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Minimal Properties of a Natural Semiotic System: Response to commentaries on *"How molecules became signs"*

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> *"Every manifestation of information, semiosis and meaning we have been able to study experimentally has a physical form. Neglect of their dynamical (energetic) ground tends towards dualism or idealism, leaving the causal basis of semiosis and the causal powers of representations mysterious. Consideration of the necessary physical requirements for the embodiment of semiotic categories imposes a discipline on semiotics required for its integration into the rest of science." — John Collier* (1999: 111).

1. Introduction: "One Long Argument"

Charles Darwin famously described his *Origin of Species …* as only the beginning outline of one long argument (Darwin, 1866). It is an argument that remains still in process a century and a half hence. As Don Favareau (2021: 603) charitably comments on the sweep of my career-long engagement with semiotic issues, this target article is a sort of progress report of my long effort to bring semiotic thinking into mainstream natural science. As the many diverse supportive and critical commentaries demonstrate, there is still much more to be done before this is one long argument is completed. The sort of dialogue that these proposals, challenges, and responses initiate will hopefully move the biosemiotics argument a number of steps forward. Alas, in this brief response to commentaries I cannot hope to do justice to the wealth of ideas that have been generated in the sixteen extensive commentaries that both challenge and expand on topics from the target article. As a result, I must apologize in advance for the many comments that I have been unable to respond to, in order to focus on a few of the most critical commentaries. By focusing on these criticisms and exploring the apparent incompatibilities they suggest I hope to highlight issues most likely to illuminate some of the more fundamental challenges of the field.

In my target article "How molecules became signs" (Deacon, 2021), I endeavored to show how semiosis can be understood in terms of molecular evolution, without invoking any atypical physical-chemical properties or taking an extrinsic observer perspective. In other words, I attempt to identify the minimal properties that are necessary and sufficient for a physical system to be able to use a molecule (such as RNA) as a sign to be "about" the properties of and relationships between other molecules. It is intended to provide what amounts to a *proof of principle* of molecular-level interpretation using a simple-as-possible model system in which no special physical-chemical properties are invoked.

This is not to suggest, however, that this is the only possible means by which molecular aboutness could have evolved. Nor can I claim that all the chemistry has been worked out. Nor does this account exclude other origins-of-life and origins of genetic information scenarios. Indeed, there are many ways in which this account is complementary to many of these alternatives; a point that I will return to below.

I believe the merits of this approach derive from its simplicity and lack of assumptions. By only considering basic chemical dynamics, it avoids introducing incompletely understood processes that we take for granted in living cells and makes possible an exhaustive account of the properties and processes involved, at least in its simple form. In this way, even if the account falls short of fully accounting for the origin of molecular semiotics, it will be more likely to expose any critical assumptions that might otherwise go unnoticed, and ultimately will allow the claims of this approach to be empirically tested.

2. Realizability

It is interesting that no one argues that a simple autogenic virus is an implausible molecular complex. Indeed, many acknowledge that it is likely to be empirically realizable. Whether or not one is willing to call its properties "semiotic" and describe its chemical interactions as a form of "interpretation," there is little dispute over the claims being made about its behavioral dispositions despite its abstract and generic characterization. Of course, innumerable details and initial conditions have been left to the imagination, and not even the general type of molecules is specified.

I predict that sooner or later autogenic virus-like forms will be discovered in e.g., sea water or deep petroleum deposits, or even on other planets. The chemical plausibility of autogenic virus-like forms suggests that a fairly simple search procedure (such as sampling for virus-like protein complexes that lack nucleotides) could screen for their existence.
Though the virus analogy suggests that protein-like molecules are involved, all that is assumed is that the component molecules are capable of catalytic and self-assembling interactions, which includes a large range of possible molecular candidates. For the current purpose, however, considering such chemical detail is irrelevant.

In many respects, as Howard Pattee (2021: 567) cautions, the chemistry I invoke becomes increasingly speculative at each step from simple autogenesis to template-based autogenesis. This is not true with respect to simple autogenesis, however, which only assume known viral and catalytic chemistry. Although I invoke no chemically implausible step in the formation of a linear template molecule, the binding of catalysts to such a template, or the offloading of some of the dynamical constraints of reciprocal catalysis onto this template, many of the relevant chemical details are framed in abstract terms. This is why I describe it only as a "proof of principle," not a specific chemical model.

But at this stage, all existing chemical models of the origins of life and the evolution of genetic information are equally abstract and speculative, whether in RNA-World scenarios, protocell models, or autopoietic theories. Indeed, I would argue that the advantage of the autogenic approach is that the introduction of every new step from simple autogen to template autogen is at least described without logical jumps that merely presuppose the appearance of some new property, such as RNA aboutness or autopoietic individuation. In this respect, the autogenic scenario can at least provide a plausible empirically explicit alternative to compare to other currently popular scenarios.

Nevertheless, my adherence to chemical processes that can be found in the nonliving world — which I consider to be a virtue of the autogenic virus — others see as a problem. Consider a comment by Tom Froese. He finds my approach limiting because I adhere "to a narrow form of naturalism, in which the only permissible explanatory factors are those captured

by the natural sciences" (Froese, 2021: 657-658). He favors "a more relaxed form of naturalism, in which the subjective side of life can also make a difference in its own right." I don't interpret him to suggest that we need to introduce mysterious nonphysical properties in order to explain semiosis, but before considering this I believe that it important to first attempt to explain semiosis solely in terms of well-known chemical and physical principals. Only if this is shown to be impossible should we consider introducing "subjective" factors. Otherwise, I fear that semiotically laden concepts such as 'genetic information' or 'cell signaling' will remain heuristic glosses based on anthropomorphic metaphors and only used for rhetorical effect in biology.

3. Autogenesis vs. Autopoiesis, Viruses vs. Cells

Tom Froese is justifiably critical of the fact that I don't review the "venerable tradition" of paradigm models that he describes as "bounded self-production" (Froese, 2021: 659). This is a fair criticism. Neither in this article nor in my other discussions of autogenesis have I systematically compared it to these many models attempting to articulate the critical abstract properties that define life. Of course, space limitations precluded such a review in the target article and also in the response. But more to the point, I believe that there are methodological reasons for distinguishing the autogenic approach from these more philosophically motivated approaches, and that treating them as variants of a common paradigm misses something important.

First, my intention is not to attempt an account of the defining principles of life or even the origins of life. This difference in motivation is well-exemplified by comparing the molecular framing of autogenesis versus the abstract principles approach that is common to most discussions of autopoiesis, such as exemplified by such principles as operational closure, bounded self-reproduction, autonomous agency, metabolism-repair, and so on. Instead, the molecular relationships and component dynamics of the autogenic model are the focus of my analysis, and specifically whether it is possible to derive the relevant semiotic properties from that chemistry alone. This is not a typical philosophical endeavor, even though it has philosophical implications. In this respect, my methodology is more characteristic of biological science than the philosophy of biology, and might better be contrasted with protocell theories.

Second, my goal in the target article is considerably narrower than to characterize life, or to analyze such abstract properties as autonomy, agency, and normativity. I am instead interested in grounding the use of semiotic concepts in ways that are consistent with the methods of current molecular biology. As a result, it is irrelevant whether an autogenic virus is categorized as alive or not, so long as its organization and dynamical dispositions provide plausible models of semiotic processes.

Third, autopoietic and protocell theories are all based on a cellular paradigm, whereas autogenesis is based on a viral paradigm. Although many commentators take issue with my use of this noncellular logic, none seemed to reflect on my motivation for departing from the standard paradigm. This shift in framing is telling. First, the very fact that viruses appear to straddle the life/nonlife boundary recommends them as a relevant model system for this most basic level of analysis. Second, it provides a figure/ground reversal that helps to disentangle basic semiotic processes from processes that are additionally required for the far more complex semiosis of cellular life. Because autogenesis is not based on a cellular paradigm, it also defies classification as either a metabolism-first, information-first, or containment-first theory. These classic attributes of cell function are also distinguished with respect to their predominant

biochemical medium—proteins, carbohydrates, nucleic acids, and lipids, respectively. This distinction naturally leads many to take a sort of reverse-engineering approach in which these functions are analytically distinguished from one another as though capable of existing separately and just combined to generate life. In contrast, one implication of the autogenic viral paradigm is that these functional attributes are inseparably entangled in a basic functional synergy that is not decomposable. They only become analytically and materially distinguishable with the increase in cellular complexity.

4. Agency, enactivism, and work

The reactive dynamics of an autogenic virus is considered problematic both by critics and supporters of this approach. Because autogenic self-repair and self-reproduction are only initiated in response to extrinsic perturbation rather than by an intrinsic process, many commentators argue that this leaves out an essential property of semiotic interpretation.

For example, while being receptive to the logic of the autogenic approach, Don Favareau (2021: 605) nonetheless wonders whether "…relying merely on the happenstance of externally-induced breakages" instead of internalized control of reproduction or repair, lea ves autogenesis without semiotic agency. And Tom Froese makes this point even more emphatically when he concludes that: "It can therefore be doubted whether this kind of extrinsically caused reactivity is sufficient for Deacon to attribute to the system any kind of intrinsic activity. If this shift from extrinsic to intrinsic cannot be secured, the model would be lacking the most essential ingredient on which Deacon's semiotic notion of normativity depends" (Froese, 2021: 659). In fact, I believe that autogenesis demonstrates that "intrinsic activity" is *not* essential to either semiosis or normativity. All that's needed is some intrinsic disposition to counter an impending threat to its organizational integrity once it's detected.

I understand the motivation for this intuition, however. It is implicit in the animate/inanimate distinction that is often used to loosely distinguish life from nonlife. But this is obviously not a diagnostic feature. No one considers a battery-powered animated toy more alive than a dormant seed. And we are not confused by the inert form of many spores, which are able to persist in an inert state for years. Nor are we doubtful whether a women's eggs fertilized in vitro and stored for years in liquid nitrogen are potential humans. Being temporarily inert in a state of suspended animation is not the same as being dead, so long as re-animation is possible when conditions are right. Yet the lack of intrinsically initiated activity is one of the reasons for the reluctance to attribute life to viruses.

Something more basic than intrinsic animacy is involved. To identify what that is we need reconsider the role played by work in our understanding of agency. To deconstruct the concept of thermodynamic work, I consider how Stuart Kauffman and colleagues (Kauffman et al., 2007) have described it. They distinguish two independent factors: a source of spontaneous energy flow and constraints on that flow. The unconstrained release of energy is inevitably problematic for life, but the carefully constrained release of energy, channeled in specific ways, is critical to life. more importantly, these to aspects of thermodynamic work can arise independent of one another. For living processes, the sources of metabolic energy can be quite diverse, and is mostly external to the organism. Thus, depending on the species, it can be provided by solar radiation, the energized molecules spewed from deep sea volcanic vents, or the consumptions of other organisms. Once acquired, however, it can be converted to a form that can

be stored internally as potential energy, ready for future use. What matters more is the locus of the constraints that organize how that energy is released to perform work.

Consider for example the thermodynamic work involved in spinning a flagellum in order to propel a bacterium. For this to be possible the bacterial cell must first build up a store of potential energy. This potential energy source is acquired in the form of nutrients previously harvested from its environment. When metabolized, the energy that is liberated is channeled into the activation of ATP molecules which cause the flagellar motor to turn. What matters is not where this potential energy comes from but how the release of this energy is constrained by organism structures so that it does work that is beneficial. Two critical constraints are (1) the conditions that trigger the release of constraints on the flow of energy, and (2) the constraints that channel how this flow of energy performs the relevant work.

In this respect, autogenesis differs from many more complex forms of life with respect to constraint 1. Unlike most cellular lifeforms, but like a virus, an autogenic system does not initiate self-preserving or self-reproducing work. It only shifts from a dormant to an active phase in response to an external stimulus. But like all forms of life, the ultimate source of energy and raw materials that constructs and sustains a simple autogenic virus is derived from its environment. It just lacks the capacity to accumulate and store potential energy.[1]

In contrast, a dormant seed or spore will use stored energetic resources to kick start development when conditions are right. And yet, like autogenesis, the initiation of dynamical constructive activity in dormant seeds and spores is triggered by specific extrinsic conditions. This sensitivity to extrinsic conditions is a function of intrinsic constraints that determine the change from a dormant to a dynamic state with respect to this extrinsic influence. But neither autogens, viruses, nor fungal spores autonomously initiate their transition from dormancy to activity. In these cases, the environment is the source of work that releases constraints that have prevented potential dynamical interactions. The constraints thereby removed are immediate interpretants of this environmentally relevant sign. They are like switches that, when flipped by a small amount of extrinsically applied work, remove constraints that have prevented other forms of work from occurring.

So, unless we are willing to argue that seeds and spores (as well as many other organisms) are incapable of biosemiosis, it would be inconsistent to deny this capacity to an autogenic or parasitic virus. From this I conclude that being able to internally initiate and generate the energetics of action is not a necessary precondition for a system to have interpretive capacity. Although interpretation is a process that requires work, it is the potential to constrain and channel energy release that is critical, irrespective of the source of that energy. It is the source of those constraints that determines the ultimate locus of semiotic agency, not the source of energy.

Nevertheless, the ability of an autogenic virus to acquire and store energy *is* discussed in the target article in terms of the generation and storage of nucleotide molecules with their ability to acquire and transport energy in the form of phosphate residues. The possible relevance of this

[1] Actually, this is not quite true. The very fact that an inert autogenic virus is a stable far-from-equilibrium structure means that breaking down its structure could liberate energy. This would happen if breakage happens in an environment lacking in relevant substrates. Indeed, it is its particular far-from-equilibrium state (a constrained state) that provides its potential to organize work on its own behalf. But the energy that drives the work of autogenic reconstruction is not derived from the breakdown of autogenic components; it only derives from catabolic breakdown of environmentally available substrates.

to automous agency was not pursued further and only its relevance to template formation was considered.

5. What Constitutes Interpretant Production?

Because of the virus-like logic of simple autogenesis, the anthropocentric connotations of the concept of interpretation make it seem quite counter-intuitive that semiosis could be instantiated in terms of molecular interactions alone. So, for example, it's not surprising that many biologist would agree with Howard Pattee (2021: 567), that the translation from nucleotide sequence to protein folding "… leaves no freedom or need for an interpreter or any interpretive process … [and that] Interpretive intervention makes sense only at higher levels." But wherever one draws the line, the same emergent challenge must be faced: how can molecules *become signs* about anything.

This approach also requires a departure from Peirce's vision of semiotic relations, which was largely described in cognitive terms. To avoid infinite regress in explaining the semiotic capacities of creatures with minds, however, we ultimately need to identify a lowest level below which there is no semiosis. Though many might argue that this threshold is crossed only at the emergence of complex brains, biosemiotics extends semiosis to the border between life and nonlife. Such a huge explanatory gulf is problematic for those like Ruth Millikan who are interested in an account of semiotic activities at the level of creatures with minds. As a result, she wonders how the autogenic account can hope to provide a "… general characterization of what is to qualify as an 'interpretant' in his new sense" (Millikan, 2021: 582). So, she asks for "a short statement in everyday terms what the general nature of his kind of interpretant is supposed to be."

Efforts to explain the sorts of higher level semiotic processes characteristic of mental processes implicitly take for granted the supportive semiotic processes taking place at the cellular and molecular levels of the organism. This most basic level of semiotic analysis must inevitably fall short of providing an account of the sorts of interpretive processes that constitute cognition. As Miguel García-Valdecasas points out, this undermines any simple "life-mind continuity assumption." Indeed, multiple nested levels of nested semiotic processes must have evolved to bridge this chasm (García-Valdecasas, 2021: 617). Still, I believe that there are necessary semiotic homologies that extend from molecules to minds in the living word, so that even an analysis at the most basic level can yield insights relevant to even the most complex mental semiotic processes.

Importantly, at this most basic level, it is apparent that interpretation is not merely an epistemological process, but is intrinsically also ontological; i.e. it is at least indirectly about the existence of this epistemological capacity itself. Interpretation at the autogenic level is a response to an existential threat. It is the integrity of this intrinsically unstable far-from-equilibrium complex that is at stake. The environmental perturbation that initiates new catalysis is interpreted by the process of autogenic reconstitution as representing this threat to the continued persistence of this system and its self-maintaining disposition. Because the initiated response specifically counters this threat, it represents this possibility of extinction to the system in terms of the work that prevent this from occurring. Thus, autogenic interpretation involves a represented object (the system's potential nonexistence), its immediate physical correlate (the breach that is a sign of this object), and an intrinsically organized physical response (an interpretant) that "mirrors" this

object in terms of the system's countervailing activity. In these terms, both autogenic and mental semiotic capacities have evolved to preserve their own interpretive infrastructure.

6. Replication

A number of the commentaries agree with me that simple template replication is too simple to account for biosemiotic functions. For example, Cliff Joslyn (2021: 666) says: "… the bottom line is that copying is not sufficient for sign processes in living systems," and Tom Dickins (2021: 639) comments: "I most certainly would not base a theory of biological information on replication." And he goes on to state: "… to the best of my knowledge no one in fact does this." On the contrary, I think that many do take this position, although mostly in a context that tacitly assumes replication *in organisms*.

As a case in point, The Harvard biologist David Haig begins his commentary defense of the RNA-World hypothesis with the following sentence. "RNAs can do many things. They can store information, act in the world, and respond to the world" (Haig, 2021: 651). He could have gone on to list the many ways that RNA molecules are also involved in regulating the epigenetics of cell differentiation and metabolism as well as much else. These claims are missing one vitally important caveat, however. These remarkable capacities of RNA molecules are only exhibited within a living cell or some artificial context that emulates a cell's interpretive capacities. Otherwise, RNA molecules are just inert and quite delicate polymers. Clearly, despite the rhetorical simplification, Haig is also assuming this context when he says that RNA molecules can serve these many biosemiotic functions. Molecular biologist just assumes that it 'goes without saying' that such functions are taking place within living cells. But in this context it needs to be said. These are not properties *intrinsic* to RNA molecules. These are functions that RNA molecules have taken on over the course of evolution in service of the preservation and reproduction of cell functions, which also includes replication of these molecules.

From an external observer's perspective there is a tendency to project onto inanimate objects properties that are actually reifications of our descriptive interpretations. For example, employing a rhetorical attribution of intrinsic semiotic agentive properties to molecules, similar to the way Richard Dawkins (1976) famously described genes as "selfish," John Stewart claims that RNA "acts in its own interests" and that RNA molecules have "evolutionary interests" (Stewart, 2021: 646). Even if this terminology is used merely as a heuristic analogy, it still begs the question of the origin of these properties. The question is not whether RNA molecules can serve many semiotic and regulatory functions—they can—but rather whether they can do these things without extensive cellular support, and if not, how they could have acquired these capabilities in the first place.

The RNA-World hypothesis for the origin of life is a variant of what many have called the "naked replicator" hypothesis: i.e., that molecular replication is sufficient to constitute the conditions that initiated the evolutionary process. Justification for the RNA-World hypothesis was, of course, provided by the discovery that RNA molecules can serve both as templates for replication and also as catalysts (ribozymes) that can facilitate other chemical reactions (e.g. facilitating the formation of peptide bonds in a ribosome). Although the RNA-World hypothesis is in this way not merely a naked replicator paradigm, it nevertheless is somewhat ambiguous about whether replication is about anything; i.e. provides information about what constitutes adaptation to prevailing conditions.

This raises two classic questions. First, in what sense is it appropriate to describe a copy as representing that which it copies? And second, does being copied also provide information to the replica about its relationship to the environment in which this occurred?

Of course, a replica *can* represent the form that it replicates to an external observer aware of both. But is this also an intrinsic property? Does the copy represent what it copies to itself? And what about the adaptive significance of *being copied*? As with a footprint in wet sand or a wax impression made by a signet ring, each can serve to represent its missing cause. But to whom or what? Not to the foot or ring, of course. Their correlation by causal and formal correspondence is a simple material fact. It is not fundamentally different than the relationship between a rock and the hole left behind when it is pried from the ground. Representation must be more than this.

Specifically, it assumes something that isn't intrinsic to the two correlates of this physical relationship; that is something more than their relationship to one another. This extrinsic perspective is provided by an interpretive process. And this has certain nontrivial requirements. So, for example, a fly buzzing nearby and sensing a footprint or wax impression would still be incapable of interpreting each as representing something other than what they are. These physical artifacts are *affordances* for a system with the appropriate interpretive competence. They become signs when interpreted. What requires explanation, then, is what this interpretive competence entails. Copying is relevant to biosemiosis, but only if that which is copied provides information about something else for some end. An outside observer (such as a biologist or philosopher) could interpret the structure of an RNA molecule as representing its antisense precursor, but it is a step too far to assume that the one molecule interprets the other.

Nevertheless, much RNA-World research *is* relevant to the autogenic logic presented here; just not playing an originative role. Indeed, the evolution of template-based autogenesis, as described in the target article, provides the context in which a theory of molecular pattern replication becomes relevant. Because of the causal correlation and homomorphism between dynamical organization and molecular template structure in the template assisted autogenic process, different template patterns can acquire differential selective value. In the case of a template molecule that re-presents the dynamical constraints of the system, differential replication of the template is a consequence of how its structure constrains the dynamics of the system of which it is a part, irrespective of any other intrinsic molecular property. So, its continued existence is a function of its relational properties, not just its intrinsic properties. This exemplifies a fundamental difference between basic chemistry and biosemiotic chemistry.

But the evolutionary value of a template molecule is only realized if, besides benefiting the system of which it is a part, it can be replicated independently. This process is left unexplained in the model of template-aided autogenesis. So, the extensive body of molecular biological research into the nature and origins of RNA replication is not just consistent with autogenic theory, it provides information about the sorts of chemical processes that are essential to the plausibility of template-based autogenesis. It's just that, from an autogenic perspective, template replication is subordinate to biosemiosis, not its origin.

7. From generic template to RNA structure

This opens the door to a reconsideration of the relevance of RNA-protein interactions. The idealized description that I present in the target article (modeled on protein-DNA binding) was merely a heuristic approach for demonstrating the plausibility of correspondence relation

between nucleotide sequence and catalyst structure. This is a simplified stand-in for a generic template-substrate relation. With respect to RNA functions, this simplification ignores the likely relevance of the complex three-dimensional structures that single-stranded RNA molecules can assume. This may provide a bridging step to the three dimensional protein-folding logic that Howard Pattee (2021) focuses on in his commentary.

Proteins are not the only polymeric molecules where the sequence of monomeric units influences how it folds into a three-dimensional structure. The nucleotide sequence of a single-stranded RNA molecule also influences its three dimensional "folding," but by a very different mechanism. Cross-linkage between different segments of the same RNA strand in which exact or nearly complementary nucleotide sequences can produce hairpin and branched configurations. So, RNA and proteins have two quite distinct mechanism by which a monomer sequence (of nucleotides or amino acids, respectively) contributes to three-dimensional polymeric structure. These two kinds of structures are also complementary: RNA annealing produces branch-like structures and protein folding produces sheet and globular structures. These two logics come together in RNA-protein complexes, like the ribosome, in which multiple RNA and protein molecules provide some of the most basic functional elements of all cells. The autogenic template logic might therefore involve binding of protein-like catalysts to three-dimensional RNA template structures. In this way, a link between three-dimensional structure and nucleotide sequence can be multiply realized, with considerably greater degrees of freedom.

8. 1-2-3 Repeat: an Open-Ended Semiotic Scaffolding Logic

The title of the target article was intended to direct attention to a basic scaffolding logic. This didn't succeed. None of the otherwise quite incisive commentaries engaged with what I tried to portray as a universal semiotic architectonic. The three types of autogenic structures described in the target article were presented to exemplify a general principle of semiosis that goes beyond what Peirce might have envisioned (though not inconsistent with his underlying architectonic). The hierarchy of autogenic forms vaguely parallels the constructive logic of iconic, indexical, and symbolic interpretive capacities, though in ways that should be conceived in far more generic terms. Framed as a nested hierarchy of affordances, it shows how interpretation based on covariance or isomorphism (form) provides the foundation for interpretation based on causal involvement or correlation (physicality) which provides the foundation for interpretation that can be displaced from any formal or physical attributes of its object of reference. Indeed, understanding this last step, which enables interpretation irrespective of any intrinsic sign vehicle affordances, is critical to the power of semiosis. This is why at the end of the target article I show how this scaffolding logic is recapitulated in DNA-mRNA-tRNA-protein-folding processes and how this enables DNA to recursively modulate DNA expression. This in turn contributes to the theme-and-variation logic of multicellular organism phenotypes.

My claim is that to create displacement of sign vehicle properties from the properties of what is represented, two intervening re-representing steps are required. Representation based on isomorphism linked to representation based on correlation creates a form of interpretive distance that maintains representation despite the lack of any common feature. This disconnect makes it possible for new levels of semiosis to emerge from the distinct affordances intrinsic to a prior sign medium as well as recursive semiotic relations. Both are exemplified by the molecular biology of genetics discussed in the penultimate section of the target article and exemplified by its final two figures. So, the 1-2-3-repeat logic of basic molecular genetics takes the form of 1)

DNA-mRNA and mRNA-tRNA *isomorphisms*, 2) tRNA-amino acid and amino acid to amino acid polymerization *contiguities*, and 3) protein-context interactions producing protein folding. This multi-step semiosis enables the complete displacement of protein structure from the linear constraints that gave rise to it. At the same time it maintains continuity of information despite this complete discontinuity of physical properties. It is what enables molecular interactions to be mediated by higher order isomorphism and physical interactions based on protein geometry, and yet to be regulated by DNA sequence information. This is of course the point that Howard Pattee (2021) was making in his commentary. What the 1-2-3-repeate account adds to his analysis is both a general account of the semiotic logic that makes this displacement possible as well as an explanation of how displacement enables open-ended semiotic scaffolding and recursive complexity.

This brings us full circle to Pattee's original question: "How Does a Molecule Become a Message?" I hope that this analysis has provided a plausible biosemiotic account of how this could have originated.

9. Conclusions

The incredible sophistication and diversity of issues that have been brought to light by this exercise demonstrates that there are many fundamental conceptual problems yet to be resolved before biosemiotics can be seamlessly integrated into the natural sciences. But I remain convinced that this is both possible and valuable. Unfortunately, in this short response piece I have only been able to comment on a fraction of many insightful commentaries. As a result, I have mostly focused on topics that reflect major paradigmatic differences, potential areas of consilience, and tacit assumptions that are illuminated by the apparent incompatibilities of our different approaches. Although this tends to frame my commentary to commentaries as engaging in debate, my hope is that my responses will be taken not as criticisms but as openings for future dialogue. Both the critical and supportive aspects of these many commentaries have forced me to reflect more carefully on the ambiguities and holes in my reasoning. I hope, in return, that my proposal and responses have likewise contributed a small step further along in our collective one long argument.

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