

Joint Bio-Energy Institute (JBEI). http://jbei.org/.

Jonsen, Albert. *The Birth of Bioethics*. Oxford: Oxford University Press, 2003.

Kelle, Alexander. Synthetic Biology & Biosecurity Awareness In Europe. Bradford Science and Technology Report No.9, 2007.

Keller, Evelyn Fox. What does synthetic biology have to do with biology? *BioSocieties* 4, 291-302, 1 September 2009.

Kelly, Jason R. *et al.* (2009). Measuring the activity of BioBrick promoters using an in vivo reference standard. *Journal of Biological Engineering* 3:4 doi:10.1186/1754-1611-3-4.

Kevles, Daniel and Leroy Hood. *The Code of Codes*. Cambridge: Harvard University Press, 1992.

Khalil, Ahmad S. and James J. Collins, "Synthetic biology: applications come of age," *Nature Reviews Genetics* 11, 367-379, 2010.

Khushf, George. "Upstream Ethics in Nanomedicine: A Call for Research." *Nanomedicine* 2(4): 511-21, 2007.

Kleinman, Arthur, Renee Fox, and Allan Brandt, eds. *Bioethics and Beyond*. *Deadalus* 128(4), 1999.

Knight, Tom. "Idempotent Vector Design for Standard Assembly of Biobricks." Whitepaper, 2003. Online at: http://openwetware.org/images/b/bd/BBFRFC9.pdf

Kwok, Roberta. "Five hard truths for synthetic biology," *Nature* 463, 288-290, Published online 20 January 2010. Available at doi:10.1038/463288a, 2010.

Lash, Scott, Bronislaw Szerszynski, and Brian Wynne, eds. *Risk, Environment and Modernity: Towards a New Ecology*. London: Sage Publications. 1996.

Latour, Bruno and Stephen Woolgar. *Laboratory Life: The Social Construction of Scientific Facts.* Beverly Hills: Sage Publications, 1979.

Lentzos, Fillippa, Gaymon Bennett, Jef Boeke, Drew Endy and Paul Rabinow. Visions and Challenges in Redesigning Life. *BioSocieties*, Volume 3, Issue 03, Sep 2008 , 311-323, 2008.

Lucks, JB, Qi L, Whitaker WR, Arkin AP. "Toward scalable parts families for predictable design of biological circuits." *Current Opinion in Microbiology* (6): 567-73, 2008.

Luhmann, Niklas. *Die Gesellschaft der Gesellschaft*, 2 vols. Frankfurt-am-Main: Suhrkamp, 1997.

Luhmann, Niklas. *Risk: A Sociological Theory*. New York: Aldine Transaction, 2005.

Martin, *et al.* Synthetic Metabolism: Engineering Biology at the Protein and Pathway Scales. *Chemistry and Biology* v16, Issue 3, 27 March 2009, 277-286, 2009.

Maurer, Stephen *et al*. From Understanding to Action: Community-Based Options for Improving Safety and Security in Synthetic Biology. 2006. Whitepaper accessed online May 31, 2010 http://gspp.berkeley.edu/iths/UC%20White%20Paper.pdf

Mutalik VK, Nonaka G, Ades SE, Rhodius VA, Gross CA. "Promoter strength properties of the complete sigma E regulon of Escherichia coli and Salmonella enteric." *Journal of Bacteriology* Dec;191(23):7279-87, 2009.

National Scientific Advisory Board for Biosecurity. http://oba.od.nih.gov/biosecurity/biosecurity.html

Nowotny, Helga, Peter Scott, and Michael Gibbon. *Re-Thinking Science: Knowledge and the Public in an Age of Uncertainty*. Oxford: Wiley-Blackwell, 2001.

O'Malley, M, Powell, A, Davies, and Calvert, J. Knowledge-making distinctions in synthetic biology. *BioEssays* 30(1): 57–65, 2008.

Parens, Erik, J Johnston, and Jacob Moses. "Do We Need 'Synthetic Bioethics'?" *Science* 321(5895): 1449, 2008.

Pauly, Phillip. *Controlling Life. Jacques Loeb and the Engineering Ideal in Biology.* Oxford and New York: Oxford University Press.1987.

Pence, Gregory. *Who is Afraid of Human Cloning?* New York: Rowman and Littlefield, 1998.

Purnick, P. and R. Weiss. The Second Wave of Synthetic Biology: From Modules to Systems. *Nature Molecular and Cell Biology* June v.10: 410-422, 2009.

Rabinow, Paul. *French DNA: Trouble in Purgatory*. Chicago: Chicago University Press, 1999.

Rabinow, Paul. *Anthropos Today: Reflections on Modern Equipment*. Princeton: Princeton University Press, 2002.

Rabinow, Paul. *Marking Time: On the Anthropology of the Contemporary*. Princeton: Princeton University Press, 2007.

Rabinow, Paul. *Symbolic Domination: Cultural Form and Historical Change in Morocco*. Chicago: University of Chicago Press, 1975.

Rabinow, Paul. *French Modern: Norms and Forms of the Social Environment*. Chicago: University of Chicago Press, 1989.

Rabinow, Paul. "The Biological Modern." *ARC Concept Note No. 6*, February 2006. Online at http://anthropos-lab.net/wp/publications/2007/08/conceptnoteno6.pdf. Accessed December 2010.

Rabinow, Paul and Nikolas Rose. Biopower Today. *BioSocieties*, 1, 195–217, 2006.

Rabinow, Paul and Gaymon Bennett. *Designing Human Practices: An Experiment with Synthetic Biology*. Chicago: Chicago University Press, 2012.

Rabinow, Paul and Gaymon Bennett. "Human Practices: Interfacing Three Modes of Collaboration." In Bedau and Parke, eds. *The Ethics of Protocells: Moral and Social Implications of Creating Life in the Laboratory*. Cambridge: MIT Press, 2008b.

Rabinow, Paul and Gaymon Bennett. "From Bioethics to Human Practices, or Assembling Contemporary Equipment." In da Costa and Philips, eds. *Tactical Biopolitics Art, Activism, and Technoscience*. Cambridge: MIT Press, 2007.

Rabinow, Paul and Gaymon Bennett. "Synthetic biology: ethical ramifications 2009. *The Journal of Systems and Synthetic Biology* December 3(1-4), 2009.

Rabinow, Paul and Gaymon Bennett. From Bioethics to Human Practices, or Assembling Contemporary Equipment. In da Costa and Philips, eds. *Tactical Biopolitics Art, Activism, and Technoscience*. Cambridge: MIT Press, 2007.

Rabinow, Paul, George Marcus, James D. Faubion, and Tobias Reese, *Designs for an Anthropology of the Contemporary*. Durham: Duke University Press, 2008.

Rabinow, Paul and Talia Dan Cohen. *A Machine to Make a Future: Biotech Chronicles*. Princeton: Princeton University Press, 2005.

Rai A, and Boyle J. "Synthetic Biology: Caught between Property Rights, the Public Domain, and the Commons." *PLoS Biology* 5(3): 58, 2007.

Registry of Standard Biological Parts. http://partsregistry.org/Main_Page.

Rasmussen, Steen *et al.* eds. *Protocells: Bridging Nonliving and Living Matter*. Cambridge: MIT Press, 2008.

Rhodius, Virgil A. and Vivek K. Mutalik. "Predicting strength and function for promoters of the Escherichia coli alternative sigma factor, σE." *PNAS* February 16, vol. 107, no. 7, 2854–2859, 2010.

Ro, Dae-Kyun *et al*. "Production of the antimalarial drug precursor artemisinic acid in engineered yeast." *Nature* 440(7086): 940-3, 2006.

Rose, Nikolas. *et al*. Special issue on genomics. *Biosocieties* 1(1), 2006.

Ross J. and A. Arkin. "Complex systems: from chemistry to systems biology." *Proceedings of the National Academy of Sciences USA*, 106(16): 6433-4, 2009.

Schmidt M., Kelle A., Ganguli A, de Vriend H. eds. *Synthetic Biology: The Technoscience and its Societal Consequences*. Berlin: Springer Academic Publishing, 2009.

Shapin, Steven. *The Scientific Life: A Moral History of a Late Modern Vocation*. Chicago: University of Chicago Press, 2008.

Shreeve, Robert. *The Genome War, How Craig Venter Tried to Capture the Code of Life and Save the World*. New York: Alfred Knopf, 2005.

Stano *et al.* Semisynthetic Minimal Cells: New Advancements and Perspectives. In Rasmussen, *et al.* eds. *Protocells: Bridging Nonliving and Living Matter*. Cambridge: MIT Press, 2008.

Steen, Eric J, *et al*. "Metabolic engineering of Saccharomyces cerevisiae for the production of n-butanol." *Microbial Cell Factories* 7:36, 2008.

The Synthetic Biology Project, Woodrow Wilson International Center for Scholars. http://www.synbioproject.org/

The Presidential Commission for the Study of Bioethical Issues. http://bioethics.georgetown.edu/pcbe/index.html

The President's Council on Bioethics. "Archived Website." http://bioethics.georgetown.edu/pcbe/index.html

Tian, J., H. Gong, N. Sheng, X. Zhou, E. Gulari, X. Gao, and G. Church. Accurate multiplex gene synthesis from programmable DNA microchips. *Nature* 432:1050-4, 2004.

Weber, Max. Objectivity in social sciences and social policy. In *The Methodology of the Social Sciences*, trans. Edward Shils and Henry Finch, New York: The Free Press, 1949.

Weber, Max. "Science as a Vocation." In *From Max Weber*, Gerth and Mills, eds. Oxford: Oxford University Press, 1958.

Wilsdon, James, and Rebecca Willis. *See-Through Science: Why Public Engagement Needs to Move Upstream*. London: Demos, 2004.

Yearly, Steven. The ethical landscape: identifying the right way to think about the ethical and societal aspects of synthetic biology research and products. *Interface: Journal of the Royal Academy* published online 15 May 2009.

Zoloth, Laurie. Second Life: Some Ethical Issues in Synthetic Biology and the Recapitulation of Evolution. In *The Ethics of Protocells: Moral and Social Implications of Creating Life in the Laboratory*. Cambridge: MIT Press, 2008.

NOTES

[1] Foucault, *The Government of the Self and Others*, 219.
[2] The BIOFAB is a multi-institutional undertaking, initially supported by the National Science Foundation as a supplement to the Synthetic Biology Engineering Research Center (http://synberc.org, and connecting researchers UC Berkeley, Stanford, and the Lawrence Berkeley National Laboratories, see: http://biofab.org/about.
[3] George Canguilhem, "The Living and Its Milieu," in *Knowledge of Life*, Marrati and Meyers, eds. (New York: Fordham University Press, 2008).
[4] www.synberc.org; Baker, Church, Collins, Endy, Jacobson, Keasling, Modrich, Smolke and Weiss, "Engineering Life: Building a Fab for Biology," *Scientific American* June (2006): 44 – 51; Purnick and Weiss, "The Second Wave of Synthetic Biology: From Modules to Systems," *Nature Molecular and Cell Biology* June (2009) v.10: 410-422.
[5] Paul Rabinow and Gaymon Bennett, *Designing Human Practices: An Experiment with Synthetic Biology* (Chicago: Chicago University Press, 2012).
[6] Drew Endy, "Foundations for engineering biology." *Nature* 438(7067): 449-453.
[7] Albert Jonsen, *The Birth of Bioethics*; John Evans, *Playing God?: Human Genetic Engineering and the Rationalization of Public Bioethical Debate* (Chicago: Chicago University Press, 2001).
[8] Sheila Jasanoff, *Designs on Nature: Science and Democracy in Europe and the United States*. (Princeton: Princeton University Press, 2005).
[9] See the archived meetings at: http://www.tvworldwide.com/events/bioethics/100708/
[10] Lorraine Daston and Peter Galison, *Objectivity* (Cambridge, MA: MIT Press, 2007).
[11] Steven Shapin, *The Scientific Life: A Moral History of a Late Modern Vocation* (Chicago: University of Chicago Press, 2008).
[12] Rabinow and Bennett, "The Setting," in *Designing Human Practices*.
[13] Anonymous review of *Designing Human Practices.*
[14] Paul Rabinow in Rabinow, Marcus, Faubion, and Reese, *Designs for an Anthropology of the Contemporary* (Durham: Duke University Press, 2008), 59.
[15] As of 2010, the Alfred P. Sloan Foundation is supporting coordinated projects on security at the J. Craig Venter Institute, bioethics at the Hastings Center, and public and policy discourse at the Woodrow Wilson International Center for Scholars. The EC has funded the Austrian Academy of Sciences Institute of Technology Assessment, the University of Zurich Ethics Centre, and Isthmus through the Synbiosafe project. The UK's BBSRC, through their "Networks in synthetic biology" project, funds "Networks in synthetic biology," which includes science studies researchers at Oxford, Nottingham, Cambridge, and Edinburgh, among others. And EuroSYNBIO is entering a first round of funding for "societal" research, having received proposals for coordinated research among scholars in Switzerland, Belgium, Germany, Austria, the UK, and the US (a consortium of which the Human Practices Thrust at SynBERC is a proposed partner).
[16] Michel Foucault, *The Hermeneutics of the Subject: Lectures at the Collège de France 1981-1982*, eds. ed. Frédérique Gros, François Ewald, Alessandro Fontana, Arnold Davidson, trans. Graham Burchell (New York: Palgrave MacMillan, 2005).
[17] Paul Rabinow and Gaymon Bennett, "From Bioethics to Human Practices, or Assembling Contemporary Equipment," in *Tactical Biopolitics Art, Activism, and Technoscience*, da Costa and Philips, eds. (Cambridge, MA: MIT Press, 2008).
[18] From *Bios-Technika* at http://bios-technika.net
[19] Albert Jonsen, *The Birth of Bioethics* (Oxford: Oxford University Press, 2003)..
[20] Helga Nowotny, Peter Scott, and Michael Gibbon, *Re-Thinking Science: Knowledge and the Public in an Age of Uncertainty*. (Oxford: Wiley-Blackwell, 2001); Paul Rabinow, *French DNA: Trouble in Purgatory* (Chicago: Chicago University Press, 1999).
[21] Albert Jonsen, *The Birth of Bioethics*.
[22] U.S. centers include: The Center for Nanotechnology and Society at Arizona State University, David Guston, director; The Center for Society and Genetics at UCLA, Chris Kelty, PI; and The Center for Bioethics at University of South Carolina, George Khushf, director. European centers include: The BIOS Center at the London School of Economics, Nikolas Rose, director; and the Organization for International Dialogue and Conflict Management, Markus Schmidt, director.

[23] Weber, "Science as a Vocation"
[24] Cf. Stavrianakis, Bennett, Rabinow, "Encountering Stasis," ARC Studio 05, http://anthropos-lab.net/studio/episode/05/
[25] Rabinow and Bennett, "Principles of Design 2006-2007," in *Designing Human Practices*.
[26] François Flahaut, *La méchanceté* (Paris: La Découverte, 1998).
[27] Paul Rabinow, *Marking Time: On the Anthropology of the Contemporary* (Princeton: Princeton University Press, 2007); Rabinow *et al*. *Designs for an Anthropology of the Contemporary* (Durham: Duke University Press, 2008); Paul Rabinow, *The Accompaniment: Assembling the Contemporary* (Chicago: University of Chicago Press, 2011).
[28] Michel Foucault, "Questions of Method," in *Ethics, Subjectivity and Truth*, Vol. 1 of *The Essential Works of Michel Foucault 1954-1984*, Rabinow, ed. (New York: The New Press, 1997).
[29] Gordon Wakefield, "Spirituality, forms of," in *The Oxford Companion to Christian Though*, Hastings, Mason, Pyper, eds. (Oxford and New York: Oxford University Press, 2000).
[30] Foucault, *Hermeneutics of the Subject*, 29.
[31] Ibid., 11.
[32] Rabinow and Bennett, http://bios-technika.net
[33] Rabinow and Bennett, "Lessons Learned 2010," in *Designing Human Practices*.
[34] Baker *et al.*, "Engineering Life: Building a Fab for Biology,"
[35] Endy"Foundations for engineering biology"; Andrianantoandro, Basu, Karig, and Weiss, "Synthetic biology: new engineering rules for an emerging discipline," *Nature Molecular Systems Biology* v.2: E1-14.
[36] Christina Smoke, "Building Outside the Box: iGEM and the BioBricks Foundation," *Nature Biotechnology* 27, 1099 - 1102 (*2009*).
[37] Rabinow and Bennett, "Synthetic Biology: Ethical Ramifications, 2009," *The Journal of Systems and Synthetic* December, 2009.
[38] Gibson *et al.*, "Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome," *Science* 2 July 2010: vol. 329. no. 5987, pp. 52 – 56.
[39] George Church, "Let us go forth and safely multiply," *Nature* 438: 423.
[40] Martin, *et al.*, "Synthetic Metabolism: Engineering Biology at the Protein and Pathway Scales," *Chemistry and Biology* v16, Issue 3, 27 March 2009, 277-286.
[41] Purnick and Weiss, "The Second Wave of Synthetic Biology: From Modules to Systems."
[42] Ibid.
[43] Paul Rabinow and Talia Dan Cohen, *A Machine to Make a Future: Biotech Chronicles*, (Princeton: Princeton University Press, 2005).
[44] Michel Foucault, "Questions of Method," in *Ethics, Subjectivity and Truth*, Vol. 1 of *The Essential Works of Michel Foucault 1954-1984*, Rabinow, ed. (New York: The New Press, 1997).
[45] Paul Rabinow, *Marking Time: On the Anthropology of the Contemporary* (Princeton: Princeton University Press, 2007); Rabinow *et al*. *Designs for an Anthropology of the Contemporary* (Durham: Duke University Press, 2008).
[46] Rabinow and Bennett, "Lessons Learned 2010," in *Designing Human Practices*.
[47] Schmidt, Kelle, Ganguli, de Vriend eds., *Synthetic Biology: The Technoscience and its Societal Consequences* (Berlin: Springer Academic Publishing, 2009).
[48] Niklas Luhmann, *Risk: A Sociological Theory* (New York: Aldine Transaction, 2005).
[49] Paul Rabinow, "Epilogue," in *Biosecurity Interventions: Global Health and Security in Question*, eds. Andrew Lakoff and Stephen Collier (New York: Columbia University Press, 2008).
[50] Rabinow and Bennett, "Principals of Design 2006-2007," in *Designing Human Practices*.
[51] Rabinow and Bennett, "Lessons Learned 2010," in *Designing Human Practices*.
[52] Michel Foucault, "12 January 1983," in *The Government of the Self and Others, Lectures at the Collège de France 1982-1983*, ed. Frédérique Gros, François Ewald, Alessandro Fontana, Arnold Davidson, trans. Graham Burchell (New York: Palgrave MacMillan, 2010).
[53] Foucault, "2 February 1983," in *The Government of the Self and Others.*
[54] Ibid.
[55] Rabinow and Bennett, "Lessons Learned 2010," in *Designing Human Practices*.
[56] Foucault, "2 February 1983," in *The Government of the Self and Others.*
[57] Michel Foucault, "Questions of Method," in *Essential Works of Foucault (1954-1984), Volume 3: Power*, eds. James D. Faubion, series ed. Paul Rabinow (New York: The New Press, 2001), 233.
[58] http://synberc.org/
[59] http://newscenter.berkeley.edu/2010/01/20/biofab_synthetic_biology/

[60] 2009 American Recovery and Reinvestment Act, online at: http://www.recovery.gov/About/Pages/The_Act.aspx
[61] Baker, *et al*. "Engineering Life: Building a Fab for Biology." *Scientific American* June: 44 – 51, 2006.
[62] Drew Endy, "Foundations for engineering biology," *Nature* 438, 449-453 (24 November 2005); Baker *et al.* "Engineering Life."
[63] Drew Endy, Adam Arkin, and Jay Keasling, "Project Summary: the SynBERC BIOFAB Facility," Proposal to the National Science Foundation, 2010, 1.
[64] Endy, Arkin, and Keasling, "BIOFAB Facility," 1.
[65] Max Weber, "Objectivity in social sciences and social policy," in *The Methodology of the Social Sciences*, trans. Edward Shils and Henry Finch, New York: The Free Press, 1949.
[66] Endy, Arkin, and Keasling, "BIOFAB Facility," 1.
[67] Ibid.
[68] The National Science Foundation ERC Year SynBERC Six Site Visit Team, "Sixth Annual Renewal Report," April, 2011.
[69] Endy, Arkin, and Keasling, "BIOFAB Facility," 1.
[70] Ibid.
[71] See Paul Rabinow and Gaymon Bennett, "Lessons Learned 2010,) in *Designs for Human Practices: An Experiment with Synthetic Biology* (Chicago: Chicago University Press, 2012).
[72] Adam Arkin and Drew Endy, "A standard parts list for biological circuitry," DARPA white paper October 1999, doi:1721.1/29794; Baker *et al.* "Engineering Life."
[73] Endy, Arkin, and Keasling, "BIOFAB Facility," 1.
[74] Ibid., 11.
[75] Ibid., 2.
[76] The National Science Foundation ERC Year SynBERC Five Site Visit Team, "Fifth Annual Renewal Report," March, 2010.
[77] Endy, Arkin, and Keasling, "BIOFAB Facility," 4.
[78] Dae-Kyun Ro, *et al*. "Production of the antimalarial drug precursor artemisinic acid in engineered yeast," *Nature* 440(7086): 940-3, 2006.
[79] Christina Smolke, "Building outside of the box: iGEM and the BioBricks Foundation" *Nature Biotechnology* Dec. 27(12) 1099-102, 2009.
[80] Synthetic Biology Project, Woodrow Wilson Center, "Trends in synthetic biology research funding in the united states and Europe," Research Brief, June 2010. Available at: http://www.synbioproject.org/process/assets/files/6420/final_synbio_funding_web2.pdf
[81] BBC Research, "Synthetic Biology: Emerging Global Markets," Forecasting Report, June 209. Available at: http://www.bccresearch.com/report/synthetic-biology-bio066a.html.
[82] Luis Campos, "That Was the Synthetic Biology That Was," in *Synthetic Biology: The Technoscience and Its Societal Consequences,* Markus Schmidt et al., eds. (New York: Springer Academic Publishing, 2009).
[83] See Endy, "Foundations," and Steven A. Benner and A. Michael Sismour, "Synthetic Biology," Nature Reviews Genetics 6, 533-543 (July 2005).
[84] Baker *et al.* "Engineering Life."
[85] Ibid., 51.
[86] Tom Knight, "Idempotent Vector Design for Standard Assembly of Biobricks," whitepaper, 2003. Online at: http://openwetware.org/images/b/bd/BBFRFC9.pdf/
[87] Baker *et al.* "Engineering Life," 51.
[88] Arkin and Endy, "A standard parts list."
[89] Ibid.
[90] Robert Cook-Deegan, *The Gene Wars: How Science, Politics and the Human Genome Project* (New York: Norton, 1995); Robert Shreeve, *The Genome War, How Craig Venter Tried to Capture the Code of Life and Save the World* (New York: Alfred Knopf, 2005).
[91] See, for example, Michael B. Elowitz & Stanislas Leibler, "A synthetic oscillatory network of transcriptional regulators," *Nature* 403, 335-338 (20 January 2000); Harold Abelson, *et al*., "Amorphous Computing," Technical Report on Logic, Programming, and DNA, available at: http://hdl.handle.net/1721.1/5929, 1999.
[92] Knight, "Idempotent."
[93] Figure created by Lance Martin.

[94] J. Christopher Anderson, *et al.*, " BglBricks: A flexible standard for biological part assembly," *Journal of Biological Engineering* Jan 20 4(1):1, 2010; Fillippa Lentzos, Gaymon Bennett, Jef Boeke, Drew Endy and Paul Rabinow, "Visions and Challenges in Redesigning Life," *BioSocieties*, Volume 3, Issue 03, Sep, 311-323, 2008.
[95] Andrianantoandro, Basu, Karig, and Weiss, "Synthetic biology: new engineering rules for an emerging discipline," *Nature Molecular Systems Biology* v.2: E1-14, 2006; J. Ross and A. Arkin, "Complex systems: from chemistry to systems biology," *Proceedings of the National Academy of Sciences USA*, 106(16): 6433-4, 2009.
[96] Smolke, "Building outside of the box."
[97] Anderson *et al.*, "BglBricks."
[98] S. Khalil & James J. Collins, "Synthetic biology: applications come of age," *Nature Reviews Genetics* 11, 367-379 (May 2010), doi:10.1038/nrg2775.
[99] Smolke, "Building outside of the box."
[100] Daisy Ginsberg, "Building new life forms at the iGEM Jamboree," Wired online at http://www.wired.co.uk, 9 November 2009.
[101] Jeffery Tabor, *et al.*, "A Synthetic Genetic Edge Detection Program," *Cell* 137, 1272–1281, June 26, 2009.
[102] Anderson *et al.*, "BglBricks."
[103] Evelyn Fox Keller, "What does synthetic biology have to do with biology?" *BioSocieties* 4, 291-302 (1 September 2009); Paul Rabinow and Gaymon Bennett, "Synthetic biology: ethical ramifications 2009," *The Journal of Systems and Synthetic Biology* December 3(1-4), 2009.
[104] Baker *et al.*, "Engineering Life,"; Andrianantoandro *et al*. "Synthetic Biology."
[105] Canton, Labno, Endy, "Refinement and standardization of synthetic biological parts and devices." *Nature Biotechnology* 26(8): 787-793, 2008.
[106] Adam Arkin, "Setting the standard in synthetic biology," *Nature Biotechnology* 26(8): 771-774, 2008.
[107] Endy, "Foundations; Andrianantoandro *et al*., "Synthetic Biology."
[108] Arkin, "Setting the Standard"; Julius Lucks, *et al.*, "Toward scalable parts families for predictable design of biological circuits," *Current Opinion in Microbiology* (6): 567-73, 2008.
[109] Kenneth Burke, *Permanence and Change* (Indianapolis: Bobbs-Merrill, 1965).
[110] Rabinow and Bennett, "Synthetic biology."
[111] Adam Arkin and Daniel Fletcher, "Fast, Cheap and somewhat in control," *Genome Biology*, 7, 114, 2006; Priscilla E. M. Purnick and Ron Weiss, "The second wave of synthetic biology: from modules to systems." Molecular Cell Biology, June Volume 10: 410-23, 2009.
[112] Oxford English Dictionary Online.
[113] Foucault, "Questions of Method," 233.
[114] Foucault, *The Government of the Self and Others, Lectures at the Collège de France 1982-1983*, eds. Frédérique Gros, François Ewald, Alessandro Fontana, Arnold Davidson, trans. Graham Burchell (New York: Palgrave MacMillan, 2010), 97.
[115] Drew Endy, "iGEM - Drew Endy Defining Synthetic Biology," at http://www.youtube.com/watch?v=XIuh7KDRzLk; Drew Endy, "Foundations for engineering biology," *Nature* 438, 449-453 (24 November 2005), see especially page 449 "COMIC 1. Adventures in Synthetic Biology," available at http://www.nature.com/nature/comics/syntheticbiologycomic/.
[116] Endy, "Foundations."
[117] Endy, Presentation at SynBERC Site Review, February 2007.
[118] http://synberc.org/.
[119] http://biobricks.org/.
[120] http://partsregistry.org/Main_Page; http://2011.igem.org/Main_Page.
[121] Endy, "Foundations," 450.
[122] Ibid.
[123] Ibid.
[124] Ibid., 451.
[125] Ibid.
[126] See James D. Faubion, *Modern Greek Lessons: A Primer In Historical Constructivism* (Princeton: Princeton University Press, 1995); Paul Rabinow, "Assembling Untimeliness," unpublished essay; and Harold Bloom, *A Map of Misreading* (Oxford: Oxford University Press, 1975).
[127] Priscilla E. M. Purnick and Ron Weiss, "The second wave of synthetic biology: from modules to systems." Molecular Cell Biology, June 2009 Volume 10: 410-23; Czar, Anderson, Bader, and Peccoud, "Gene synthesis demystified," *Trends in Biotechnology* 2009 27(2): 63-72.

[128] Drew Endy, Testimony at the Presidential Commission for the Study of Bioethical Issues hearings on synthetic biology, "Overview and Context of the Science and Technology of Synthetic Biology
Transcript from July 8, 2010, in Washington, D.C. Available at: http://bioethics.gov/transcripts/synthetic-biology/070810/overview-and-context-of-the-science-and-technology.html
[129] Roberta Kwok, "Five hard truths for synthetic biology," *Nature* 463, 288-290 (2010), Published online 20 January 2010, available at doi:10.1038/463288a.
[130] Canton, Labno, Endy, "Refinement and standardization of synthetic biological parts and devices." *Nature Biotechnology* 26(8): 787-793, 2008.
[131] Evelyn Fox Keller, "What does synthetic biology have to do with biology?" *BioSocieties* 4, 291-302 (1 September 2009).
[132] Endy, "Foundations."
[133] Steven A. Benner and A. Michael Sismour, "Synthetic Biology," Nature Reviews Genetics 6, 533-543 (July 2005); S. Khalil & James J. Collins, "Synthetic biology: applications come of age," *Nature Reviews Genetics* 11, 367-379 (May 2010), doi:10.1038/nrg2775
[134] Barry Canton, Labno, Endy, "Refinement and standardization of synthetic biological parts and devices." *Nature Biotechnology* 26(8): 787-793, 2008.
[135] Adam Arkin, "Setting the standard in synthetic biology," *Nature Biotechnology* 26(8): 771-774, 2008.
[136] Jason R. Kelly, *et al*., "Measuring the activity of BioBrick promoters using an in vivo reference standard," *Journal of Biological Engineering*, 2009 3:4. Online publication available at: doi:10.1186/1754-1611-3-4.
[137] MIT Registry of Standard Biological Parts at http://partsregistry.org/Main_Page
[138] Kwok, "Five Difficult Truths"
[139] Georges Canguilhem, "Machine and Organism," in *Knowledge of Life*, eds. Paolo Marrati and Todd Meyers, trans. Stefanos Geroulanos and Daniela Ginsburg (New York: Fordham University Press, 2008), 88.
[140] Keller, "Biology."
[141] Steven Shapin, *The Scientific Life: A Moral History of a Late Modern Vocation* (Chicago: University of Chicago Press, 2008).
[142] Ibid., 151.
[143] John Dewey, *Liberalism and Social Action*, (New York: G. P. Putnam's Sons, 1935).
[144] See Faubion, *Modern Greek Lessons* and Rabinow "Assembling Untimeliness."
[145] Mutalik, *et al.*, "Promoter strength properties of the complete sigma E regulon of Escherichia coli and Salmonella enteric," *Journal of Bacteriology* 2009 Dec;191(23):7279-87; Virgil A. Rhodius and Vivek K. Mutalik, "Predicting strength and function for promoters of the Escherichia coli alternative sigma factor, σE," *PNAS* February 16, 2010, vol. 107, no. 7, 2854–2859.
[146] See Paul Rabinow and Gaymon Bennett, "From Manifestos to Research Programs," in *Designs for Human Practices: An Experiment with Synthetic Biology* (Chicago: Chicago University Press, 2012).
[147] See Paul Rabinow and Gaymon Bennett, "The Second Wave of Human Practices," in *Designs for Human Practices: An Experiment with Synthetic Biology* (Chicago: Chicago University Press, 2012).
[148] http://www.biofab.org/humanpractices
[149] Steven Shapin, *The Scientific Life*, 5.
[150] Ibid., 5
[151] Ibid.
[152] Cf. "The Diagnostic" at *Bios-Technika*: http://bios-technika.net/diagnostics.php
[153] Georges Canguilhem, "The Living and Its Milieu," in *Knowledge of Life*, eds. Paolo Marrati and Todd Meyers, trans. Stefanos Geroulanos and Daniela Ginsburg (New York: Fordham University Press, 2008), 108.
[154] See Ahmad S. Khalil & James J. Collins, "Synthetic biology: applications come of age," *Nature Reviews Genetics* 11, 367-379 (May 2010), doi:10.1038/nrg2775; Priscilla E. M. Purnick and Ron Weiss, "The second wave of synthetic biology: from modules to systems," Molecular Cell Biology, June 2009 Volume 10: 410-23; and Andrew D. Ellington, "Man versus Machine versus Ribozyme," PLoS Biol. 2008 May; 6(5): e132. Published online 2008 May 27. doi: 10.1371/journal.pbio.0060132.
[155] See http://bios-technika.net/concepts.php#veridiction.
[156] Gabaldon *et al*, "The Core of a Minimal Gene Set: Insights from Natural Reduced Genomes," in *Protocells: Bridging Nonliving and Living Matter*, Rasmussen, Steen *et al.* eds. (Cambridge: MIT Press, 2008); Roberta Kwok, "Five hard truths for synthetic biology," *Nature* 463, 288-290 (2010), Published online 20 January 2010, available at doi:10.1038/463288a.
[157] Adam Arkin, "Setting the standard in synthetic biology," *Nature Biotechnology* 26(8): 771-774, 2008.

[158] Jefferey Skerker *et al*., "Evolution, ecology and the engineered organism: lessons for synthetic biology," *Genome Biology*, 10: 114, 2009; Jason R. Kelly, *et al*., "Measuring the activity of BioBrick promoters using an in vivo reference standard," *Journal of Biological Engineering*, 2009 3:4. Online publication available at: doi:10.1186/1754-1611-3-4.
[159] Cf. Eric Haseltine and Frances Arnold, "Synthetic gene circuits: Design with directed evolution," *Annual Review of Biophysics and Biomolecular Structure*, 36: 1-19, 2009; Skerker *et al*., "Evolution."
[160] Cf. Anthony Forster and George Church, "Towards synthesis of a minimal cell," *Molecular Systems Biology* 2:45, 2006; Peter Carr and George Church, "Genome Engineering," *Nature Biotechnology* 27, 1151-1162, 2009.
[161] Cf. Haseltine and Arnold, "Gene circuits."
[162] Cf. David Sprinzak and Michael Elowitz, "Reconstruction of genetic circuits," *Nature* 438, 443-448, 2006.
[163] Cf. Haseltine and Arnold, "Gene circuits"; Adam Arkin and Daniel Fletcher, "Fast, Cheap and somewhat in control," *Genome Biology*, 7, 114.
[164] Georges Canguilhem, "The Living and Its Milieu."
[165] Ibid., 100.
[166] Ibid., 99.
[167] Ibid., 100.
[168] Ibid.
[169] Ibid., 103.
[170] Ibid.
[171] Ibid., 109.
[172] Ibid., 111.
[173] Ibid.,
[174] Ibid., 113.
[175] Ibid., 115.
[176] Ibid., 113.
[177] Ibid.
[178] Ibid., 118.
[179] Ibid.
[180] David Graeber, *Toward and Anthropological Theory of Value* (New York: Palgrave, 2001), 16.
[181] For details on the ERC Program see: http://www.erc-assoc.org/index.htm
[182] Sheila Jasanoff, *Science at the Bar: Law, Science, and Technology in America* (Cambridge: Harvard University Press, 1997).
[183] See Priscilla E. M. Purnick and Ron Weiss, "The second wave of synthetic biology: from modules to systems." Molecular Cell Biology, June 2009 Volume 10: 410-23; Czar, Anderson, Bader, and Peccoud, "Gene synthesis demystified," *Trends in Biotechnology* 2009 27(2): 63-72; and Rabinow and Bennett *Designing Human Practices: An Experiment With Synthetic Biology* (Chicago: Chicago University Press, 2012).
[184] Paul Rabinow, *Marking Time: On the Anthropology of the Contemporary* (Princeton: Princeton University Press, 2007).
[185] See Paul Rabinow, *Anthropos Today: Reflections on Modern Equipment* (Princeton: Princeton University Press, 2003), 3.
[186] Rabinow and Bennett, *Designing Human Practices*.
[187] Ibid.
[188] The National Science Foundation ERC Year SynBERC Five Site Visit Team, "Fifth Annual Renewal Report," March, 2010.
[189] Rabinow and Bennett, *Designing Human Practices*.
[190] The Synthetic Biology Engineering Research Center Annual Report, 2011.
[191] The National Science Foundation, "Fifth Annual Renewal Report," March, 2010.
[192] Ibid.
[193] Ibid.
[194] Ibid.
[195] Ibid.
[196] Gaeber, *Value*.
[197] Paul Rabinow, "France in Morocco: Technocosmopolitanism and Middling Modernism," *Assemblage* No. 17 (Apr., 1992), pp. 52-57.
[198] Rabinow, "France in Morocco."

[199] "Shame," Oxford English Dictionary, online.
[200] Jason R. Kelly, *et al*., "Measuring the activity of BioBrick promoters using an in vivo reference standard," *Journal of Biological Engineering*, 2009 3:4. Online publication available at: doi:10.1186/1754-1611-3-4.
[201] Kelly, *et al*. "Reference standard."
[202] Ibid.
[203] Ibid.
[204] Ibid.
[205] Paul Rabinow, "France in Morocco: Technocosmopolitanism and Middling Modernism," *Assemblage* No. 17 (Apr., 1992), pp. 52-57.
[206] Philip Pauly, *Controlling Life: Jacques Loeb & the Engineering Ideal in Biology* (Oxford: Oxford University Press, 1987).
[207] Graeme Gooday, *The Morals of Measurement: Accuracy, Irony, and Trust in Late Victorian Electrical Practice* (Cambridge: Cambridge University Press, 2004.
[208] The article is "France in Morocco: Technocosmopolitanism and Middling Modernism"; the longer work is *French Modern: Norms and Forms of the Social Environment*
[209] Rabinow, "France in Morocco," 53.
[210] Ibid,. 54.
[211] Ibid.
[212] Priscilla E. M. Purnick and Ron Weiss, "The second wave of synthetic biology: from modules to systems," Molecular Cell Biology, June 2009 Volume 10: 410-23.
[213] Rabinow, "France in Morocco," 54.
[214] Purnick and Weiss, "The second wave."
[215] Michel Foucault, *The Hermeneutics of the Subject: Lectures at the Collège de France 1981-1982*, eds. ed. Frédérique Gros, François Ewald, Alessandro Fontana, Arnold Davidson, trans. Graham Burchell (New York: Palgrave MacMillan, 2005), 17.
[216] Dan Gibson, John Glass, *et al*. "Creation of a bacterial cell controlled by a chemically synthesized genome," *Science* 2010 Jul 02; 329(5987): 52-6
[217] Gibson, *et al.* "Creation," 52
[218] George Church, "Sizing up the 'synthetic cell': Nature asked eight experts about the implications of the J. Craig Venter Institute's latest creation," *Nature* published online 20 May 2010, doi:10.1038/news.2010.255.
[219] Arthur Caplan, "Sizing up the 'synthetic cell': Nature asked eight experts about the implications of the J. Craig Venter Institute's latest creation," *Nature* published online 20 May 2010, doi:10.1038/news.2010.255.
[220] Niklas Luhmann, *Observations on Modernity*, trans. William Whobrey (Palo Alto: Stanford University Press, 1998).
[221] America Magazine Staff, "Vatican Greets First Synthetic Cell With Caution," *America*, published online http://www.americamagazine.org/content/signs.cfm?signid=428.
[222] Ibid.
[223] Laurie Zoloth, "Second Life: Some Ethical Issues in Synthetic Biology and the Recapitulation of Evolution," in *The Ethics of Protocells: Moral and Social Implications of Creating Life in the Laboratory*, eds. Bedau and Parke (Cambridge: MIT Press, 2008); Henk van den Belt, "Playing God in Frankenstein's Footsteps: Synthetic Biology and the Meaning of Life," *Nanoethics* (2009) 3:257–268.
[224] Elizabeth Pennsi, "Synthetic Genome Brings New Life to Bacterium," *Science* 21 May 2010 vol. 328, 958-9.
[225] Paul Rabinow, *Anthropos Today: Reflections on Modern Equipment* (Princeton: Princeton University Press, 2003).
[226] Georges Canguilhem, "Monstrosity and the Monstrous," in *Knowledge of Life*, eds. Paolo Marrati and Todd Meyers, trans. Stefanos Geroulanos and Daniela Ginsburg (New York: Fordham University Press, 2008), 134.
[227] Gibson, *et al.* "Creation."
[228] Canguilhem, "Monstrosity," 135.
[229] Quoted from the JCVI website at: http://www.jcvi.org/cms/research/projects/first-self-replicating-synthetic-bacterial-cell/overview/
[230] Hannah Landecker, *Culturing Life: How Cells became Technologies* (Cambridge: Harvard University Press, 2008).
[231] Canguilhem, "Monstrosity," 134.
[232] Ibid., 136.

[233] Priscilla E. M. Purnick and Ron Weiss, "The second wave of synthetic biology: from modules to systems," Molecular Cell Biology, June 2009 Volume 10: 410-23.
[234] Georges Canguilhem, "Machine and Organism," in *Knowledge of Life*, eds. Paolo Marrati and Todd Meyers, trans. Stefanos Geroulanos and Daniela Ginsburg (New York: Fordham University Press, 2008).
[235] Ibid., 88.
[236] Ibid.
[237] Ibid.
[238] Dae-Kyun Ro, *et al*. "Production of the antimalarial drug precursor artemisinic acid in engineered yeast," *Nature* 440(7086): 940-3, 2006.
[239] Canguilhem, "Monstrosity," 90.
[240] Adam Arkin and Drew Endy, "A standard parts list for biological circuitry," DARPA white paper October 1999, doi:1721.1/29794.
[241] http://www.jcvi.org/cms/research/projects/first-self-replicating-synthetic-bacterial-cell/overview/
[242] Canguilhem, "Monstrosity," 91.
[243] Ibid., 76.
[244] Ibid., 78.
[245] Ibid., 90
[246] Ibid., 93.
[247] Ibid.
[248] Zoloth, "Second Life"; and Paul Wolpe, Testimony at the Presidential Commission hearings on synthetic biology. Available at: http://bioethics.gov/transcripts/synthetic-biology/070910/ethics-of-synthetic-biology.html.
[249] Leon Kass, *Life, Liberty, and the Defense of Dignity* (New York: Encounter Books, 2002).
[250] Steven Shapin, *Never Pure: Historical Studies of Science as if It Was Produced by People with Bodies, Situated in Time, Space, Culture, and Society, and Struggling for Credibility and Authority* (Baltimore: The Johns Hopkins University Press, 2010).
[251] Foucault, *The Hermeneutics of the Subject*, 17.
[252] Rabinow, *et al*., *Designs for an Anthropology of the Contemporary* (Durham: Duke University Press, 2008).
[253] America Magazine Staff, "Vatican Greets."
[254] John Dewey, *Reconstruction in Philosophy*, enlarged edition (Boston: Beacon Press, 1957). On reconstruction and human practices see Rabinow and Bennett, *Designs* chapter 3.
[255] Foucault, *The Government of the Self and Others, Lectures at the Collège de France 1982-1983*, eds. Frédérique Gros, François Ewald, Alessandro Fontana, Arnold Davidson, trans. Graham Burchell (New York: Palgrave MacMillan, 2010), 183.
[256] The materials in this chapter were developed in connection with Stavrianakis, Bennett, and Rabinow, "Truth-speaking: The Instance of The Presidential Commission for the Study of Bioethical Issues and Synthetic Biology,"ARC Studio 02 http://anthropos-lab.net/studio/episode/002/
[257] Office of the President, "Letter from the President," on the Commission's website at http://bioethics.gov/documents/Letter-from-President-Obama-05.20.10.pdf
[258] The Presidential Commission for the Study of Bioethical Issues, "New Directions: The Ethics of Synthetic Biology and Emerging Technologies," Report to the President, December 2010. Available online at: http://bioethics.gov/documents/synthetic-biology/PCSBI-Synthetic-Biology-Report-12.16.10.pdf, 15.
[259] Presidential Commission, "Synthetic Biology," 119.
[260] The President's Council on Bioethics, materials archived at: http://bioethics.georgetown.edu/pcbe/
[261] Strianakis, Bennett, and Rabinow, "Truth Speaking: The Instance of the Presidential Commission for the Study of Bioethical Issues and Synthetic Biology," ARC Studio 2, http://anthropos-lab.net/studio/episode/002/, accessed March 30, 2011.
[262] Michel Foucault, "12th January, 1983," in *The Government of the Self and Others, Lectures at the Collège de France 1982-1983*, ed. Frédérique Gros, François Ewald, Alessandro Fontana, Arnold Davidson, trans. Graham Burchell (New York: Palgrave MacMillan, 2010).
[263] Presidential Commission hearings on synthetic biology, "Overview and Context of the Science and Technology of Synthetic Biology, Transcript from July 8, 2010, in Washington, D.C. Available at: http://bioethics.gov/transcripts/synthetic-biology/070810/overview-and-context-of-the-science-and-technology.html
[264] Ibid.
[265] Ibid.
[266] Ibid.

[267] Ibid.
[268] Presidential Commission hearings on synthetic biology, "Applications of Synthetic Biology," Transcript from July 8, 2010, in Washington, D.C. Available at: http://bioethics.gov/transcripts/synthetic-biology/070810/applications-of-synthetic-biology.html
[269] Max Weber, "Science as a Vocation," in *From Max Weber*, Gerth and Mills, eds. (Oxford: Oxford University Press, 1958).
[270] Paul Wolpe, Testimony at the Presidential Commission hearings on synthetic biology. Available at: http://bioethics.gov/transcripts/synthetic-biology/070910/ethics-of-synthetic-biology.html.
[271] Presidential Commission hearings on synthetic biology, "Benefits and Risks of Synthetic Biology," Transcript from July 8, 2010, in Washington, D.C. Available at: http://bioethics.gov/transcripts/synthetic-biology/070810/benefits-and-risks-of-synthetic-biology.html.
[272] Ibid.
[273] Ibid.
[274] Presidential Commission hearings on synthetic biology, "Ethics of Synthetic Biology," Transcript from July 8, 2010, in Washington, D.C. Available at: http://bioethics.gov/transcripts/synthetic-biology/070810/ethics-of-synthetic-biology.html.
[275] Ibid.
[276] Foucault, *The Government of the Self and Others*, 183.
[277] Ibid., 173-4.
[278] Michel Foucault, "19th January, 1983," in *The Government of the Self and Others, Lectures at the Collège de France 1982-1983*, ed. Frédérique Gros, François Ewald, Alessandro Fontana, Arnold Davidson, trans. Graham Burchell (New York: Palgrave MacMillan, 2010).
[279] http://bioethics.gov/transcripts/synthetic-biology/070910/ethics-of-synthetic-biology.html.
[280] Paul Wolpe, Testimony
[281] Sondra Wheeler, Testimony at the Presidential Commission hearings on synthetic biology. Available at: http://bioethics.gov/transcripts/synthetic-biology/091310/philosophical-and-theological-perspectives.html.
[282] See Paul Rabinow, *Making PCR: A Story of Biotechnology* (Chicago: University of Chicago Press, 1997); Steven Shapin, *The Scientific Life: A Moral History of a Late Modern Vocation* (Chicago: University of Chicago Press, 2008);
[283] Presidential Commission, "Synthetic Biology."
[284] Ibid., 135.
[285] Ibid., 139.
[286] Ibid., 140.
[287] James D. Faubion, "Toward an Anthropology of Ethics: Foucault and the Pedagogies of Autopoiesis," *Representations* 74, Spring 2001, 83.
[288] Michel Foucault, *The Government of the Self and Others*, *Lectures at the Collège de France 1982-1983*, ed. Frédérique Gros, François Ewald, Alessandro Fontana, Arnold Davidson, trans. Graham Burchell (New York: Palgrave MacMillan, 2010), 219.
[289] Webb Keene, "Life with Others and the Anthropology of Ethics," UC Berkeley Anthropology Department Lecture Series Colloquium, April 19, 2010.
[290] Hubert Dreyfus and Paul Rabinow, *Michel Foucault: Beyond Structuralism and Hermeneutics*, 2nd ed. (Chicago: University of Chicago Press, 1983).
[291] James D. Faubion, "Toward an Anthropology of Ethics: Foucault and the Pedagogies of Autopoiesis," *Representations* 74, Spring 2001, 83-104.
[292] Faubion, "Autopoiesis," 84.
[293] Albert Jonsen, *The Birth of Bioethics* (Oxford: Oxford University Press, 2003).
[294] Paul Rabinow, *French DNA: Trouble in Purgatory* (Chicago: University of Chicago Press, 1999); Helga Nowotny, Peter Scott, and Michael Gibbon, *Re-Thinking Science: Knowledge and the Public in an Age of Uncertainty* (Oxford: Wiley-Blackwell, 2001); Sheila Jasanoff, *Designs on Nature: Science and Democracy in Europe and the United States* (Princeton: Princeton University Press, 2007).
[295] For a diagnostic overview of these prior efforts see http://bios-technika.net/diagnostics.php
[296] See Paul Rabinow and Gaymon Bennett, *Designs for Human Practices: An Experiment with Synthetic Biology* (Chicago: University of Chicago Press, 2012).
[297] See Rabinow and Bennett, *Designs* as well as Faubion, "Autopoesis"

[298] Anthony Stavrianakis, Gaymon Bennett, and Paul Rabinow, "Fieldwork in Affect," http://anthropos-lab.net/studio/episode/04/
[299] To see further experimental efforts visit the ARC Studio at http://anthropos-lab.net/studio/
[300] Faubion, "Autopoiesis," 92.
[301] Ibid., 94.
[302] Ibid.
[303] Luc Boltanski and Laurent Thevenot, *On Justification: Economies of Worth*, trans. Catherine Porter (Princeton: Princeton University Press, 2007).
[304] Cf. Paul Rabinow, "Introduction," in *Making PCR*
[305] Ian Hacking, *Historical Ontology* (Cambridge, MA: Harvard University Press, 2004).
[306] James D. Faubion, *The Shadows and Lights of Waco: Millenialism Today* (Princeton: Princeton University Press, 2001).
[307] Paul Rabinow, *The Accompaniment: Assembling the Contemporary* (Chicago: University of Chicago Press, 2011).
[308] Foucault, 209.
[309] Ibid., 219.
[310] Ibid.
[311] Ibid., 227.
[312] Rabinow, *Anthropos Today: Reflections on Modern Equipment* (Princeton: Princeton University Press, 2003); see also *Bios-Technika* at http://bios-technika.net.
[313] Foucault, 228-229
[314] Foucault, 229
[315] Ibid.
[316] Ibid. 228
[317] Ibid. 230
[318] Ibid., 239.
[319] Ibid., 238.
[320] Michel Foucault, *The Hermeneutics of the Subject: Lectures at the Collège de France 1981-1982*, eds. ed. Frédérique Gros, François Ewald, Alessandro Fontana, Arnold Davidson, trans. Graham Burchell (New York: Palgrave MacMillan, 2005), 437.
[321] Thanks to Paul Rabinow and Anthony Stavrianakis with whom the reconstructive work in this prologue to the near future was undertaken. Cf. Stavrianakis, Bennett, and Rabinow, ARC Studios 1-6 at: http://anthropos-lab.net/arcstudio/
[322] See especially, Stavrianakis, Bennett, and Rabinow, "Fieldwork in Affect: Diagnosis, Inquiry, Reconstruction," ARC Studio 04 at: http://anthropos-lab.net/studio/episode/04/.
[323] Foucault, *Hermeneutics*, 293-8.
[324] For one experiment in tests of the object see Paul Rabinow and Gaymon Bennett, "Diagnostics" at http://bios-technika.net/diagnostics.php.
[325] Foucault, *Hermeneutics*, 298-304.
[326] We have begun to experiment with giving form to these questions. See *Bios-Technika* "Cases," at: http://bios-technika.net/cases.php.
[327] Foucault, *Hermeneutics*, 437-447.
[328] These are the overarching themes of the *Bios-Technika* experiment (http://bios-technika.net), as well as ARC Studios 4-6 (http:/anthropos-lab.net/arcstudio/.
[329] Stavrianakis, Bennett, and Rabinow, "Ethics: Directives," http://anthropos-lab.net/studio/episode/003/.
[330] Foucault, *Hermeneutics*, 453-487.
[331] Thanks to Paul Rabinow for drawing special attention to the passages in Foucault on the problem of the future in the care of the self. See his unpublished "Assembling Untimeliness: Permanently & Restively."
[332] Rabinow, "Assembling Untimeliness."