NBER WORKING PAPER SERIES

STAR SCIENTISTS, INSTITUTIONS, AND THE ENTRY OF JAPANESE BIOTECHNOLOGY ENTERPRISES

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Working Paper 5795

NATIONAL BUREAU OF ECONOMIC RESEARCH
1050 Massachusetts Avenue
Cambridge, MA 02138
October 1996

This research has been supported by grants from the University of California's Pacific Rim Research Program, the Alfred P. Sloan Foundation through the NBER Research Program on Industrial Technology and Productivity, the National Science Foundation (SES 9012925), and the University of California Systemwide Biotechnology Research and Education Program. We acknowledge very useful comments from Jeff Armstrong, Takaji Ishimaru, Sam Kortum, Robert Lipsey, Scott Stern, Maximo Torero, Kazuo Ueda, and participants in presentations at the Pacific Rim Allied Economics Associations' 2nd Biennial Conference, Hong Kong, January 1996, the NBER Japan Project meetings, May 1996, and the NBER Science & Technology Policy Meeting, August 1996. Benedikt Stefansson and Akio Tagawa were primarily responsible for developing the Japanese firm data set and conducting the analysis. We are indebted to a remarkably talented team of post-doctoral fellows Zhong Deng, Julia Liebeskind, and Yusheng Peng and research assistants Paul J. Alapat, Jeff Armstrong, Cherie Barba, Rajesh Chakrabarti, Lynda J. Kim, Kerry Knight, Edmundo Murrugara, Amalya Oliver, Alan Paul, Jane Ren, Erika Rick, Benedikt Stefansson, Yui Suzuki, Akio Tagawa, Maximo Torero, Alan Wang, and Mavis Wu. This paper is part of NBER's research program in Productivity. Any opinions expressed are those of the authors and not those of the National Bureau of Economic Research.

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ABSTRACT

Advance of science and its commercial applications are in a close, symbiotic relationship in the U.S. biotechnology industry. Comparing Japan and the U.S., the structure of the science appears broadly similar, but the organization of the biotechnology industry is quite dissimilar. In the U.S., some 77 percent of new biotechnology enterprises (NBEs) were dedicated new biotechnology firms (NBFs) started for this purpose while 88 percent of Japanese biotech firms in our data base were subunits of existing firms (NBSs). We report pooled poisson regression estimates of the relation of NBE births in Japan to top-producing "star" scientists and other variables. While a similar process is at work in Japan and America, stars in Japan induce entry of significantly fewer NBEs than in the U.S. and preexisting economic activity plays a greater role. We find no such significant difference for entry of keiretsu-member and nonmember firms within Japan. We relate the significant Japan-U.S. differences to Japan's relatively compact geography and institutional differences between the higher-education and research funding systems, the venture-capital and IPO markets, cultural characteristics and incentive systems which impact scientists' entrepreneurialism, and tort-liability exposures. The relative importance of these factors and whether differences in organization of biotechnology result in substantial differences in productivity and international competitiveness are issues for future research.

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STAR SCIENTISTS, INSTITUTIONS, AND THE ENTRY OF JAPANESE BIOTECHNOLOGY ENTERPRISES

by Michael R. Darby and Lynne G. Zucker

The world's research-based economies -- preeminently the U.S., Japan, and northwestern Europe -- derive their very high and growing standards of living from their ability to create scientific innovations and exploit them commercially. Since 1975, biotechnology has provided an archetypal example of breakthroughs in basic science creating technological opportunities which drive the transformation of existing industries and the creation of new ones. With our associates, we have examined the linkages between bioscientific advance and commercial applications in the United States in a series of papers reviewed in Zucker and Darby (1996). This work validates the importance of "**star**" scientists -- defined as those discovering more than 40 genetic sequences and/or authoring 20 or more articles reporting such discoveries up through early 1990 -- in determining where and when firms begin to use biotechnology and which of them are most successful.[1] There are 327 of these stars worldwide, of whom 207 worked in the U.S. and 52 in Japan, with the U.K. next largest with 30 stars.[2] We identify a star scientist as "**active**" at a particular place and time if he or she has written three or more articles in this and the two preceding years with location determined by the last affiliation given for the star.

Since we have an internationally unbiased census of genetic-sequence discoveries used to define our stars, it is immediately attractive to see whether they play such a key role in the commercialization of biotechnology in Japan. There are a number of geographic, institutional, and cultural differences between the two countries which suggest that the process will be characterized by interesting differences. In this paper, we consider those underlying differences and their potential effects on the process of entry of firms into biotechnology, examine the empirical determinants of entry in Japan and whether the process differs between members and non-members of keiretsus, and make an initial comparison of the effects of the principal determinants between Japan and the U.S. While we find little evidence of significantly different processes between Japanese keiretsu members and non-members, we do find that stars have a significantly weaker (but still significantly positive) influence on entry in Japan than they do in the United States, consistent with the institutional differences in the two countries.

I. Structural Differences between Japan and the U.S.

Over 1993-1995 we did fieldwork involving interviews with over 50 university and research-institute scientists, executives and scientists at Japanese biotech and financial firms, and government officials. Our respondents identified a number of structural differences between Japan and the United States, differences which they primarily saw as impediments on the Japanese side explaining the lag of their industry behind that in the U.S. (A particularly well organized version of the consensus Japanese view was provided for use in our discussions by one of our respondents and appears as Appendix Table A.) From our reading and observations, we have identified several other factors that may affect the process of entry. We shall discuss what appear to be the key underlying differences after summarizing what is known about the industry and its scientific base in the two countries.

Science Base and Its Commercial Application

As indicated previously, there is a unified data base (GenBank) reporting all genetic-sequence discoveries. The GenBank accession number is normally required by editors as a condition of publication, and scientific and commercial incentives for demonstrated priority ensure that scientists promptly report their discoveries.[3] There is no such universe to provide a frame for identifying the new biotechnology enterprises ("**NBEs**") commercially applying the breakthroughs in recombinant DNA and other basic technologies. In our terminology, NBEs are either dedicated, newly-formed new biotechnology firms ("**NBFs**") or subsidiaries or other subunits of pre-existing firms ("**NBSs**"). Depending on the directory or directories a researcher uses, for example, there are between 500 and perhaps 2500 NBEs in the U.S. alone. Using a more stringent definition of whether the enterprise is actually involved in using the breakthrough technologies, Zucker, Darby, and Brewer (1997) identified 751 NBE births from 1976 to April 1990.

We have attempted to apply a similar definition to NBEs in Japan, and have identified 277 NBEs either born or beginning use of biotechnology between 1975 and 1989 inclusive as described in Data Appendix A.1. Of these, only 12.3 percent are NBFs compared to 77.3 percent in the U.S.[4] We are not confident that the definitions are strictly comparable, nor is a simple count of NBEs our preferred measure of the total activity in the area. Unfortunately, however, many NBFs are nonpublic and report very little information while most NBSs do not report information with sufficient detail to distinguish between activities involving traditional technologies and the new biotechnologies.

Figures 1 and 2 plot the number of stars ever active and the number of NBEs born up to early 1990 by the Bureau of Economic Analysis functional economic areas ("**BEAs**") for the U.S. and by prefectures for Japan. We see in both the U.S. and Japan that there is a high correlation in the locations of NBEs and star scientists. Of course, this apparent correlation cannot prove causation since it may reflect the effects on each of third factors such as population or employment distribution which might determine where both stars and NBEs are located.

Geography

The U.S. is characterized by a rich variety of patterns across the BEAs: Some large areas have great universities and others do not, the same is true for medium and smaller regions. Nor do all great universities, even those among the strongest in the biosciences have similar numbers of star scientists as we define them. All together, the U.S. geography provides us with sufficient variation to characterize as a natural experiment. In Japan, people, firms, and universities are much more concentrated, particularly in the Tokyo area and around Osaka and Kyoto in the Kansai. This makes it more difficult statistically to distinguish the effects of stars and other measures of intellectual human capital from measures of economic activity. Fortunately, we do have information not only on where stars have been active but also when and thus are able to draw some conclusions where otherwise it might be impossible.

The simple map in Figure 2 illustrates a substantive as well as statistical way in which Japan's geography might result in different impacts of local stars on regional development: With the population and economy concentrated like a dumbbell along the Tokaido shinkansen line, few stars are located more than three hours from some 90 percent of the existing firms. Thus, it is conceivable that Kyoto's scientists could contribute actively to commercial applications of biotechnology at NBEs located in Tokyo and vice versa. These issues are particularly important in explaining entry into biotechnology. Once we know the firms which are actively using the new technology, we can look at specific linkages between stars and NBEs to predict the success of those NBEs (see Zucker, Darby, and Armstrong 1994), but that is the subject of another paper.

University Structure, Policies, and Culture

Japanese experts in industry, academe, and government all emphasize aspects of the Japanese national university system as playing an important role in the lag of Japanese biotechnology behind that in the U.S. (see, e.g.,Zucker and Darby 1994). In part, they argue that the university system reflected generally poor support for basic research and placed greater stress on an explicitly "market-driven rationale, which skewed the interest into electronics and computers fields, or into the heavy 'strategic' industries of the 1960s and 70s -- steel, materials, automotives, and chemicals. When genetic engineering breakthroughs appeared suddenly on Japan's borders, there were literally no researchers in Japan working in genetic engineering." (Yoriko Kishimoto 1989, pp. 41-42.)

Such concerns can be overdone, however, since Japan has progressed rapidly in both bioscience and its commercialization and by 1990 ranked second only to the U.S. Our concern in this paper is not so much why Japan's production of star scientists is both smaller (proportionately) and later than in the U.S.,[5] but whether and why Japan systematically made less of this smaller endowment than was the case in the U.S. On this latter issue, much concern is expressed that biotechnology without America's scientist-entrepreneurs is like Hamlet without the Prince of Denmark. The university structure is seen as preventing Japanese professors from starting NBFs or aggressively working with NBSs, something which would be culturally difficult, and, so far as start-up NBFs are concerned, financially impossible. That is, the university system is seen as part of a triad (university/finance/culture) which eliminates the scientist-entrepreneur and reduces the pressure for change which would be present if the members of the triad were not all effective blocks.[6]

Only the national universities have sufficient resources in Japan to play a significant role in building the science base for biotechnology; so our remarks will be confined to those. A basic precept is that the faculty are fully employed by the government in the university and thus it is illegal for them to profit from their work by consulting for pay or starting a firm as a principal. In the U.S., scientist-entrepreneurs starting NBFs typically retained their academic positions at least until their firm was well established and they were multimillionaires; in Japan, the academic is legally required to give up his or her position and laboratory in order to profit from commercialization. Technology transfer is supposed to be paid for by Japanese professor's salaries, but since there are no incentives to do so it tends to fall to the end of the professor's to-do lists. Further, in many cases commercialization of research output may require permission from the relevant Ministry (usually Health and Welfare), which creates a *de facto* barrier to entry of new firms to exploit university breakthroughs.[7]

We were surprised that 40 percent of Japanese stars at some time in their publishing career up to 1990 either published as or (much more frequently) with an employee of a firm, a higher rate even than the 33 percent in the United States; stars in Japan and the U.S. show substantially more such ties than those in any other country.[8] Subsequently, additional fieldwork indicated that incentives were stronger than might at first appear. First, firms are allowed to send talented employees (in strictly limited numbers) as doctoral students working in the laboratories of professors of their choice. These students are extremely valuable to the professor because they expand the workforce in a way which is impossible to do with research grants in universities since every hire confers lifetime employment. Furthermore, these students are able to bring research funds which permit purchase of new equipment and reagents that otherwise would not be available and the students serve as liaisons between their employers and the professor who might, for example, request that the firm's laboratory take over laborious work such as sequencing material by Monday. Thus, with the professors forbidden to go work with the firms, the firms can work with them by providing in-kind research support.

A number of NBEs indicated that they also frequently had understandings to place productive professors in extraordinarily well-paid advisory positions after the professors' mandatory retirement. Annual unreported cash payments (similar in magnitude to the professor's salary) were also made by at least some of the NBEs. Executives at the same NBEs which reported making such payments also indicated that they preferred to work with American scientists at ten times the total cost but with clear title to the resulting intellectual property rights.

We conclude that there are workable incentives of various shades from white to very dark gray for star scientists to actively collaborate with NBEs, but that these incentives are still smaller than in the U.S. and that the opportunity to start a firm while a professor is nonexistent. Critics of the national university system, which is currently undergoing reform in response to such critiques, also point to the relatively noncompetitive nature of research funding and salaries so that Japanese academics have little experience in the entrepreneurial arenas of grantsmanship and competitive job offers.

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 (JHSF) sponsored by the Ministry of Health and Welfare, the Japan Biotechnology Association (JBA) sponsored by Ministry of International Trade and Industry, and the Society for Techno-innovation of Agriculture, Forestry, and Fisheries (STAFF) sponsored by the Ministry of Agriculture, Forestry, and Fisheries. 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.

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, NBE executives describe the quangos 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 the contributing firms to fund research done at those firms related to the quango's goals.

Financial Market Support for Venture Firms

The best U.S. biotechnology companies may report negative accounting profits for 10 or 15 years as their research and development investment is written off while successful products take years of testing prior to F.D.A.approval and marketing. (Non-pharmaceutical applications have yielded faster accounting profits but smaller market values to date.) In Japan, in the absence of family wealth which played an important role for a handful of entrepreneurial NBFs, it has been nearly impossible to start an independent NBF both because of a lack of venture capital firms to finance the first 5-10 years of the NBF's life and then an initial public offering (IPO) market to take out the venture capitalists' investment at a profit long before any accounting net income is in prospect.[9] (See Zucker and Darby 1994 and Kishimoto 1989 for details; however, innovations initiated by the Ministry of Finance in 1994 and 1995 may move the Japanese capital markets toward the American model in the future.[10])

In practice, the structure of the Japanese capital markets has precluded the pattern of NBF formation seen in the U.S. and the structure of the universities greatly has reduced the number of potential founding scientist-entrepreneurs. Thus, we understand why entry into commercial application of biotechnology in Japan has occurred nearly exclusively through adoption of the technology by pre-existing firms (NBSs). It is an empirical question addressed below, however, whether this difference in pattern of entry in fact significantly retards the rate of entry relative to the science base.

Threat of Product Liability Litigation

Although Japanese observers have not remarked on the threat of product liability litigation as playing a role in the development of commercial applications of biotechnology, this may be because they were searching for factors which have retarded that development in Japan relative to the United States. Clearly, product liability is, in comparison, a non-issue in Japan. This could also serve to explain why biotechnology is more likely to be adopted by large established firms in Japan than in the U.S. where that adoption could be construed as literally betting the company, particularly in the earlier years. As a result, we believe that it is not possible to conclude from the lack of NBFs in Japan, that their absence proves that commercialization is slowed. In fact, if product liability were sufficiently important, it could reverse that presumption.

Cultural Differences with Respect to Entrepreneurialism

As alluded to above, many respondents commented on the differential status or honor given to the professor relative to the individual involved in commerce.[11] "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." (Zucker and Darby 1994)

The cultural value placed on lifetime employment also works against university or other star scientists moving to the NBSs as employees or being effective there if they did. Certainly, it is inconsistent with a professor leaving the university to start a NBF. We note, however, that the biographies of top biotech scientists and executives in Japan generally reflect more than one change in employer, suggesting that lifetime employment is honored more with words than in practice. Thus while the Japanese culture is certainly consistent with university professors staying aloof from the world of commerce and sticking to the university, we find some evidence that it does not present an absolute bar either to collaboration with firms or to changing jobs if the incentives are right.

II. Determinants of Births of NBEs in Japan

Since we have already learned a great deal about the process of NBE entry in the United States, we follow Zucker, Darby, and Brewer (1997) to the extent possible given the availability of data and the problems of multicollinearity which arise within the more limited geography of Japan where many of the explanatory variables used in the U.S. are highly correlated. Basically, we look to measures of intellectual capital and to economic variables to explain entry of firms, entering them in groups both to give an idea of marginal contribution and stability of the prior coefficients.

Because NBSs are much more common in Japan, multiple locations where biotechnology is utilized are potentially more important than in the U.S. For our empirical work in Japan, we experimented with two definitions of entry: One includes only entry at the primary location and the alternative includes entry at both primary and one or more secondary locations. Since we have only one year for entry for each firm, the former definition probably gives a more accurate picture of the timing of entry in Japan while cumulating entry on the second definition probably gives a more accurate description of the geographical distribution of biotechnology in Japan. For this purpose, we searched the *Science Citation Index* for biotech-relevant publications by scientists at each of the 277 Japanese NBEs in order to uncover any additional locations and correct instances in which corporate headquarters rather than laboratory or plant locations were reported in our directory source. With secondary locations included, there were a total of 416 entries into biotechnology from 1975 through 1989.

Analogous to Zucker, Darby, Brewer (1997), our data are in panel form for each of the 47 Japanese prefectures for each of the years 1975-1989 for a total of 705 observations. We are attempting to explain counts of entries by new biotechnology enterprises for each prefecture and year. Since there are many zeroes among these non-negative integers, we estimate poisson regressions using LIMDEP (Version 7.0). In Section III below, we estimate separate regressions to explain the number of entries by keiretsu-member and nonmember firms for each prefecture and year. In order to conserve space, the regression results reported in Tables 1-4 are all for the definition of entry which includes secondary locations. Restricting the definition of entry to primary locations in fact resulted in only one difference in significance levels, as noted below.

We measure intellectual capital both by counts of how many stars and their collaborators are "active" in each prefecture in each year and also by the number of main professors and the total resources for bioscience research institutes at major universities in the prefecture (see Data Appendix A.2 for details). As in the U.S., the economic variables are total employment in the prefecture as a measure of its size and average earnings in the prefecture as a measure of the skill level of its labor force (see Data Appendix A.3 for details).[12]

The first column (a) of Table 1 estimates a simple model of entry of enterprises into biotechnology based on the numbers of active stars and collaborators by year and prefecture. In Japan, stars have a strong positive effect and collaborators have a significant negative effect.[13] As in the U.S., there appears to be a nonlinear relationship which is captured in the second column (b) of Table 1 by adding the product of the number of stars and collaborators. This eliminates the negative direct effect of collaborators and instead the negative interaction coefficient suggests that the more new people to whom the stars are teaching the new technology the less is the effect of the stars on entry into biotechnology. However, the significance of both collaborators and the star•collaborator interaction term is unstable as the model is expanded to account for other resources in the area; so the influence of collaborators may not be reliably determined from the limited geography of Japan. We believe that geography's limits on the variation in Japanese conditions is the most likely explanation, in part, because when we experimented with artificially limiting the U.S. birth analysis data set to only California BEAs, we found that similar instability resulted.

The final column (e) of Table 1 presents the full model, in which stars (as always) have a significantly positive effect on the probability of entry of NBEs in the prefecture. Total employment and average earnings also have highly significant positive effects. The coefficients of the number of main professors and total research funding for bioscience labs in major university research institutes are insignificant in the full model, in contrast to model (c) which includes all the intellectual human capital variables only and in which they are both significant. We explored the multicollinearity among these two variables and the economic variables a bit further by dropping each in turn from models (c) and (e): We found that either the number of main professors or total research funding is highly significant and positive in model (c) if entered alone but neither is significant if entered alone in model (e) with the economic variables. Thus, while the distribution of major universities is such that, unlike the U.S., we cannot find an effect for them separate from the areas in which they are located, a significant positive effect remains for our measure of very specific intellectual human capital in the form of star scientists.

The fourth regression (d) in Table 1 indicates that, similar to results in Zucker, Darby, and Brewer (1997) for the U.S., the explanatory factor of the economic variables alone is about equivalent to that of the star and collaborator counts alone (compare the log-likelihoods for columns a and d), but significantly less than that of the intellectual capital variables as a group (column c). As in the U.S., where and when star scientists are active has a strongly positive and significant independent effect on where and when NBEs entered into biotechnology, and this effect is always separate from and in addition to the effects of research support for university scientists and the general economic conditions of the prefecture.

Thus the Japanese data validate the qualitative conclusions in our previous work for the U.S. alone on the importance of intellectual human capital in general, and particularly the role of individual star scientists in promoting births of NBEs in an area and the regional economic development which they imply.

III. Are Entry Patterns Different for Keiretsu Member Firms?

Keiretsus, large groups of related firms typified by cross-shareholding and financial relations with a central bank, are generally viewed as a distinctive and important aspect of Japanese industrial organization. One hypothesis is that members of a keiretsu are more likely to engage in risky, long-horizon investments such as biotechnology because of their low cost of capital and implicit risk-sharing arrangements and superior information network for monitoring innovation. An alternative hypothesis is that management of keiretsu-member firms are more entrenched and less likely to be alert to new innovations such as biotechnology. In this section, we examine whether their entry pattern in fact differs significantly from that estimated for non-member firms.

Since keiretsus are largely informal groupings, there is no generally agreed definition or listing of which firms are members of which keiretsu. The situation is somewhat easier for vertical groupings more analogous to American conglomerates in structure, but it is debatable whether those groups should be counted as keiretsus at all. David Weinstein generously has provided us with the data set constructed for Weinstein and Yishay Yafeh (1994) which lists member firms for four different definitions of keiretsu: (a) The Big 6 are the DKB, Fuyo, Mitsui, Mitsubishi, Sanwa, and Sumitomo horizontal groups. (b) The Big 8 are the Big 6 plus the Industrial Bank of Japan and Tokai groups. (c) The Big 8 + Vertical definition is the broadest, adding to the Big 8 firms that are members of vertical groups. (d) The Big 6 Presidents Club definition is the narrowest, including only the inner circle of Big 6 firms whose CEOs belong to their group's Presidents Club.[14]

Using in turn each of these four definitions of keiretsu memberships, we divided our entry counts by prefecture and year into the number of entries by firms identified as members of a keiretsu and the number of entries by all other firms. We replicated Table 1 for the member and non-member counts separately for each definition, and also stacked the two count variables in a third regression for ease in testing the hypothesis that the coefficients of each of the variables -- but not the constants -- are the same in each regression pair.[15] We do not include the constant terms in the test as they will differ simply because keiretsu-member firms are relatively infrequent and thus should (as a group) have a different, lower base frequency of entry. For each Keiretsu definition, from broadest to narrowest, Table 2 reports the χ^2 statistics for these tests of equality for the coefficients of regression forms (b) through (e) from Table 1 together with a memorandum of the share of keiretsu-member entry to total entry into biotechnology.[16] In regressions involving only the stars, collaborators, and their product, most of the definitions involve significant differences in regression coefficients. In regressions involving all the intellectual human capital variables, these significant differences mostly disappear. There is no evidence of significant differences between the keiretsu and non-keiretsu coefficients for either the full model or for regressions including only total employment and average wages by prefecture.

We explore keiretsu/non-keiretsu differences further in Table 3. This Table reports the star-collaborator-product and full-model regressions for the split samples for the broadest keiretsu definition (Big 8 plus vertical groups) which also follows the dominant pattern with respect to the significance tests in Table 2. Two models are reported in Table 3, one including only stars, collaborators, and their interaction, and the other full model with all the variables. The χ^2 statistics reported for each pair of regressions is that for the corresponding stacked regression from Table 2. The message of Table 3 seems to be that even where the differences in the process of entry for keiretsu members and non-member is *significantly* different in a statistical sense (columns a and b), the differences are very small and are not likely to be of much economic significance.

Even the statistically significant differences reported in Table 2 may be the result of a data problem. Since keiretsu-member firms are generally larger and likely to have more secondary locations than non-members, coding secondary locations as entering in the same year as primary locations (which in fact probably entered earlier) may differentially shift the entry pattern by membership category. In fact, when we used the primary-locations-only entry definition in regressions not reported here, the corresponding χ^2 statistics were in every case lower than those reported in Table 2 and none of the values were significant.

In Figure 3 we plot the cumulative entry as a percentage of type-specific total entry for keiretsu members and nonmembers separately, using the primary-location-only definition of entry. Even after eliminating apparent bias from misdating secondary locations, a higher proportion of keiretsu members appear to have entered early in the process than is the case for nonmembers. Since the underlying processes are indistinguishable, these differences presumably reflect subtle differences in geographical distribution by membership category.[17]

IV. Differences between Japanese and American NBE Entry Processes

A particularly interesting question is whether the structural differences between Japan and the United States result in detectible differences in the linkage between the science base and its commercialization. Since it is difficult to find many variables which are strictly comparable across countries, we must address this question with stripped down models which consider only the numbers of stars and collaborators and total employment in the local area.[18]

For the common years 1976-1989 in both data sets, the first column (a) of Table 4 reports the results from a pooled Japan-US poisson regression for NBE entry by year and area based on only a constant and the number of stars and collaborators in each. In this simple model, both the number of stars and the number of collaborators have a significantly positive effect on births of NBEs. In the remaining four columns of Table 4 we explore different models which include both the values of the variables for both countries and those values interacted with JDUMMY where JDUMMY is 1 for Japanese observations and 0 for U.S. observations. Thus, the interaction terms measure the *additional* impact of the variable in Japan compared to the U.S. Therefore, the combined coefficients for Japanese stars and collaborators in column (b) are 0.158 +0.184 = 0.342 and 0.040 - 0.132 = -0.092, respectively. These differ slightly from the values in column (a) of Table 1 because of the shorter overlapping sample.

Since on average Japanese prefectures have nearly twice as large populations as American BEAs, the probability of a birth in a prefecture might well be larger on average than in a BEA, so we want to test for structural differences that shift the coefficients of the variables in Japan relative to the coefficients in the U.S. For an individual coefficient, whether the value of the JDUMMY interaction coefficient is significantly different from 0 is an appropriate test if it is maintained that all the other coefficients are in fact different. The χ^2 JDUMMY interactions =

0 statistic near the bottom of the table reports the test of the hypothesis that there is no significant difference, except for the constant, in the entry process between Japan and the U.S. (i.e., that all the coefficients of the interaction terms are zero). In contrast to the similar analysis conducted in Section III above for members and non-members of keiretsus, in every case this χ^2 statistic confirms that there are significant differences between the processes in the U.S. and Japan.[19]

Considering first the full model in column (e), we see that stars and collaborators have weaker effects on local developments -- as measured by NBE births -- in Japan than in the U.S. and that firms are more likely to enter in Japan where there is already more economic activity. This is certainly consistent with the arguments presented in Section I above which suggest that there are strong structural impediments in Japan to the deep involvement in commercialization characteristic of many U.S. professors/scientist-entrepreneurs. The greater importance of agglomeration factors in Japan, as indicated by the large coefficient on Total Employment x JDUMMY, may also reflect the institutional structure in which NBEs often get what collaboration they can with star scientists at national universities by sending their employees to the stars' labs rather than the stars coming to the firms. (In the U.S., it is in both the NBE's and the scientist's interests for the university scientist to work at the firm in order to strengthen the case that the university does not have a property interest in the results of the research.) If the NBE's employees are working in the university lab, rather than vice versa, then it is less important that the NBE be located locally to conserve the star's time.

In columns (c) and (d), we see that even in the absence of internationally-comparable additional university-based measures of intellectual human capital, counts of stars and collaborators and their interaction alone make a somewhat greater marginal contribution as measured by increases in the log-likelihood than does total employment in explaining the pattern of entry of NBEs into biotechnology in Japan and the U.S., with their combined explanatory power considerably greater than either alone.

Figure 4 shows the cumulative densitites of Japanese and American NBE entry, where each is measured as a cumulative percentage of total entry for each country and where the primary-location-only definition of entry is used for Japan.[20] The patterns are very similar with a relatively small lead on the part of Japan apparently explicable by differences in definition of the start of the process with entry in Japan definitionally starting in 1975 and in the U.S. definitionally starting in 1976. Note, however, in Figure 5 that NBE entry by non-members of keiretsus virtually overlaps the U.S. pattern while entry by keiretsu members is concentrated in relatively earlier years. Again, we cannot determine whether this reflects some anomaly in reporting practices or whether it is a possible indication of a real timing difference in entry for keiretsu member firms relative to non-member firms in Japan and firms in the United States.

Given the relatively small coefficients on Japanese stars and collaborators reported in Table 4, an important issue for future research and for policymakers is whether structural differences in Japan in comparison with the U.S. have resulted in the under-utilization of the science base -- particularly the intellectual human capital embodied in the stars and their collaborators -- in terms of its impact on commercial development in Japan or whether instead these structural differences have only spread the impact of stars on commercialization more widely throughout Japan.

V. Summary and Conclusions

This paper has explored one aspect of the perceived lag of Japanese commercialization of biotechnology relative to the U.S. We have reported evidence that star scientists in Japan, like the U.S., play an independent role in the location and timing of the formation of the biotechnology industry over and above that which could be predicted by measures of bioscience research resources at major universities and by economic factors of agglomeration and labor quality. Taken together the measures of intellectual human capital contribute more to the explanatory power of our regressions than do the economic variables.

Although stars play an important role in determining where and when the biotechnology industry was formed in Japan, that role is significantly smaller -- and the role of preexisting economic activity greater -- than in the United States. This significant quantitative difference is consistent with a number of structural factors -- including university policies which weaken the scientists' incentives to be involved in commercialization, absence of a venture capital/IPO market necessary for long-term nurturing of biotech startups, and cultural inhibitions on professors becoming scientist-entrepreneurs -- which have been seen as interfering with Japan's ability to exploit its science base commercially. Support for the importance of these factors is found, moreover, since Japanese star bioscientists induce significantly less entry of NBEs than do similar scientists in the U.S. We found little evidence that the entry of keiretsu-member firms followed a significantly different process than that of non-members. While our results strictly apply to the formative years of the industry, factors governing its early evolution likely shape the industry's market structure at maturity (Steven Klepper and Elizabeth Graddy 1990).

As frequently happens in research, we see more questions raised than answered. First, while Japanese star scientists are quite rarely principals or employees of new biotech firms -- or indeed of pre-existing firms which have adopted biotechnology -- in other work underway we find that academic stars are slightly more likely than U.S. scientists to coauthor publications with employees of NBEs in their country. (Stars in both the U.S. and Japan are substantially more involved in publishing as or with employees of NBEs than stars in other countries.) Such evidence of bench-level collaboration with star scientists was shown in Zucker, Darby, and

Armstrong (1994) to be a powerful predictor of the success of NBEs in terms of the numbers of product in development and on the market and of growth in employment. We plan to investigate whether the Japanese system, with smaller financial incentives for the stars and less clear property rights for the firms, can produce similar results in terms of NBE success.

We also believe that it is important to investigate whether the fact that Japanese firms doing biotechnology are much more likely to have been pre-existing firms with their own technological identities rather than new firms built around particular competencies in biotechnology also plays a role in limiting the success of the Japanese economy in commercializing its science base.

In the U.S. work summarized in Zucker and Darby (1996) there is substantial evidence of a symbiotic relationship between the progress of basic science and the stars' role in enhancing commercial success in biotechnology. With respect to the Japanese science base, it is important to investigate the role of Japanese university and science and technology policies in limiting the early science base and promoting the catch-up process. We also want to investigate whether the weaker ties between university stars and commercialization in Japan has slowed the progress of basic science in Japan as well as limited the nation's payoff from its investment in the science base. In closely related work underway, we are investigating the causes and effects of distinctive Japanese patterns of scientific collaboration within and across universities and other institutions with respect to the growth and transmission of bioscience in Japan.

Finally, we plan to quantify the effects of particular policies and institutional arrangements on the development and commercialization of bioscience by expanding our data set to include a range of countries with sufficient variation in policies and institutions to identify separate effects of each. We also hope to explain the distinctive pattern of migration of stars within the APEC region and its role in the diffusion of science and the development of the region's economies.

Data Appendix

All data on stars and their collaborators was derived from the universe in *GenBank* (1990), and hand-pulled and coded records for each of the stars' articles therein as detailed in the Data Appendix to Zucker, Darby, and Brewer (1994), which also provides conceptual and procedural background on the variables detailed here.

A.1. New Biotechnology Enterprises

Attempting to develop a data set comparable to the one we developed for the U.S., we started by licensing a machine readable data base (North Carolina Biotechnology Center 1992). As with the U.S. NBE data set, we added additional NBEs based on their listings in *Bioscan* (1989-1994). Finally, we added additional NBEs from Nikkei Biotechnology (1990) based on lengthy discussion with Mr. Mitsuru Miyata (Editor-in-Chief) and Ms. Ikuko Uchiyama (Staff Editor) of *Nikkei Biotechnology* which enabled us to distinguish those firms actually using the new technologies from those which were listed as a courtesy to subscribers hoping to improve their stock price. Nikkei Biotechnology (1994) was used to fill in missing data.

As noted, seven eighths of these companies had founding dates prior to their entry into biotechnology and so were classed as NBSs. Apparent response bias led early entrants to report 1975 as the date of entry, which we accepted as the earliest date of entry even though it is doubtful that entry occurred before 1976 given the lag observed in U.S. in applying the key Cohen-Boyer discovery (Stanley Cohen, A. Chang, Herbert Boyer, and R. Helling 1973) in the U.S. In four cases, very early entrants gave dates of entry before 1975, apparently referring to earlier technologies; these were constrained to 1975.[21]) This gave us dates of entry for 242 firms. For another 35 firms, no entry dates were available in any of our data sources. Since there was valuable location data associated with the firms, we estimated the entry date of these firms by drawing entry dates from the same distribution as recorded for firms in their prefecture with known entry dates.

Typically, these NBEs were large enterprises with many locations and often the headquarters address was listed as the NBE's location regardless of where biotechnology actually was being applied. Akio Tagawa developed an ingenious method to locate NBEs by searching the *Science Citation Index* online by firm name for 1983-1993 to see where scientists affiliated with each firm were writing bioscience articles. For those firms which could be thus located, the most frequent location was designated the primary location and any other locations were designated secondary locations. Otherwise, the listed location was retained. In each case, the date of entry into biotech from our directory sources was used for all locations since we had no other information.

Application of these procedures yielded a total of 277 Japanese NBEs with the same number of primary locations and an additional 139 secondary locations for 74 of these NBEs.

A.2. Japanese University Research Resources

Our university research resources information is taken from a comprehensive directory published by the Japan Association for the Advancement of Science (Nihon Gakujutsu Shinkokai, 1990) which has listings for all of the scientific research institutions in Japan affiliated to universities. This source, in addition to general information such as institute names, addresses, phone numbers, and year of establishment, also contains very detailed information such as director names, numbers of researchers, research divisions within institutions, researcher names, research objectives, and information about research oriented resources. It is published yearly.

We first collected information from this directory about all of the research institutes that perform research in bioscience related fields, and compiled them. In particular, the numbers of full professors, associate professors, assistant professors, and other researchers, as well as the total resources for each relevant institute was recorded.

The relative size and structure of Japanese research institutes is quite clear from the way in which the entries are listed. Institutes generally are broken down into smaller research divisions, each of which has a specific research agenda, and each of which is led by what we call a "main professor," who is usually a full professor but often an associate professor. Thus, the number of main professors or research divisions gives us a very good indicator of how large the universities' institutes are. Typically, it would suffice to simply count the number of full professors who are affiliated to each institute, but in many cases, there was no full professor, and so an associate professor was counted. It is for this reason that we have used a variable No. Main Professors which counts their number by prefecture, in contrast to simply using "full" professor.

We also collected information about the total amount of yearly resources for each of the relevant institutes. This figure also is another measure of the relative size of the institutions. Because we were concentrating on relative size of the institutions based on university and ultimately location of the university by prefecture, we collected the information for the research institutes from the 1990 directory, which includes information for the years 1987 and 1988.

In the end, all of the data was combined and sorted based on the universities to which the various research institutes belong, and the cumulative data is what we used for this study. Because we were only interested in the top research oriented universities in the country, we used a minimum cut-off of three main professors per university to qualify for the analysis, and all others were considered too small to significantly contribute. Our variable Total Research Funding is the sum (in millions of yen) across all such universities in a given prefecture.

Note that both No. Main Professors and Total Research Funding have the same values for a given prefecture for each year in the analysis, thus serving together as a type of modeled fixed effect component in our regressions.

A.3. Japanese Economic Variables

The main prefecture-level economic variables used are Total Employment (total employment in the given prefecture in a given year) and Average Earnings (average earnings per employed person in the given prefecture in a given year). These variables were obtained for the years 1975-1990. Japanese data at the sub-national level is unusually difficult to obtain, as we found out in acquiring the information for these variables. Almost all data on labor and employment is reported at only the national level. Thus, we had to combine several sources to compile the necessary information for these variables: Policy Planning and Research Department, Minister's Secretariat, Ministry of Labour (1975-1990), Statistics Bureau, Management and Coordination Agency (1976, 1981, 1986, 1991), Asahi Shinbunsha (1975-1990), Kokuseisha (1988), and Bureau of Statistics (1991).

Total Employment (in thousands) was listed irregularly in the various sources, and while there was some overlap among sources which served for confirmational purposes, much of the information was obtained through the above sources in different editions. In the end, we were able to obtain consistent data only for the years 1975, 1977, 1979, 1980, 1985, 1987, and 1990. The remaining years were filled in by interpolation from the obtained data.

Average Earnings was calculated from the average cash earnings per worker per month over a twelve month period for all of the 47 prefectures in Japan and compared for consistency to the national average. Cash earnings is defined as the amount of money earned before deductions for income tax, for social insurance contributions, for union dues, and for payment for goods purchased. Cash earnings specifically include semi-annual bonuses, which in Japan are (or were) typically equivalent to another six months' worth of income. The yearly cash earnings were divided by 12 to find the average monthly cash earnings for each prefecture and year. Finally, we adjusted this amount for inflation by dividing by the consumer price index for the central city of each of the prefectures in Japan for each year during the period 1975-1990. The basic cash earnings data were found in successive annual editions of the Yearbook of Labour Statistics during this period.

We also experimented with a third economic variable, the Earnings/Price Ratio as an estimate of the (all-equity) cost of capital. This figure is the inverse of the price/earnings ratio as reported in Nihon Ginko Tokeikyoku (1975-1990) for the Tokyo Stock Price Index, or TOPIX, based on all First Section stocks on the Tokyo Stock Exchange.

REFERENCES

Asahi Shinbunsha, *Asahi nenkan* [Asahi Annual], Tokyo: Asahi Shinbunsha, 1975-1990. (16 different vols.)

Bioscan, Volumes 3-8, 1989-1994.

Bureau of Statistics (Tokeika), *Rodo tokei yoran* [Directory of Labour Statistics], Tokyo: Ministry of Health and Welfare (Koseisho), 1991.

Cohen, Stanley, A. Chang, Herbert Boyer, and R. Helling, "Construction of Biologically Functional Bacterial Plasmids *in vitro*," *Proceedings of the National Academy of Sciences*, 1973, 70: 3240-3244.

GenBank, Release 65.0, machine readable data base, Palo Alto, CA: IntelliGentics, Inc., September 1990.

Japan Association for the Advancement of Science (Nihon Gakujutsu Shinkokai), *1990-nen daigaku kenkyujo yoran* [Directory of Scientific Research Institutes of Universities of Japan, 1990], Tokyo: Dai Nippon, 1990.

Kishimoto, Yoriko, "A Historical Perspective on Japan's Biotech Boom," *Venture Japan*, 1989, 2(1): 41-43.

Klepper, Steven, and Elizabeth Graddy, "The Evolution of New Industries and the Determinants of Market Structure," *The Rand Journal of Economics*, Spring 1990, 21(1): 27-44.

Kokuseisha, *Deta de miru kensei, '89-90: Nihon kokusei zue chiiki tokeiban* [Prefectural Information through Data '89-90], Tokyo: Kokuseisha, 1988.

Nihon Ginko Tokeikyoku, *Keizai tokei nenpo* [Economic Statistics Annual], Tokyo: Nihon Ginko Tokeikyoku, 1975-1990. (16 different vols.)

Nikkei Biotechnology, *Biotechnology Guide Japan, 1990-1991*, Japan-America Management, Ltd., trans., New York, NY: Stockton Press, 1990. [Translated from the Section on Japanese Companies in *'89 Sekai no Baio Kigyo 800sha*, (The World's 800 Bioindustry Companies.)]

Nikkei Biotechnology, *94/95 sekai no baio kigyo 2000-sha* ['94/'95 World's 2000 Bioindustry Corporations], Tokyo: Nikkei Business Publications, 1994.

North Carolina Biotechnology Center, *North Carolina Biotechnology Center Japanese Companies Database*, machine readable data base, Research Triangle Park, NC: North Carolina Biotechnology Center, April 16, 1992.

Odagiri, Hiroyuki, and Akira Goto, "The Japanese System of Innovation: Past, Present, and Future," in Richard R. Nelson, ed., *National Innovation Systems: A Comparative Analysis*, Oxford: Oxford University Press, 1993.

Policy Planning and Research Department, Minister's Secretariat, Ministry of Labour, Japan (Rodo daijin kanbo seisaku chosabu), *Rodo tokei nenpo* [Yearbook of Labour Statistics], Tokyo: Daiwa Printing, 1975-1990. (16 different vols.)

Statistics Bureau, Management and Coordination Agency, Japan (Somucho tokei kyoku), *Kokusei chosa hokoku* [The Population Census of Japan], Tokyo: Nihon Tokei Kyokai, 1976, 1981, 1986, 1991. (4 different vols.)

Steiner, Robert, "Japan Launches New Stock Exchange to Stimulate Small, Expanding Firms," *Asian Wall Street Journal*, July 24, 1995, p. 18.

Ueda, Kazuo, "Institutional and Regulatory Frameworks for the Main Bank System," in Aoki and Patrick, eds., *The Japanese Main Bank System*, Oxford: Oxford University Press, 1995.

Ueda, Kazuo, *An Economic Analysis of the Hollowing Out of the Japanese Financial Industry*, Tokyo: Nikkei Shinbun Sha, 1996. (in Japanese)

Weinstein, David E., and Yishay Yafeh, "Japan's Corporate Groups: Collusive or Competitive? An Empirical Investigation of *Keiretsu* Behavior," *Journal of Industrial Economics*, December 1995, 43(4): 359-376.

Wooldridge, Jeffrey M., "On the Application of Robust, Regression-Based Diagnostics to Models of Conditional Means and Conditional Variances," *Journal of Econometrics*, January 1991, 47: 5-46.

Zucker, Lynne G., and Michael R. Darby, "The Organization of Biotechnology Science and Its Commercialization in Japan," UCLA Institute for Social Science Research Working Papers in the Social Sciences, vol. 6, no. 1, August 1994.

Zucker, Lynne G., and Michael R. Darby, "Star Scientists and Institutional Transformation: Patterns of Invention and Innovation in the Formation of the Biotechnology Industry," *Proceedings of the National Academy of Sciences*, 1996 in press.

Zucker, Lynne G., Michael R. Darby, and Jeff Armstrong, "Intellectual Human Capital and the Firm: The Technology of Geographically Localized Knowledge Spillovers," National Bureau of Economic Research Working Paper No. 4946, December 1994.

Zucker, Lynne G., Michael R. Darby, and Marilynn B. Brewer, "Intellectual Capital and the Birth of U.S. Biotechnology Enterprises," National Bureau of Economic Research Working Paper No. 4653, February 1994.

Zucker, Lynne G., Michael R. Darby, and Marilynn B. Brewer, "Intellectual Human Capital and the Birth of U.S. Biotechnology Enterprises," *American Economic Review*, March 1997, 87(1): in press.

FOOTNOTES

1. See particularly, Zucker, Darby, and Marilynn B. Brewer (1994, 1997) and Zucker, Darby, and Jeff Armstrong (1994). The first of these contains an extensive data appendix describing in detail how the star scientists were identified.

2. Two caveats should be noted: (a) We only have data for the affiliations of stars on each of their publications reporting genetic-sequence discoveries up to April 1990. (b) There is substantial movement across national boundaries: Counting stars once in each country they ever published, increases the total stars to 425 from the 327 unique individuals. Of the 52 Japanese stars, 33 published only in Japan; 8 published first in the U.S. and then moved to Japan; 6 published first in Japan and then moved to the U.S.; 1 published first in Japan, moved to the U.S. and then back to Japan; 1 published first in Japan, moved to a third country and then back to Japan; and 3 published first in third countries and then moved to Japan.

3. Each genetic sequence entering GenBank for the first time is assigned a primary accession number (our measure of a genetic-sequence discovery).

4. In the U.S. data, Zucker, Darby, and Brewer (1997) could definitively classify only 511 NBFs and 150 NBSs, with the remaining 90 NBEs lacking data to classify or (in 18 cases) being problematic joint venture cases; 511 is 77.3 percent of 661. The 34 Japanese NBFs were identified as such on the basis of having a company founding date after 1974, while the remaining 243 NBEs with founding dates before 1975 were classified as NBSs.

5. The growth of the underlying science base is certainly a central concern in the larger research program of which this paper is a part.

6. More generally, the role of the university is notable by its absence in Hiroyuki Odagiri and Akira Goto's (1993) overview of the Japanese national innovation system.

7. We are indebted for this point to Kazuo Ueda, who has studied similar barriers in the financial industry (Ueda 1995, 1996).

8. Copublication is generally agreed by scientists and executives to be an excellent indicator of alignment of interests.

9. Zucker, Darby, and Brewer (1997) report a significantly negative coefficient on the number of venture capital firms in poisson regressions explaining births of NBEs. This appears to be related to their tendency to package the efforts of several star scientists into one larger enterprise. We do not regard this as proving that the presence of startup-supporting venture capital firms reduces the overall number of firms established.

10. In particular, in response to widespread concern about financial market regulations blocking entry of new firms in emerging industries, in July 1995 the Japanese Ministry of Finance approved establishment of the Frontier Market which for the first time will allow small companies with little earnings history to sell shares to the public. (Robert Steiner 1995)

11. One measure of the value of that differential status is this: In the U.S. there was a significant net outflow of star scientists from university faculties to firms; no such outflow occurred in Japan.

12. Zucker, Darby, and Brewer (1997) also included a count of the number of venture capital firms in the BEA eligible to finance start-up NBFs, but such a variable would be uniformly 0 in Japan during this period. In addition, we experimented in regressions not reported here with the (TOPIX) earnings-price ratio as a measure of the nationwide cost of capital. This variable performed even more poorly than in the U.S. case (see Zucker, Darby, and Brewer 1997) with perverse (positive) coefficients wherever it was entered. We believe that this occurred because, varying by year but not prefecture, it serves as a fixed effects proxy for the year and, in our sample, covaried positively with underlying factors impacting positively on NBE entry. It is

frequently argued that the managers of Japanese firms are so insulated from stock-market pressure that the absence of a significant negative effect is not entirely surprising.

13. Zucker, Darby, and Brewer (1997) report that both stars and collaborators have positive effects in the corresponding model for the U.S. Differences between the U.S. and Japan will be explored in Section IV below. Note, however, that in long-run poisson regressions (not feasible here because of the smaller number of prefectures than U.S. BEAs) Zucker, Darby, and Brewer (1997) do find some evidence of negative effects of the number of active collaborators.

14. The two broader definitions (b) and (c) were based on "Dodwell Marketing Consultants' *Industrial Groupings in Japan.*" The narrower definitions (a) and (d) were based on "*Keizai Chosa Kyokai's Keiretsu no Kenkyu* (KNK)." (Weinstein and Yishay Yafeh 1994, p. 367.)

15. See Section IV below for details on the stacked regressions and associated Wald test as the technique is applied to testing for equality of coefficients for entry in Japan and the U.S.

16. These stacked regressions are not reported in full since the coefficient estimates are identical to those in the separate regressions, representative examples of which are reported in Table 3 below.

17. Alternatively, the differences which are visually apparent may not be statistically significantly so. Further, these differences may reflect remaining differential reporting bias in which larger firms are more likely to claim to have been doing biotechnology from the beginning since nearly 10 percent of keiretsu firms report entering biotechnology in the earliest possible year.

18. In the United States we use BEAs as the local areas corresponding to prefectures in Japan.

19. The χ^2 statistic is not reported for column (d) since in that case there is only one interaction term and the significant coefficient for Total Employment x JDUMMY is sufficient to demonstrate structural differences.

20. There are a relatively small number of NBSs in the U.S. for which secondary locations are included among the NBEs if separate entry dates could be obtained for entry at each location.

21. Entry dates for NBSs are generally less reliable than for NBFs, and this is especially so in Japan where many firms declare themselves early entrants in biotechnology referring to older fermentation and other production methods based on living organisms, and not to the "new" biotechnology based on recombinant DNA, monoclonal antibodies, and other new techniques.

Table 1
Poisson Regressions of Entry of New Biotech Enterprises by Year and Prefecture in Japan, 1975-1989

	(a)	(b)	(c)	(d)	(e)
Constant	-0.775***	-0.862***	-1.112***	-3.291***	-4.662***
	(0.037)	(0.040)	(0.054)	(0.545)	(0.511)
Active Stars	0.341***	0.362***	0.137***	-	0.082***
	(0.021)	(0.015)	(0.019)		(0.025)
Active Collaborators	-0.092***	-0.001	-0.024	-	-0.061**
	(0.012)	(0.012)	(0.016)		(0.023)
Ac. Stars x Ac. Collabs.	-	-0.008***	-0.003**	-	-0.001
		(0.001)	(0.001)		(0.001)
No. Main Professors	-	-	-0.087***	-	0.019
			(0.008)		(0.013)
Total Research Funding-Univ.	-	-	0.022***	-	-0.003
			(0.001)		(0.003)
Total Employment in Pref.	-	-	-	0.527***	0.495***
				(0.056)	(0.070)
Average Earnings in Pref.	-	-	-	0.046**	0.084***
				(0.017)	(0.016)
Log-likelihood	-758.4	-746.4	-677.1	-752.33	-592.7
L-1 restricted	-923.4	-923.4	-923.4	-923.4	-923.4

Significance levels: * < 0.05, ** < 0.01, *** < 0.001
Notes: Standard errors (adjusted by Wooldridge 1991, Procedure 2.1) are in parentheses below coefficients. N = 705.

Table 2
Wald Tests for Equality of Coefficients for
Entry of Keiretsu and Non-Keiretsu New Biotech Enterprises
in Poisson Regressions by Year and Prefecture in Japan, 1975-1989

Variables Included -- Equality of Coefficients Tested Groupwise[a]	χ^2 Statistics[a] by Definition of Keiretsu[b]			
	Big 8 + Vertical	Big 8	Big 6	Big 6 Pres. Club
Active Stars, Active Collaborators, Ac. Stars x Ac. Collabs.	8.40* [3]	8.61* [3]	5.03 [3]	7.84* [3]
Above variables + No. Main Professors, Total Research Funding-Univ.	9.67 [5]	12.03* [5]	11.36 [5]	9.71 [5]
Above variables + Total Employment, Average Earnings in Pref.	9.85 [7]	11.80 [7]	10.80 [7]	10.00 [7]
Only Total Employment in Prefecture, Average Earnings in Prefecture	2.46 [2]	2.42 [2]	0.81 [2]	2.45 [2]
Memo: Share of Keiretsu-Members in Total Entry	0.365	0.317	0.310	0.168

Significance levels: * < 0.05, ** < 0.01, *** < 0.001

Notes: [a]The reported statistics are distributed χ^2 with the degrees of freedom reported below each in square brackets on the null hypothesis that the coefficient for each variable is the same for entry of keiretsu-member and non-member firms in poisson regressions in which the number of births of each type are counted separately.

[b]Keiretsu membership is defined by comparing our firms with those listed as in a keiretsu of a particular type for four different definitions in a data set generously supplied by David E. Weinstein and described in Weinstein and Yishay Yafeh (1994). The Big 6 are the DKB, Fuyo, Mitsui, Mitsubishi, Sanwa, and Sumitomo horizontal groups. The Big 8 are the Big 6 plus the Industrial Bank of Japan and Tokai groups. The Big 8 + Vertical definition adds firms that are members of vertical groups. The Big 6 Presidents Club definition is the narrowest, including only Big 6 firms whose CEOs belong to their group's Presidents Club.

Table 3
Poisson Regressions of Entry of Keiretsu-Member and Non-Member New Biotech Enterprises (Big 8 + Vertical Groups Definition) by Year and Prefecture in Japan, 1975-1989

	(a) Member Entry	(b) Non-Member Entry	(c) Member Entry	(d) Non-Member Entry
Constant	-1.745***	-1.394***	-5.962***	-4.920***
	(0.070)	(0.062)	(0.783)	(0.744)
Active Stars	0.337***	0.377***	0.040	0.108***
	(0.028)	(0.022)	(0.040)	(0.032)
Active Collaborators	-0.030	0.014	-0.105*	-0.037
	(0.030)	(0.018)	(0.042)	(0.029)
Ac. Stars x Ac. Collabs.	-0.007**	-0.008***	-0.001	-0.003
	(0.002)	(0.001)	(0.002)	(0.002)
No. Main Professors	-	-	0.017	0.021
			(0.022)	(0.018)
Total Research Funding-Univ.	-	-	-0.002	-0.004
			(0.004)	(0.003)
Total Employment in Pref.	-	-	0.475***	0.509***
			(0.111)	(0.097)
Average Earnings in Pref.	-	-	0.095***	0.077***
			(0.024)	(0.022)
χ^2 for equality of coefficients[a]	8.40* [3]		9.85 [7]	
Log-likelihood	-400.6	-517.1	-332.6	-430.7
L-1 restricted	-436.9	-662.3	-436.9	-662.3

Significance levels: * < 0.05, ** < 0.01, *** < 0.001

Notes: Standard errors (adjusted by Wooldridge 1991, Procedure 2.1) are in parentheses below coefficients. N = 705. [a]The test is for each pair of regressions (a and b, and c and d, respectively). See Table 2 and text for discussion of these Wald tests. Degrees of freedom are in square brackets below the χ^2 statistic.

Table 4
Poisson Regressions of Entry of New Biotech Enterprises by Year and Local Area in Japan and the U.S., 1976-1989

	(a)	(b)	(c)	(d)	(e)
Constant	-1.352*** (0.024)	-1.570*** (0.032)	-1.812*** (0.037)	-1.771*** (0.036)	-1.924*** (0.047)
JDUMMY	-	0.784*** (0.053)	0.929*** (0.063)	-0.053 (0.064)	0.084 (0.089)
Active Stars	0.194*** (0.017)	0.158*** (0.020)	0.244*** (0.172)	-	0.139*** (0.024)
Active Stars x JDUMMY	-	0.184*** (0.031)	0.120*** (0.025)	-	-0.069* (0.033)
Active Collaborators	0.012 (0.010)	0.040** (0.013)	0.220*** (0.013)	-	0.198*** (0.015)
Ac. Collabs. x JDUMMY	-	-0.132*** (0.018)	-0.219*** (0.020)	-	-0.203*** (0.024)
Ac. Stars x Ac. Collabs.	-	-	-0.014*** (0.001)	-	-0.010*** (0.001)
Ac. Stars x Ac. Col. x JDUMMY	-	-	0.006*** (0.002)	-	0.007*** (0.002)
Total Employment in area	-	-	-	0.423*** (0.010)	0.185*** (0.027)
Total Emplmt. x JDUMMY	-	-	-	0.249*** (0.021)	0.483*** (0.046)
χ^2 JDUMMY interactions = 0	n/a	52.3*** [2]	112.3*** [3]	n/a	244.5*** [4]
Log-likelihood	-2472.8	-2378.9	-2177.6	-2305.2	-2003.7
L-1 restricted	-3116.4	-3116.4	-3116.4	-3116.4	-3116.4

Significance levels: * < 0.05, ** < 0.01, *** < 0.001
Notes: Standard errors (adjusted by Wooldridge 1991, Procedure 2.1) are in parentheses below coefficients. N = 3220. Degrees of freedom are in brackets under the χ^2 statistics. Local areas are prefectures in Japan and the Bureau of Economic Analysis's functional economic areas in the U.S.

Appendix Table A
Comparative Analysis of Factors Related to Biotechnology Enterprise between United States 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 deregulated	strongly need deregulation
research cost(gvmt:company)	45:55	27:72
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 1991	140	18

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

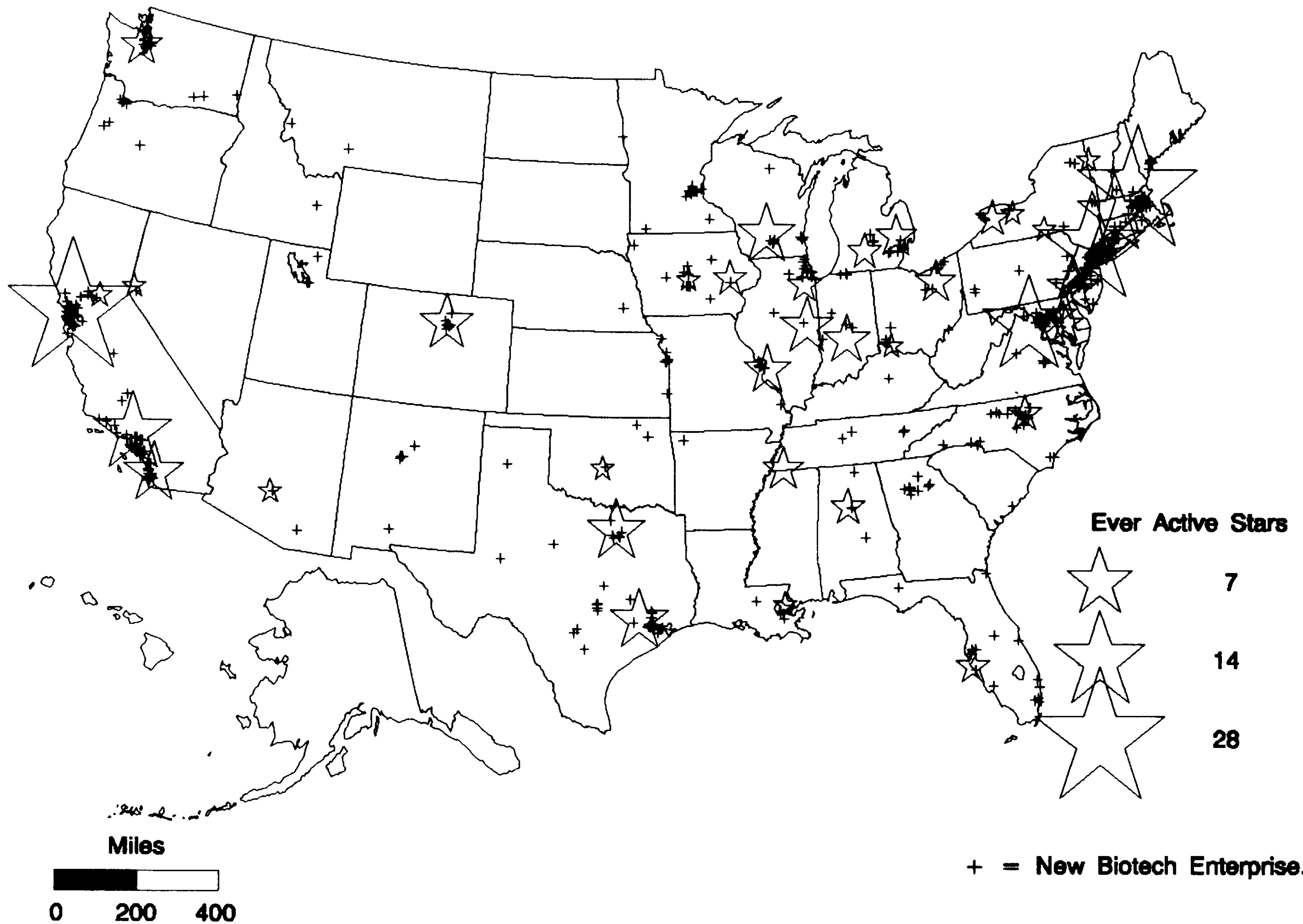
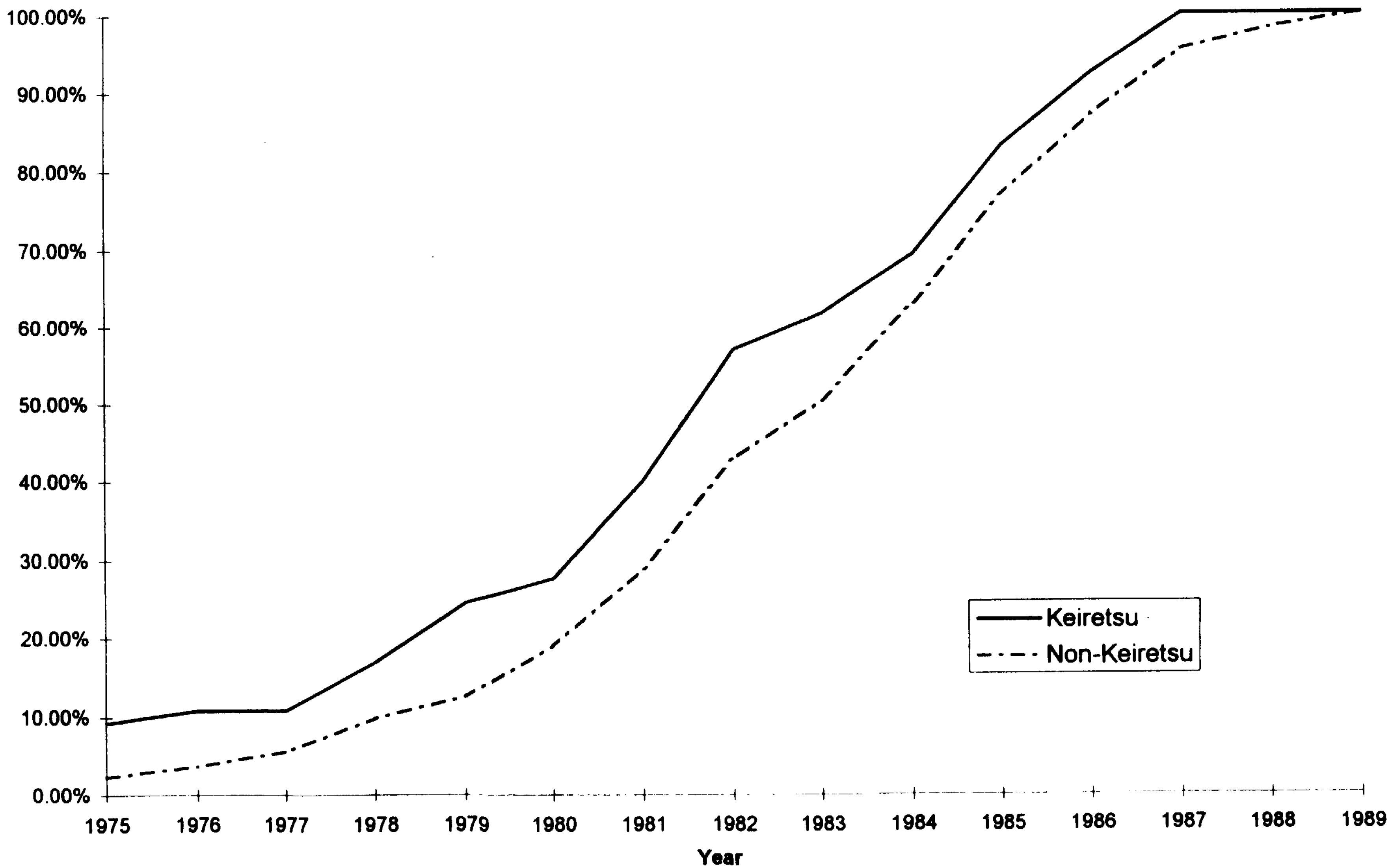


Figure 1. Active Stars and New Biotechnology Enterprises as of 1990
in the U.S.

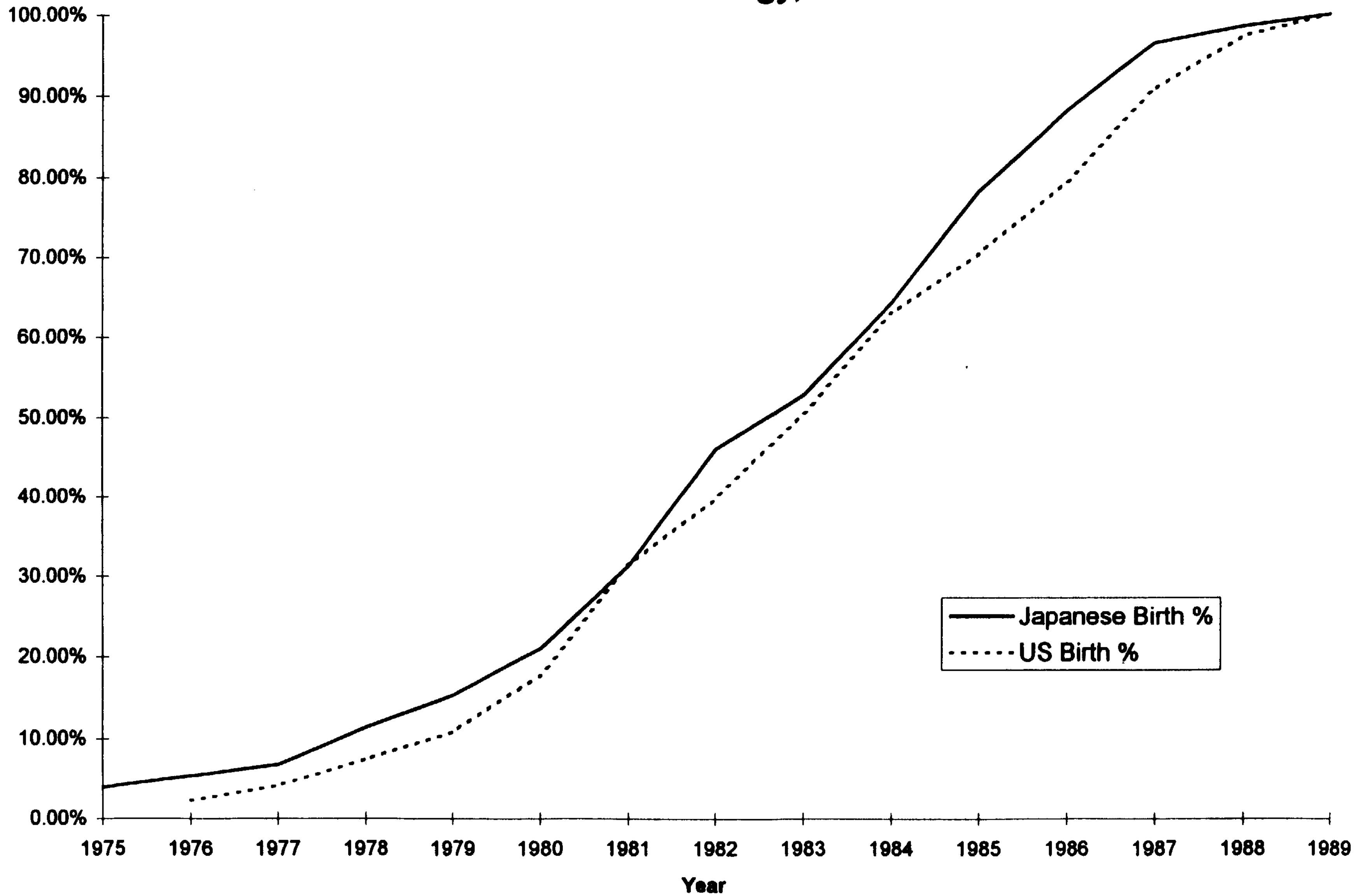
Figure 2. Active Stars and New Biotechnology Enterprises as of 1990 in Japan

Figure 3. Cumulative Densities for Entry of Keiretsu Members and Non-members into Biotechnology, 1975-1989



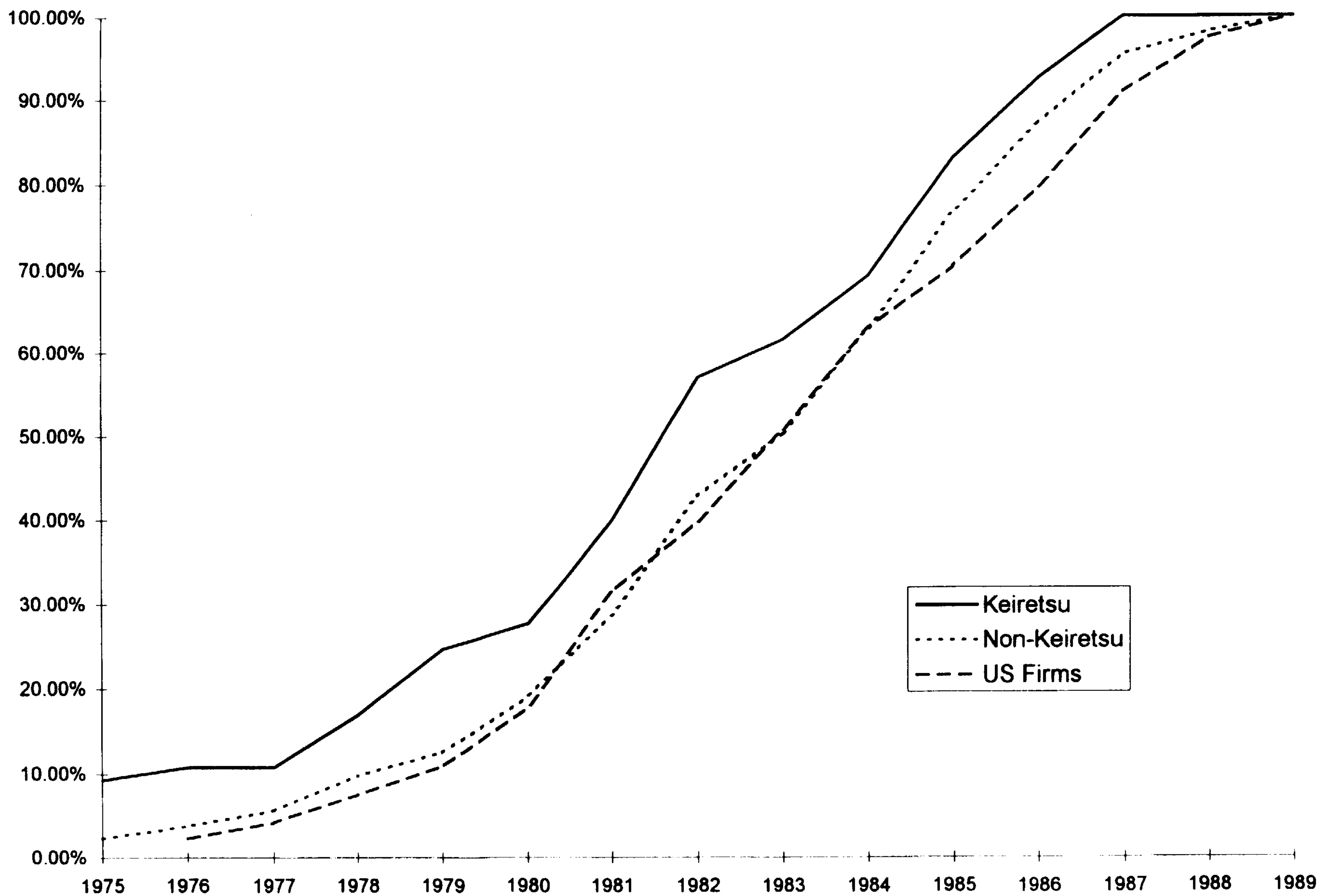
Note: Keiretsu = Entry by members of Big 8 plus Vertical Groups. Non-Keiretsu = Entry by all others.

Figure 4. Cumulative Densities for Entry of Japanese and American Firms into Biotechnology, 1975-1989



Note: Japanese Birth % = Entry by all Japanese new biotechnology enterprises to date as a percentage of total entry 1975-1989 (primary locations only). Japanese entry is defined by source to begin in 1975. US Firms = Entry by all U.S. new biotechnology enterprises to date as a percentage of total entry 1976-1989; U.S. entry is defined in the data set to begin in 1976.

Figure 5. Cumulative Densities for Entry of U.S. Firms vs. Japanese Keiretsu Members and Non-Members into Biotechnology, 1975-1989



Note: Keiretsu = Entry by members of Big 8 plus Vertical Groups. Non-Keiretsu = Entry by all other Japanese firms. Japanese entry (primary locations only) is defined by source to begin in 1975. US Firms = Entry by U.S. new biotechnology enterprises; defined to begin in 1976.