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The Organization of Biotechnology Science and Its Commercialization in Japan

by

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ABSTRACT

The biotechnology revolution is of particular interest both for the sociology of science and for industrial organization. Indeed, the closeness of progress in the basic science to applications in industry makes it impossible to understand the development of the industry without understanding the progress of the science and linkages between the two domains. In the U.S., Zucker, Darby, and Brewer (1994) demonstrates that where and when "star" scientists at the research frontier (and, in later years, their collaborators) were actively publishing were important determinants of where and when new biotechnology enterprises (NBEs) were founded. In ongoing work extending the analysis to Japan, it is seen that while the structure of science related to the new biotechnologies is broadly similar between the United States and Japan, the organization of the biotechnology industry in the two countries is quite dissimilar. In the U.S., at least 68 percent of NBEs were new biotechnology firms (NBFs) started for this purpose while 98 percent of Japanese biotech firms in our data base were subunits of existing firms. This paper reports the results of field work in Japan which was undertaken to develop understanding of the differences underlying these structural differences and to generate hypotheses for future empirical work on the development of the biotechndogy science and industry in Japan. The individuals interviewed included biotech scientists, industry executives, government officials, and officers of intermediating organizations.

Our respondents identified three major factors which interact to deter the formation of NBFs: (a) the closed nature of the Japanese system of higher education and non-competitive research funding, (b) incompleteness of the capital markets: aspecially the lack of a national venture capital industry capable of financing new firms and the related absence of initial public offerings prior to a firm's achieving substantial profitability, and (c) cultural characteristics and incentive systems which discourage Japanese entrepreneurialism generally, and particularly impact scientists. An alternative hypothesis is that U.S. incumbent firms have been deterred from entry due to U.S. tort-liability exposures. It remains for future research to determine both the relative importance of these factors and whether the two systems of organization of the biotech industry are associated with substantial differences in productivity and international competitiveness.

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The Organization of Biotechnology Science and Its Commercialization in Japan

by

Lynne G. Zucker
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Broadly enough defined, biotechnology has **been used as** long as people have baked bread and drank wine. Cross breeding of animals and growing penicillin are other examples of biotechnology. Since the mid-1970s a new biotechnology industry has emerged, driven by revoutionary advances in the biological sciences, particularly in fields such as genetic engineering and cell hybridization. This new bioscience and the associated industry are defined by their use of the new techniques, principally genetic engineering based upon taking a gene from one organism, implanting it in another, and producing the outcome of this process. The underlying technique of recombinant DNA **(rDNA)** is based on the 1973 discovery by Stanley Cohen and Herbert Boyer.' The other basic technology is **cell fusion** in which lymphocytes are fused with myeloma cells to create rapidly proliferating antibody-producing cells.'

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and for industrial organization. Indeed the closeness of progress in the basic science to applications in industry makes it impossible to understand the development of the industry without understanding the progress of the science and linkages between the two domains. In ongoing research, the authors and others have found it very useful to identify worldwide 337 leading researchers whom we termed stars on the basis of the number of genetic sequence discoveries reported up to 1990 for which they were an author and of the number of such articles. These 337 stars were listed as authors on 4,315 distinct articles in major journals. Because research discoveries frequently occurred through teams, another 7,718 scientists who were coauthors with a star but who had not themselves met the star criteria were labeled **collaborators.3** In the United States, Zucker, Darby, and Brewer (1994) demonstrates that where and when these stars (and, in later years, collaborators) were actively publishing were important determinants of where and when new biotechnology enterprises (NBEs) were founded.

In ongoing work extending the firm data base to Japan, we have observed that while the structure of science related to the new biotechnologies is broadly similar between the United States and Japan, the organization of the biotechnology industry in the two countries is quite dissimilar. Both of these points can be made be reference to Table 1. First we note that although the numbers of Japanese stars and collaborators are somewhat lower than the Japan-U.S. population ratio of 0.50, the distribution of location of scientists is nearly identical across organizational types. However, while 68 percent of NBEs in the U.S. are New Biotechnology Firms (NBFs) established since 1976 primarily to commercialize the new biotechnologies, some 98 percent of the NBEs are subunits or subsidiaries of preexisting firms in Japan. Such radically different industrial structures may or may not make much difference as to the productivity of biotechnology in the two countries. Furthermore, there

are slightly more NBEs per star in Japan than in the U.S.; so at least in terms of numbers the Japanese enterprises are as numerous as one might expect.

This paper reports the results of field work in Japan which was undertaken to develop understanding of the differences underlying these structural differences and to generate hypotheses for future empirical work on the development of the biotechnology science and industry in Japan. We conducted ten interviews in Tokyo, Osaka, and Kyoto, Japan, from November 30 through December 10, 1993. The individuals interviewed included biotech scientists, industry executives, government officials, and officers of intermediating organizations. The questions covered and respondents are listed in Appendix A. Extensive documentary material was also collected.

The authors recognize and confirmed that both the biotech science and industry, as well as the financial infrastructure, in Japan are organized differently from the United States. We do, however, believe that in a comparative study it is important to identify both areas of difference and similarity, and point to mechanisms which may reduce or amplify the importance of differences in the two systems. It is important to stress that both U.S. and Japanese firms are producing drugs based on biotechnology which, though still few in number, are responsible for both substantial revenues and alleviation of human suffering. Although the systems are somewhat different, both appear successful.

In our research on biotechnology in America, it was relatively easy to identify when firms began their biotech activities since three quarters were new firms started for this purpose. Subunits of existing firms were harder to date and locate, but relatively few in number. In contrast, 98 percent of Japanese biotech firms in our data base were subunits of existing firms. This poses both a data problem as well as the set of substantive questions as to what are the reasons for the differences in structure and do the structural differences

and their underlying causes result in substantive differences in performance between the American and Japanese biotechnology industries. While at present the new biotech firms in the U.S. seem to be somewhat ahead, it is far from certain that the better short-run strategy will also survive as an optimal long-run industrial organization. For example, the U.S. system seems to involve more concentration (and duplication) of research efforts on those areas with the highest payoffs as compared to Japan; whether this is more or less socially productive is at least debatable.'

In our work on biotech science we found that Japanese researchers were both numerous, constituting nearly 20 percent of the world total by 1985, and very productive in terms of both numbers of gene sequence discoveries and citations to their work.[5] From early reactions -- both in the U.S. and Japan -- to our findings on bioscience in Japan, it seemed as if the productivity of Japanese science was substantially underrated. This posed a question as to whether there was a flaw in our methodology for measuring the growth and diffusion of the science.

Finally, geography and timing were sufficient to link active biotech scientists in the United States to entry of new or existing firms into biotech activity, but these variables were questionable for Japan both because of some difficulties in determining either timing or location of biotech subunits of existing firms and also because of the much more compact and concentrated scientific and industrial geography of Japan with both concentrated in the Kanto region around Tokyo and in the Kansai region (Osaka and Kyoto, especially). The maps in Figure 1 plot ever-active stars and collaborators by geographic center of BEA functional economic areas for the U.S. and by prefecture for Japan (see footnote 5 for the definition of "active"). Firms are plotted by zip code for the U.S. and by city for Japan. In empirical work not reported here we are examining functional economic areas for Japan as

defined in Table 2.

I. Reasons for Reliance on Existing Firms in Japan

As shown in Table 1, the American biotech industry is dominated by new biotech firms while the Japanese industry is dominated by subunits of previously existing firms. Exploring these differences in Japan naturally leads to an emphasis on those factors in Japan which inhibit the development of new firms in Japan. However, we should not forget that there also may be an important other blade of the scissors: factors which inhibit existing U.S. firms from entry into the industry.6 We also note that while large firms in general seem to be less nimble than the small, new firms, Japanese pharmaceuticals appear to be doing a rather better job of keeping up than do their American counterparts.

Our respondents identified three major factors which interact to deter the formation of new biotech firms ("venture firms" in Japanese nomenclature): (a) the closed nature of the Japanese system of higher education and non-competitive research funding, (b) incompleteness of the capital markets, especially the lack of a national venture capital industry capable of financing new firms and the related absence of initial public offerings (IPOs) prior to a firm's achieving substantial profitability, and (c) cultural characteristics and incentive systems which discourage Japanese entrepreneurialism generally, and particularly impact scientists. We shall report on each of these in turn.

I.A. The Japanese Higher Education System

Our respondents identified a number of characteristics of higher education in Japan which they believe retard bioscience research within Japan and especially its

commercialization. There seems to be universal agreement that the private universities simply do not have the resources to compete with the national universities in this field. Lack of compensation in Japanese grants for overhead -- as is customarily given in the U.S. — converts these grants from money makers to resource drains for the private universities. This lack of competition for the governmental universities from their private counterparts is generally viewed as a significant problem relative to the American situation, particularly because of widespread dissatisfaction with aspects of the national university system. The national universities appear to be much more government operated -- as opposed to subsidized as is typical for U.S. state universities. One respondent stated that the government wants to control universities even to the level of appointments of individual professors. Another said that professors in the national universities act more like government bureaucrats than American professors. Other statements somewhat softened this picture, but there does seem to be consensus that the national universities are more subject to government control and procedures than their U.S. counterparts.

The National University System

The national university system is said to suffer from a lack of a competitive evaluation system both in hiring and retention of personnel and in allocation of research support. The basic tenure decision is made at the time of the initial hire as assistant.' The major national universities generally hire only their own graduates and the norm is no movement among universities. Some respondents believe that norm is gradually breaking down with some possibility of distinguished professors either earning their way to better universities or stepping down from there to lesser universities. Others observe that while there are exceptions, it is not unusual for a major university department to have 95 percent

of its faculty with Ph.D. degrees from that university. There does appear to be substantial migration of the more entrepreneurial faculty to the boards of the major firms. To what extent this movement ameliorates constraints in the university system is not clear to us.8

Several respondents point to the importance of personal connections in organizing research within the national universities as well as in obtaining jobs there in the first place. For example, if a researcher at Kyoto or Osaka University was pursuing research that required access to apparatus only available at the University of Tokyo, he would have to figure out some chain of relationship to the almost foreign world of the Tokyo professor controlling access to the apparatus.

The national universities are said to be organized on rigid departmental lines and this makes it difficult to organize interdisciplinary research such as is commonly needed for breakthroughs in the biotech area. Research funding comes from the Ministry of Education (ME) -- also the Ministry of International Trade and Industry (MITI) for engineering, the Ministry of Health and Welfare (MHW) for medicine and pharmacology, and the Ministry of Agriculture, Forestry, and Fisheries (MAFF) for agriculture -- down to the departmental level and is allocated there. Government research funding seems to be determined by the historic strength of the programs rather than by any dynamic assessment of the research which will be done with the money. Scientists with initiative may apply to the various institutes, usually developing proposals in concert with government and industry influentials; we are unsure whether such grants fund only the single project, or whether the whole department shares some benefits.

This departmental allocation approach eliminates the incentive present in America for researchers from different areas to collaborate to develop a complete research proposal which would be competitive for funding in a national arena. Allocations within the

departments tend to be relatively uniform among the faculty; so there is little culture of scientific entrepreneurship -- or grantsmanship -- built up by the system. Japanese faculty complain of the amount of time spent making collective decisions, primarily in meetings, and one respondent contrasted this to the management skills developed by successful scientists in American universities who must manage their own laboratories.

Several respondents report that the university system has worked much better in the electronics area both because all the relevant science is generally available within the engineering department and because MIT1 has fostered greater university/firm collaboration. It is reported that in the electronics area the national universities even have professors who worked previously for electronics firms.

Technology transfer

Technology transfer from the national universities seems to be impeded by lack of appropriate and open incentives for the faculty. Faculty are not permitted legally to accept consulting fees or honoraria. Nor can faculty members start their own firm and retain their positions in the university. In general university scientists are not aware of patent practices and thus do not have any significant entrepreneurial activity, although they may patent their discoveries under their own name according to the formal rules of the current system. If a patent is instead taken out in the name of the university, the faculty members do not receive any royalties.

There is some indication that this situation leads to informal arrangements in which firms and faculty enter into oral agreements that the firms will contribute to support faculty research at the national universities and -- in at least some cases -- make only informally agreed payments to the faculty, and the faculty members in turn will patent their discoveries

in their own names with the firm being granted a license to use the discovery. At present there is no way to determine the nature and extent of these types of arrangements since they do not have to be disclosed as public information; however, it is believed that they are quite common in practice. Such informal arrangements have the potential for somewhat alleviating the complex legal situation which creates barriers for collaboration between firms and university scientists. They do so, however, at considerable risk to the parties involved and with less efficiency than the American system of overt shared royalties. It is also reported that the implicit tax rate on overt research funding for faculty is very high -- on the order of one half by the time the funds get from the Ministry of Finance to the intended recipient, with other funds going to the university as a whole. Furthermore, the most eminent Japanese academic scientists are reported to be the most inhibited about entering into informal agreements or undertaking any arrangements under which they must delay reporting commercially valuable results until the patent application is filed. Therefore, even though university research can be commissioned relatively cheaply in Japan, major firms demonstrate a marked tendency to enter into collaborative research with American universities and their faculty members and to allocate the majority of their external funding to such research.'

An alternative view is that university faculty members would lose honor if they were directly involved with firms and that intermediating quasi-non-governmental organizations (quangos in British terminology) can foster technology transfer that would otherwise be impossible in Japan. There are three such organizations in the biotech area: the Japan Health Sciences Foundation sponsored by the MHW, the Japan Biotechnology Association sponsored by MITI, and the Society for Techno-innovation of Agriculture, Forestry, and Fisheries sponsored by the MAFF. The JHSF concentrates of pharmaceuticals and health

care, the JBA on synthesis of bulk chemicals and on processing technologies, and STAFF on agricultural applications. Each quango has a membership of 150-200 firms which fund cooperative research among universities, national research institutes, firms, and foreign scientists and institutions. These grants may encourage some interdisciplinary work, although the focus of each of the quangos is fairly narrow.

By way of example, the JHSF was established in 1986 and had a budget of Y2 billion in fiscal 1990 which has risen to Y4.4 billion in the current fiscal year 1993. These funds are used to promote research in four principal areas: development of biotechnology, development of glycotechnology and its applications to pharmaceuticals and medicine, evaluation of and advances in medical materials, and elucidation of biological host defense mechanisms. Well over half of the budget is spent on joint research programs, primarily domestic but with a small internationa! component. In addition, the JHSF plays a role in evaluating and formulating regulations and standards, providing research resources, and promoting technology transfer through symposia and conferences as well as printed and electronic information services.

The respondents do not agree on the effectiveness of these quangos: At one extreme they are viewed as an effective means of dealing with cultural and political inhibitions that prevent Japanese academics from directly dealing with firms. At the other extreme, they are viewed as off-budget means for the sponsoring ministries to tax their regulated firms for the benefit of favored national universities and institutes with a large part of the firms' contributions being returned to them to fund research done at the firms related to the quango's goals. Sorting out these divergent viewpoints provides a real challenge for empirical researchers.

Given the importance of personal relationships, the relationships between professor

and former students employed by firms may be an important channel for technology transfer in general and for creating the sort of special relationships mentioned above. These relationship are not necessarily of the dissertation chairman/Ph.D. nature, however. Some respondents indicate that firms find that newly minted Ph.D.s are often of the nature of aspiring academics who have been unable to obtain an academic position. Firms are reported instead to prefer to hire as entry scientists those with Masters degrees -- more equivalent to American All-But-Dissertation (ABD) scientists. These scientists then receive extensive on-the-job training which in some cases produces work which is submitted as a thesis for the Ph.D. degree years after leaving the university.

Nature of Bioscience in Japanese Universities

While some respondents were critical of the quality of Japanese bio-science, the preponderance of opinion reflected a guardedly positive opinion. Japanese academics are said to be narrowly focussed but very deep in understanding and mastery of their particular areas. Some respondents attribute the narrow/deep characterization to the personnel practices of the national universities. They described a doctoral student making his/her career by attaching himself/herself to a particular professor who will serve as mentor and patron, obtaining the student a job in the university. The student's training from then on is concentrated on mastering the mentor's area(s) of interest; so they lack the advantage of forced exposure to a range of other areas and viewpoints as would be typical in the American system.

The research-funding system discussed above was also frequently cited as narrowing the focus of Japanese bio-scientists instead of forcing them to interact with those from other departments and disciplines and to put their research into a broader context as part of a

competitive proposal process. While some respondents referred to impressive results from concentrated work on a particular topic by an eminent professor and his associates, another spoke eloquently of a sense of loneliness for Japanese professors because of a lack of unifying purpose. The latter respondent also observed that Japanese professors publish relatively little of their research results compared to professors working in the same areas in other countries. We were not able to resolve the accuracy or significance of this observation which was attributed to cultural norms as well as obvious differences in evaluative structures and incentives. If the observation is correct, then this would mean that our publication-based science data set under-represents the strength of Japanese scientists relative to those from other countries -- the opposite problem from the usual reaction to our results.

One respondent cautions against overstressing the narrow/deep characterization. He observes that Japan does have a few very creative bio-scientists capable of making breakthrough research and not simply following a next logical discovery. While their numbers may be small, those sorts of scientists are rare anywhere. Even one of the severest critics of the national university system argues that Japan lags the U.S. considerably less in bio-science than in its commercialization.

I.B. Capital Market Imperfections

A number of respondents report that even apparent venture firms in our data set (e.g., Hayashibara Biochemical and Nippon Gene) are more accurately characterized as continuations of and subunits of long existing family firms which provided their financing rather than new biotechnology firms (NBFs) comparable to the usual American form. While there may be special deterrents to starting biotech firms for reasons discussed in

sections I.A. above and I.C. below, we note that there are about 1.3 million corporations active in Japan, which is nearly three quarters the American rate of 3.5 million after adjustment for population differences. While the overall rate is lower, clearly some Japanese are willing and able to start businesses.

Respondents attribute the capital market inhibitions to creation of venture firms as due to the interaction of four distinct but reinforcing attributes of these markets: the lack of American-style venture capital firms, the lack of IPOs for firms without an established record of substantial profitability, the fact that the keiretsu will not buy small firms unless at distress prices, and the lack of bank financing for risky ventures without collateral.

About 120 venture capital firms exist in Japan, but they are all focussed in bringing established small and medium sized companies to the point of making the IPO. These firms have assets of about $5.5 billion (as of May 1993) with another $2.5 billion raised through sponsored partnerships. The largest of these venture capital firms by far is Japan Associated Finance Co., Ltd. (JAFCO) with about $2 billion under management. However, there appear to be no U.S. style venture capital firms which will finance a new biotech firm located in Japan for the first ten years or so before the firm either makes an IPO or is sold profitably to a large firm."

The lack of venture capital firms financing start-up companies does not appear to reflect a shorter horizon on the part of venture capital firms in Japan. In the United States, too, a typical venture capital firm is looking to something like a ten year relationship. The difference is that American firms can rely on making an IPO or profitable sale at a much earlier stage of development than in Japan. In effect, the more complete American capital markets allow the venture capital firms to act farsighted because they know that once substantial research and development results have been obtained, their investments can be

sold to other investors who will discount the future profitability to the present."

The Japanese capital markets have not to date accepted IPOs for firms which do not have a track record of proven profitability. The second section of the Tokyo Stock Exchange for smaller companies requires a minimum before tax profit of Y400 million ($3.6 million). On the over-the-counter (OTC) market JASDAQ which began on October 23, 1991, the smallest before tax profit reported by a firm making an IPO was Y258 million ($2.3 million)." While there may emerge in Japan an IPO market which could take biotech venture firms public before profitability is achieved the pressure is obviously low because such firms practically do not exist since there were no venture capital firms financing start-ups in the golden age for biotech during the 1980s. In this way we see a vicious circle of no financing for start-ups and no start-ups to lead the way as with the Genentech IPO in the U.S. in 1982.

In principle, the large groups of Japanese companies (the keiretsus) could substitute for an effective IPO market by bidding vigorously for the winners of an R&D race among independent venture firms. Indeed, this is a common outcome of successful venture capital investments in the United States. For reasons that are not clear to the authors, none of the respondents reported any such bidding and indeed indicated that if firms were bought, it would be only at distress prices.[13] Thus, one alternative means of fostering bio-ventures in Japan is eliminated. A tantalizing possibility is whether Japanese venture firms could make a successful IPO in the United States following a British precedent.

Respondents also point to a lack of uncollateralized bank financing for risky ventures as a deterrent to growth in new enterprises, in effect requiring all growth to be self-financed. While this would seem to stretch out the period of growth relative to other countries, it seems unlikely to us that bank financing would anywhere be a real alternative to venture

capital firms.

Japanese venture capital firms such as JAFCO have concentrated on financing American and European bioventures and also on their strategic alliances with Japanese firms through joint ventures and other mechanisms.

I.C. Cultural Barriers to Entrepreneurialism and Incentives to Individuals

As alluded to above, many respondents commented on the differential status or honor given to the professor relative to the individual involved in commerce. This social distance was compounded at least through the early eighties by the radical or Marxist orientation of many students and some faculty in the major universities.

Several respondents also believed that business people do not want to reveal too much to university faculty because the faculty highly value open communication and may not keep their findings confidential until patent protection of intellectual property can be obtained.

One respondent went so far as to say that firms looked to the universities primarily to supply good Japanese brains. The demand for Japanese scientists, rather than scientists trained elsewhere, probably stems in part from the value of the social network formed in the universities, providing early and privileged access to new discoveries at the university where the scientist was trained. But there also may be an element of Japanese discrimination against *gaijin* (foreigners) that leads firms to avoid hiring non-Japanese whether because of prejudice or for fear that the foreigners will ultimately choose to leave Japan and the firm.

Other respondents suggested that the faculty's desire for honor and only covert relations with firms reduced the firms' costs of obtaining Japanese academic research -- that

providing honor through creating foundations and institutes and perhaps making some informally agreed payments cost only a tenth as much as explicit payments for academic researchers in the U.S. and Europe." On retirement from the university, a professor who has maintained a close relationship with a company can become a consultant to the firm or a member of its board -- but not an employee -- without losing honor.

A second cultural factor which inhibits the creation of bio-venture firms in Japan is the national career ideal of working for a single employer until retirement. Reinforcing this factor is the importance of social contacts within organizations which make it hard for a newcomer to enter a firm from outside. Thus, leaving a firm or university to start a new firm involves disrupting that firm-based or university-based social network and possibly labeling oneself as different if not unstable. If the firms succeeds, then there is probably a net gain on these dimensions to the individual, but biotechnology is inherently risky with the prizes from a search for a new drug mainly going to whomever gets there first and can raise enough capital along the way to keep the company afloat until there are some profits. If the new venture ultimately fails, the founding scientists' career pattern is disrupted and it may be very hard to find new lifetime employment or even to establish the social network within a new organization to be successful. Since lifetime employment is itself a culturally endorsed risk-avoidance strategy, the downside risk of starting a new firm must seem enormous compared to scientists used to the American system of employment often said to be based on the revolving door."

Compounding the difficulties of the potential venture firm are the general difficulties with entry of new firms into the Japanese market place. These barriers to entry are well known and have been the subject of numerous international trade negotiations. They work for natives in much the same way as for foreigners and must deter entry in bio-industry as

well. On the other hand, since the biggest returns are in the highly regulated pharmaceutical industry where track record and personal ties play a major role in the United States as well, this factor probably should not be unduly stressed.

A cultural preference for group or team activity as opposed to the American ideal of rugged individualism may contribute to the relative evenness of allocation of funds within ranks at the national universities and the aversion to differential rewards for differential performance. The same cultural preference may restrain vigorous national competitions for scientific grants and the associated culture of scientific entrepreneurship which seems to be a short step away from starting a new firm in the United States. Scientists in both countries, however, rely on the same mode of scientific production: the research team based in the laboratory of a distinguished senior scientist. It remains for us to see how these teams differ.

A final cultural trend in Japan is its eclecticism. One respondent noted a tradition of Japan's sending people to other countries to learn their best practices starting 1000 years ago with China. While the success of Japan in judging the best in foreign economies and cultures and incorporating it at home -- often in improved form -- is legendary, it may also lead to overestimation of foreign superiority in areas of innovation. We saw that Japanese firms and investors were eager to support the innovative work done in America but less willing to support and rely on the unique breakthroughs of Japan's own scientists. Sometimes Japanese firms ended up licensing applied technologies from the United States that were based on basic Japanese discoveries -- just the reverse of many American's fear of another VCR!

II. Subunits of Existing Firms as Alternatives to New Firms in Japan

Hundreds of previously existing Japanese firms have established new biotech subunits or activities (NBSs) dealing with the commercialization of one or more aspects of bioscience. A number of respondents believe that to date these activities have lagged behind and built upon those in the United States and Europe. As explained in some detail above, collaborations with Japanese academic scientists have been less prominent than those with foreign scientists, depriving these NBSs of a potential source of innovative, competitive edge.16 These NBSs are primarily located, like the most important academic scientists, in the Osaka/Kyoto and Tokyo/Tsukuba areas. However, as indicated in Figure 1, there are significant numbers of NBSs located in other areas.

In comparison to the American industry, M.D.s are rare among the scientists in the pharmaceutical companies, with Ph.D.s more common. In part this reflects the fact that M.D.s are not simply the terminal degree in medical school, but require more research work, equivalent to a research Ph.D., and carry more status.

Some respondents believe that large Japanese firms have been dabbling in biotechnology rather than really committing major resources to the field. One explanation for this is the importance of seniority to achieving CEO or senior management status in Japan. As a result the top executives may not really be able to understand the value of the revolution in bio-science and its commercial implications. This is seen as different not only from U.S. venture firms but also some large American firms where CEOs in their forties are not uncommon.

This view seems inconsistent with the fact that a number of NBSs in Japan are deriving major revenues from biotechnology products, but may reflect an uneveness in the

level of committment.

III. Implications **for Further Work and Summary**

In ongoing work, we are analyzing diffusion of bioscience in Japan and collaborations among Japanese scientists and among Japanese and foreign scientists. We are using our understanding of the barriers to new biotech firms in Japan to inform our analysis of births and success of new biotech enterprises in Japan with a focus on comparing the roles of NBSs in Japan and the United States. These subunits appeared earlier and in larger numbers in Japan than in the United States.

In lieu of our own summary, we present here in its stead a comparative table (Figure 2) which was prepared to guide our discussions by Dr. Ryuzo Sadahiro, Executive Director of the Pharmaceuticals Group, Chugai Pharmaceutical Co., Ltd. We are endebted to him for his generous permission to use this exhibit. We do not believe that every respondent would agree with all the particulars outlined on Dr. Sadahiro's table, but we found it very useful in analyticaI1y displaying the majority of our respondents' views on the issues with which he deals.

Appendix A
List of Interviews, Respondents, Principle Questions

Principle Questions:

1. Our quantitative measures based on gene sequence discoveries and citations indicate that, after a short lag, Japanese scientists have been quite productive, accounting for 15-20 percent of the basic science compared to say 45 percent in the U.S. Others say that Japan lags behind. How would you characterize Japanese biotech discoveries? Can you help resolve this paradox?
2. Is there a uniquely Japanese focus to bioscience?
   a. Do firms encourage pursuing it? Does government?
3. What is the incentive system in Japan for bio-science?
   a. Has commercialization changed that?
   b. What has been the government role? Industry role?
   c. What are the sources of funding for basic research?
4. Where are Japanese biotech scientists typically trained?
   a. What is the role of foreign scientists? (postdocs? visitors?)
      Do universities recruit from abroad? Firms?
5. What is(are) the typical career path(s) of Japanese scientists? Postdocs? Foreign postings?
6. What is the role of the institutes? How are they linked to universities? Specific firms? Have many new institutes been created? By what organizations?
7. In the U.S., perhaps because the country is so large and scientists start new firms near their homes, we can use geography to link firms and scientists; how can we link firms to scientists in Japan?

8. What is the geographic nature of bio-science and industry in Japan? Where is it localized?

9. Is there a uniquely Japanese focus to the biotech industry?

10. Our sources on Japanese biotech are limited in the U.S. Is there a good book or information service (in Japanese is O.K.) to help us locate all biotech industry in Japan?

Interviews and Respondents:

Mr. Kuniho Sawamoto, Director General; Mr. Zenta Nakajima, Deputy Director; Mr. Hiroo Taguchi, Chief Manager-Research Division I

Institute for Monetary and Economic Studies, Bank of Japan, Tokyo [11/30/93--0: 1 5

Dr. Yoshio Suzuki, Chief Counselor; Mr. Takuma Takahashi, General Manager-Business & Management Research Department

Nomura Research Institute, Ltd., Tokyo [12/2/93--2:OO]

Dr. Itaru Watanabe, Professor Emeritus of Keio University

Corporate Adviser, Yakult Honsha Co., Ltd., Tokyo

Vice President, Science Council of Japan, Tokyo

Chairman, Society for Techno-Innovation of Agriculture, Forestry, and Fisheries, Tokyo

[Ms. Nami Matsuko of the Business & Management Research Department, Nomura Research Institute, Ltd., served as translator and elucidated several points--12/3/93--2:00]

Yoshihiro Ohtaki, Ph.D.. General Manager; Mr. Hironori Hozoji, Assistant Manager

International Investment Evaluation Department, Japan Associated Finance Co., Ltd. (JAFCO), Tokyo [12/3/93--1:45]

Yukio Sugino, Ph.D., Member of the Board

Takeda Chemical Industries, Ltd., Osaka [12/6/93--2:OO]

Norio Masaki, D.Sc., Associate Professor

Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto [12/7/93--1:15]

Lawrence J. Marnett, Ph.D., Mary Geddes Stableman Professor of Cancer Research; Director, A.B. Hancock Memorial Laboratory; Director of Research, Vanderbilt Cancer Center

Vanderbilt University Medical Center, Nashville, Tennessee, USA [participant in Kyoto biotechnology seminar--12/8/93--0:30]

Mr. Mitsuru Miyata, Editor-in-Chief, Nikkei Biotechnology; Ms. Ikuko Uchiyama, Staff Editor, Nikkei Biotechnology; Ms. Hiromi Niwa, Special Project Office

Nikkei Business Publications, Inc., Tokyo [12/9/93--2:15]

Dr. Takaji Ishimaru, Senior Managing Director; Mr. Hideo Nagoshi, Director, International Affairs

Japan Health Sciences Foundation, Tokyo [12/9/93--2:30]

Dr. Ryuzo Sadahiro, Executive Director

Pharmaceuticals Group, Chugai Pharmaceutical Co., Ltd., Tokyo [Mr. Takuma Takahashi of Nomura Research Institute accompanied us and made a number of significant points--12/10/93--1:45]

FOOTNOTES

1. Cohen, Chang, Boyer, and Helling (1973).

2. This technology is also identified by the terms monoclonal antibodies, MABs, or hybridomas.

3. For details, see the Data Appendix to Zucker, Darby, and Brewer (1994).

4. The Japan Health Sciences Foundation sponsored by the Ministry of Health and Welfare (and discussed below) has reportedly intervened to coordinate division of firm research and production programs so as to avoid competitive rivalry for the same market.

5. The biotechnology industry has been driven by advances in the biological sciences, particularly in fields such as genetic engineering and cell hybridization. During the industry's genesis in the late 1970s and 1980s a very important measure of research success is the discovery of nucleotide sequences that determine the characteristics of proteins and other molecules. In our science data set, GenBank was used to identify ail articles reporting gene sequence discoveries up to 1990 by which time the rDNA technology had devolved from high to routine science.

As outlined above in the text, we identified worldwide 337 leading researchers whom we termed "stars" on the basis of the number of sequence discoveries reported up to 1990 (for 315 individuals) and on frequency of publication of articles reporting gene sequences (which added 22 additional individuals). These 337 stars were listed as authors on 4,315 distinct articles in major journals. All of these articles were collected by hand and institutional affiliation and location were noted for each author (whether star or one of their 7,718 collaborators) on each article. We use the institutional affiliations to locate scientists: Generally a scientist is located for our analysis at the institution given in the last publication; however, scientists are said to be "born" in the year and at the institution of their first publication. The resulting authorship data file containing stars and collaborators consisted of 20,669 observations, approximately 5 authors for each of the 4,315 published articles. We have also collected data for 1982, 1987, and 1992, on the total number of citations to each of our 4,315 published articles listed in the Institute for Scientific Information's Science Citation Index.

A second screen was developed to focus on those scientists who were actively working at a particular time: a star or collaborator is **active** in any year in which he or she has published three or more articles in the three-year period ending with that year. This is a substantial screen: Only 13-l of the 213 stars who ever published in the U.S. are ever active in the U.S. while only 12.5 percent (498 out of 3983) of the collaborators who ever published in the U.S. are ever active in the U.S.: 50 of the 65 stars who ever published in Japan are ever active in Japan while only 16.6 percent (242 out of 1462) collaborators who ever published in Japan are ever active in Japan. In empirical analysis scientists are located by the affiliations in their most recent previous article. Only these active stars and collaborators are plotted in the maps presented below.

6. We particularly have in mind such factors as the American tort liability system which may make it much safer to do this research only in a stand-alone new biotech firm rather than

an existing firm with “deep pockets” (substantial assets).

7. In Japanese universities, the ranks assistant, assistant professor, and professor correspond to assistant professor, associate professor, and professor in American universities.

8. In future empirical work, our scientist data base may shed some light on both the frequency and nature of moves by Japan’s bio-scientists, although only for the most productive scientists and their coauthors.

9. One exception to the idea that Japanese academic-firm collaborations are relatively inexpensive to the firms involves establishing mini-grant programs. American firms give small grants -- perhaps $10,000 -- to young academic scientists to establish a relationship and screen for good, productive candidates for major grants. Because of the fixed costs of making an ear-marked grant through the Ministry of Finance down to the university or the fixed risks of under-the-table arrangements, this is not a viable opportunity in Japan.

10. These firms are sometimes involved with financing start-ups abroad as discussed below.

11. An alternative view of the Japanese situation is that the lack of start-up funding does not reflect incompleteness of the capital markets. Such funding vehicles, on this view, are not necessary in Japan because the keiretsu provide an efficient funding mechanism for new activities in a way which reduces shareholder-manager agency problems. On this view, the numerous American venture capital firms are due to American regulatory restrictions. We do not believe that this story holds up, however, since the banking regulatory system in Japan is even more restrictive than in the United States, there are no regulations preventing large American firms from establishing new sub-units to pursue new technologies, and venture capital firms funding startups was also a feature of the incubation of the U.S. electronics industry for which there were no significant liability issues (see footnote 6 above).

12. JASDAQ suffered from some early scandals which may reinforce caution in standards for current IPOs.

13. Stock prices of the major conglomerates do seem to react to the reputed success of their biotech subunits. On the other hand even remarkably profitable NBSs are small relative to the core businesses of their parents. For example, Kirin Brewery reportedly earned Y23 billion last year on two very successful pharmaceutical products, but stock prices declined with overall sales of beer. We believe that these biotech subunits may play a vital role in determining a firm’s long-run success as the Japanese economy transforms from medium- to high-tech production in the face of new competition in the globalized economy. Nonetheless, we are puzzled by the general belief by Japanese experts that the value of such subunits would not get reflected in competitive bids for successful bio-ventures.

14. Recall, however, that Japanese industrialists appear to prefer dealing with American academic researchers so there may be significant elements of the cost-benefit relationship omitted from the simple cost comparison.

15. Note that the two university systems are similar in their reliance on an initial screening period followed by lifetime tenure guaranteed by the university. However, the practice appears to be different. U.S. faculty more often move -- with life tenure -- to other universities, and more often will resign tenured university employment for untenured opportunities in firms or research institutes. Perhaps significantly, in America only tenured university professors can take a leave of absence -- rather than being forced to resign previous employment -- when they accept appointment as an official of the federal government.

16. Also, the scientific activity did lag a bit in development compared to the U.S., at least in the genetic sequence area (refer again to footnote 5 for discussion of our bioscience data base).

17. The discussion of biotechnology occurred in a much longer discussion of the Japanese economy.

Table 1 -- Comparison of Bioscience and Its Commercialization
United States and Japan

Description	Absolute numbers		Percentage distribution	
	U.S.	Japan	U.S.	Japan
Stars"				
Universities	163	49	76.5	75.4
Research Institutes/Hospitals	44	15	20.7	23.1
Firms	6	1	2.8	1.5
All"	213	65	100.0	100.0
Collaborators"				
Universities	2887	1122	72.5	76.7
Research Institutes/Hospitals	703	261	17.7	17.9
Firms	390	79	9.8	5.4
All	3983	1462	100.0	100.0
Bioindustry				
New Biotech Firms	511	5	68.0	2.0
All Enterprises	751	246	100.0	100.0
Enterprise/Star	3.5	3.8	n/a	n/a

Notes: **a. Stars and collaborators are located here by the institutional affiliation on their first publication in a particular country Worldwide, about one third of the stars publish in more than one country.**

b. For U.S. collaborators, "all" includes a few cases of dual affiliations not separately classified.

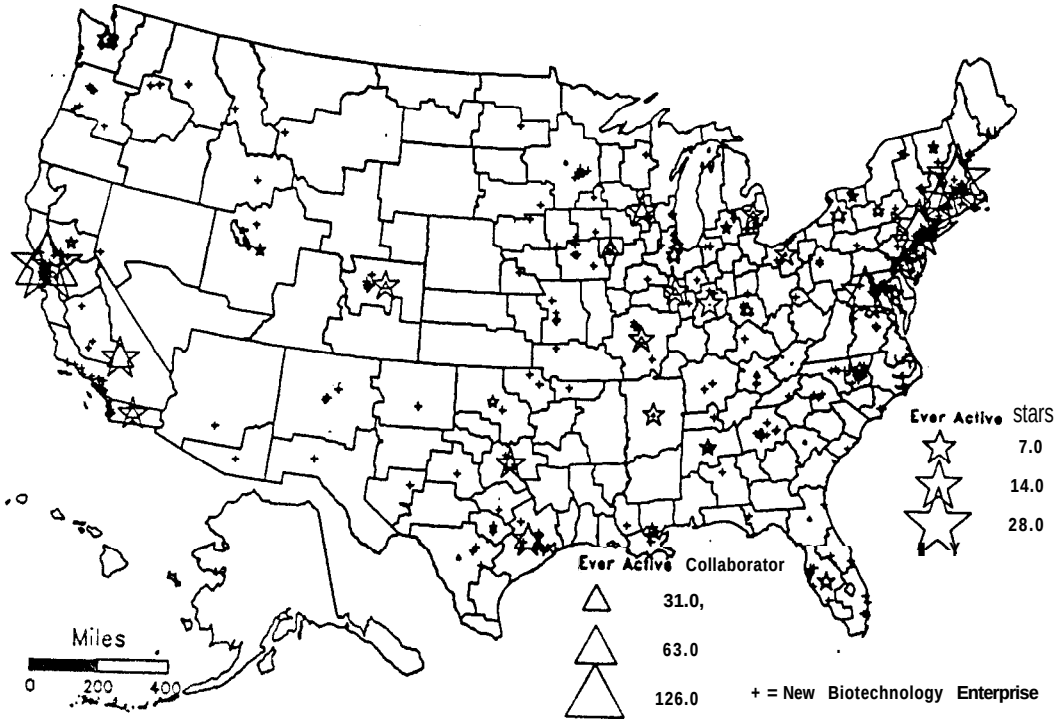
Table 2
Definitions of Functional Economic Areas for Japan

Region Name	Included Prefectures
Hokkaido	Hokkaido
Northern Honshu	Akita, Aomori, Fukushima, Iwate, Miyagi, Niigata, Yamagata
Tokyo area-immediate”	Chiba, Kanagawa, Saitama, Tokyo
Tokyo area-ring”	Gumma, Ibaraki, Shizuoka, Tochigi, Yamanashi
West-Central Honshu	Aichi, Fukui, Gifu, Ishikawa, Mie
Kansai Area	Hyogo, Kyoto, Nara, Osaka, Shiga, Wakayama
Western Honshu	Hiroshima, Okayama, Shimane, Tottori, Yamaguchi
Shikoku	Ehime, Kagawa, Koichi, Tokushima
Kyushu & Nansei Shoto Islands	Fukuoka, Kagoshima, Kumamoto, Miyazaki, Nagasaki, Oita, Okinawa, Saga

Note: a. Tokyo area-immediate and Tokyo area-ring are the two parts of the same Tokyo Functional Economic Area; however, for some analyses it is useful to separate the central area from the outer ring.

Figure 1

Active Stars, Collaborators and New Biotechnology Enterprises by BEA as of 1990 in the US



Active Stars, Collaborators and New Biotechnology Enterprises by Prefectures as of 1990 in Japan

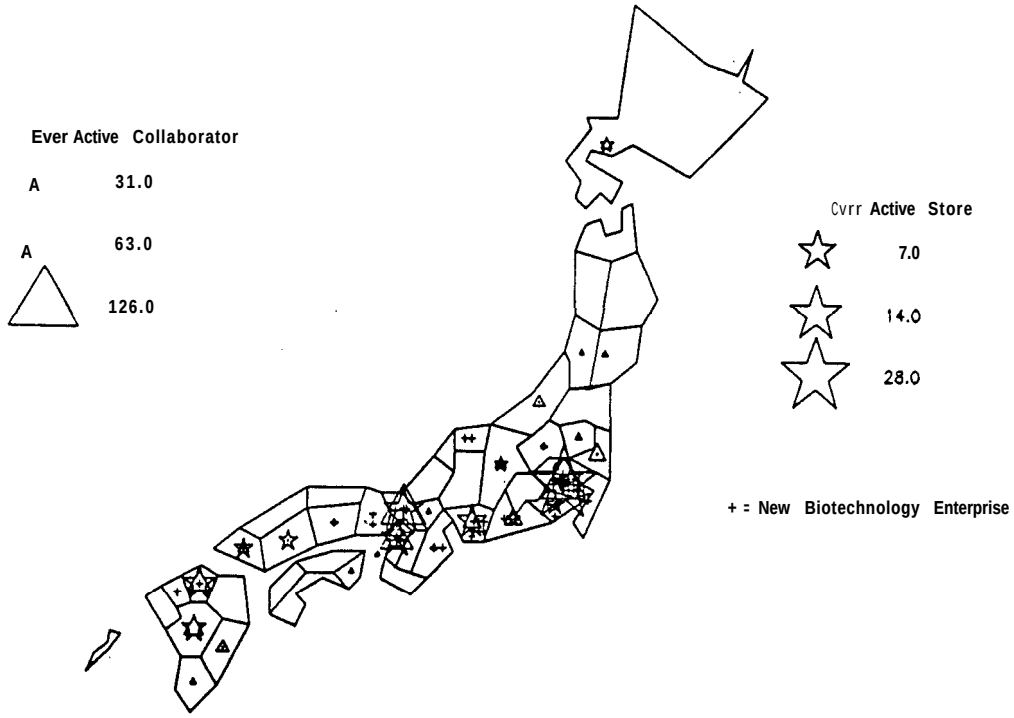


Figure 2

- Comparative Analysis of Factors Related to Biotechnology Enterprise between United Stare and Japan

		US	Japan
Academic activities			
	national/state and private univ	both strong	mostly national
	autonomy	strong	weak
	government control	modest	influential
	scientist mobility MD univ to univ	high	low
	univ to company	high	very rare
	PhD univ to univ	high	not frequent
	univ to company	high (any size OK)	high (mostly big company)
	support by company	expensive	inexpensive
	by venture capitalist	frequent	so far zero
	scientist entrepreneurship	aggressive, rewarded	essentially not allowed
	innovative mind	aggressive	
company			
	size	large to small	large to middle
	top management	relatively not age related	markedly age related
	scientist mobility	high	very low
	decision making	individually led	group consensus
	challenge spirit	risk taking	modest
Society			
	bank/venture capitalist	risk taking/frontier technology	don't take risk/asset based
	popular view	appreciate small company	appreciate large company only
	commerce law	relatively &regulated	strongly need deregulation
	research cost(gvmt:company)	45:55	27%
Patent			
	priority	date of the invention (made only in US)	date of the submission
	claim	broad(doctrine of equivalency)	limited
	number of bio-pharm in 199 1	140	18

Source: Ryuzo Sadahiro, Ph.D., Executive Director, Pharmaceuticals Group, Chugai Pharmaceutical Co., Ltd., Tokyo