ACADEMIC-CORPORATE TIES IN BIOTECHNOLOGY: A QUANTITATIVE STUDY

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The rapid commercialization of applied genetics in the mid-1970s, accompanied by a sudden rise in academic-corporate partnerships, raised questions about the impacts these linkages have had on the social and professional norms of scientists. The extent and pattern of faculty involvement in commercialization of biological research is largely an unexplored area. This article provides a quantitative assessment of the linkages between biology faculty in American universities and the newly formed biotechnology industry. The results of this study, covering the period 1985-88, show that academic scientists responded en masse to participating in the commercialization of genetics research by establishing formal associations with many of the new biotechnology companies. A data base consisting of 889 U.S. and Canadian biotechnology companies and 832 scientists who had formal ties to them was developed over a four-year period. The patterns of academic-corporate linkages are revealed by institution. Three universities with the most commercially active faculty are Harvard, Stanford, and MIT. Of the 359 biomedical scientists and geneticists who were members of the National Academy of Sciences (in 1988), at minimum, 37% had formal ties with the biotechnology industry.

Rapid commercialization of the biological sciences began several years after the 1973 discovery of recombinant DNA (rDNA) molecule techniques. Potential applications of "gene splicing" to a wide range of industrial, agricultural, and pharmaceutical products stimulated the founding of hundreds of new firms (see Figure 1). Billions of dollars of venture capital were invested in just a few years (U.S. Congress, Office of Technology Assessment

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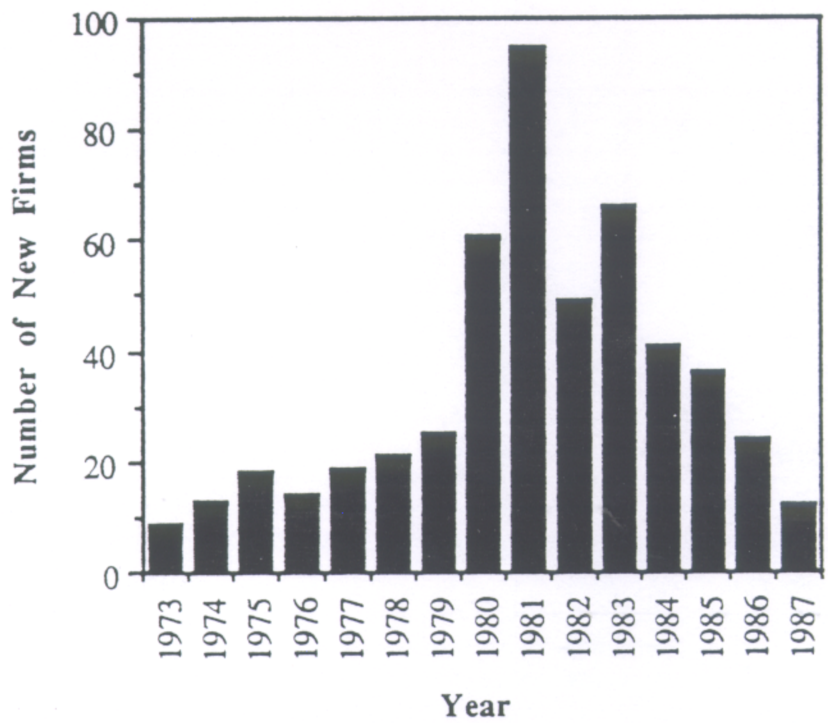

Figure 1. New biotechnology firms, by founding dates: 1973-1987 (N = 493).

1988, 80 [cited as OTA 1988]; Crawford 1986, 12-14). Academic scientists were centrally involved in the birth and development of many of these firms. While dual affiliation of scientists with universities and with for-profit companies is common in some academic fields, there is reason to believe that the practice is especially pervasive and significant in biotechnology. These linkages merit consideration for several reasons. Some possible negative consequences include potential conflicts of interest, redirection of research from basic to applied areas, erosion of openness of scientific communication, and detrimental effect on graduate training. On the other hand, positive consequences of such ties might include new and necessary sources of research funding, increased incentive for scientific innovation, increased yield of beneficial new products, more rapid technology transfer from universities and government labs to industry, and competitive advantage in international markets.

University-industry relations were the subject of intense media scrutiny and congressional oversight between 1980 and 1983. Subsequently, the commercialization and possible politicization of the biological sciences became the focus of new scholarly studies. Etzkowitz (1983, 198-233) finds the historical roots of academic entrepreneurship in early nineteenth-century German science and traces its evolution and development in pre-World War II America. Weiner (1986, 33-43) presents historical evidence that spirited debates over patenting medical discoveries raged early in this century. Blumenthal, Epstein, and Maxwell (1986, 1621-26) describe the success of the Wisconsin Alumni Research Foundation (WARF), which provided a commercial outlet to university scientists for more than a century. The works of Kenney (1986) and Dickson (1984) describe how academic institutions have sought new sources of funding and a more favorable political climate for university-industry partnerships in biology. And through a series of in-depth interviews, Etzkowitz (1984; 1989, 14-29) explores the values, motivations, and changing norms of entrepreneurial scientists and university administrators across disciplines.

Until 1984, there were many conjectures about how commercialization of applied genetics was affecting universities and their faculty, but as yet no systematic effort had been made to study these effects. In that year Harvard University's Center for Health Policy and Policy Management initiated a study that surveyed over 100 firms and more than 1,200 biomedical faculty in over 50 U.S. universities. Two published papers from that study provide the best current data on the extent and impacts of faculty-industry research relationships (Blumenthal, Gluck, Louis, and Wise, 1986, 242-46; Blumenthal, Gluck, Louis, et al., 1986, 1361-66). Also in 1984, the Office of Technology Assessment (OTA) published a study on commercial biotechnology with a chapter dedicated to university-industry relationships (U.S. Congress, Office of Technology Assessment 1984 [cited as OTA 1984]). In connection with its study, OTA sponsored a survey of six universities with strong biomedical research facilities and of 15 biotechnology companies to gain information on the factors responsible for and the nature of the new relationships in biology.

Academic-industry relations are only partly expressed through research relationships. Other types of relationships include shared patent rights, equity interests, consultantships, and managerial roles. The question we posed for our study is, Can a quantitative and objective measure be developed that exhibits the structure of faculty-industry relations across American universities but does not depend on faculty self-reports? The advantage of such a measure is that it can reveal demographic patterns while also showing the fine structure of industry-faculty associations within individual institutions. These results are important for gaining a better understanding of the potential for conflicts of interest, shifts in the research agenda, and the potential obstacles to intellectual exchange.

Method

The goal of our study is to exhibit the linkages between university faculty and the biotechnology industry during the industry's early stage of development. The years 1985-88 were chosen as the test period. The method consists of three elements. First, the term *faculty-industry linkage* was defined. Second, a system for quantifying the linkages was developed. Finally, a linkage map was constructed of commercially active faculty and the new biotechnology industry for North American colleges and universities. The university-industry relationships we chose to measure are those in which faculty have a formal association with a firm. Faculty are considered to have formal associations if they satisfy one or more of the following conditions: (a) serve as a member of the firm's scientific advisory board (SAB) or as a standing consultant; (b) hold managerial position in the firm; (c) possess substantial equity in a firm (i.e., sufficient equity to be listed in a public firm's prospectus); or (d) serve on the board of directors of a company. University biological/biomedical faculty who satisfy the criteria listed above will be called *dual-affiliated biotechnology scientists* (DABS).

Industry-university linkages as defined above represent the highest degree of scientist involvement in the commercial sector, namely, formal associations with a firm. As such, they are most likely to have consequences of concern. While the Harvard study encompasses industry-funded research relationships of any duration, the focus of this study is on those ties likely to be more enduring and involving.

Our faculty sample excludes individuals with small equity interests in a company who otherwise do not meet any of the four conditions listed above. While equity interests of any magnitude may influence behavior of faculty, small equity interests were excluded from our study because they could not be systematically identified by our method and because we sought an indicator of active and substantial firm involvement.

Between 1985 and 1988 we constructed a list of 889 U.S. and Canadian biotechnology firms. Two criteria guided the selection of firms. First, a firm must be involved in the microbiology, genetics, or biochemistry of cells. Companies that specialize exclusively in bioprocessing, fermentation, large-scale purification, and instrumentation were excluded. Second, we included only newly established (post-1973) companies, their subsidiaries, or established companies that formed new research and development divisions in biotechnology in the aftermath of the genetics revolution. Firms were located by using standard industry directories, trade association lists (e.g., Industrial Biotechnology Association), publication inventories (*Genetic Engineering News*), government studies, personal contacts, media accounts, and other sources. Under the U.S. Securities and Exchange Act, firms that issue public securities are required to file prospectuses and annual financial disclosure statements (10K reports) that include information about management personnel. By reviewing these documents, we obtained the names of university faculty who were founders, board members, major shareholders, standing consultants, or members of the firm's SAB. For private companies that are not required to issue public prospectuses, we sent a one-page questionnaire requesting the founding data, the public/private holding of the firm, whether it employed a SAB, and the names of its board members.

Pretest samples were sent first to 51 and then to an additional 53 firms during the spring of 1985; another 289 private firms were queried in March 1987. Firms that did not respond to the mail survey were contacted by telephone and asked the same questions. In August 1988, 507 remaining firms on which we had no information were sent the survey. Overall, we obtained usable information on 539 firms or 60.6% of the total list of 889.

Of the firms for which we obtained information, 54.0% (291) reported having a SAB, and 46.0% (248) responded negatively. Response bias may inflate the yes percentage somewhat, since firms with SABs might view the question as more pertinent and, therefore, be more likely to respond. Nevertheless, the overall yes percentage can be no lower than 32.7% (i.e., 291/889) Thus the proportion of all biotechnology firms with SABs is roughly between one-third and one-half. In order to determine whether nonrespondents in the final sample were systematically different from respondents, we randomly selected 95 nonrespondents from the final sample and contacted them by telephone. Of this group, 22 (23%) had SABs and 18 (19%) did not; 24 (25%) had gone out of business or were no longer at their listed address or phone number. Eight firms refused to respond to the survey. The remaining 23 (24%) did not answer repeated calls. Those firms that provided information had a 55% SAB rate (22/40), which is comparable to what we found in the mail survey. In a rapidly moving field like biotechnology, there is a substantial turnover of firms (new arrivals and bailouts) within a short time period. If we assume, conservatively, that one-half of the 350 firms that failed to respond are still in business and that 55% of these have SABs, then there are roughly another 96 SABs that we have not located.

The final data base has two parts. The first consists of 889 biotechnology companies, and the second consists of 832 scientists (including plant pathologists, microbiologists, geneticists, and biochemists) with formal relationships to biotechnology firms. As a small number of scientists hold affiliations with more than one company, they therefore appear more than once in the data base. The search yielded 927 linkages with a median SAB board size of 3 (mean = 4.3, maximum = 29; minimum = 1). If the estimated number of missing SABs (96) is multiplied by the median SAB size, then we estimate roughly that an additional 288 "missing" scientists serving on biotechnology advisory boards are not recorded in our data base.

Of the 889 firms, 286 (32%) are public, 406 (46%) are private, and 197 (22%) have an undetermined status. More than one-half the total number of firms are composed of newly established companies (post-1973), subsidiaries, or new biotechnology divisions of established companies.

The data base represents aggregated entry points in the biotechnology field for firms and DABS. Although there has been some winnowing of firms during the four-year period and some scientists have retired from academe or disaffiliated from a firm, these data points remain included so long as a scientist or a firm meets the criteria at any time during 1985-88.

Patterns of Linkage

As noted, our survey of biotechnology firms revealed that 291 (32.7%) have SABs. New firms are more likely than established firms to have SABs, since displaying intellectual capital can help attract financial backing. Many private firms treat their SAB membership as proprietary information. Moreover, new firms are constantly forming, and some may have been missed in our surveys. Despite these limitations, a data map with over 800 DABS reveals the structural relationships between a nascent industry and the academic sector.

Our demographic analysis of the biotechnology industry shows that the highest concentrations of new biotechnology firms are in California, Massachusetts, Maryland, New Jersey, and New York, in descending order. Nearly 40% of the firms are located in California (OTA 1988, 68; see Figure 2).

Start-up companies frequently sought financing based on the promise of the techniques, in some cases without explicit product ideas, prototypes, or patents in hand. Having prominent scientists on the firm's SAB can bolster the confidence of prospective investors. The data indicate that faculty from large, prestigious universities were most heavily involved in the promotion

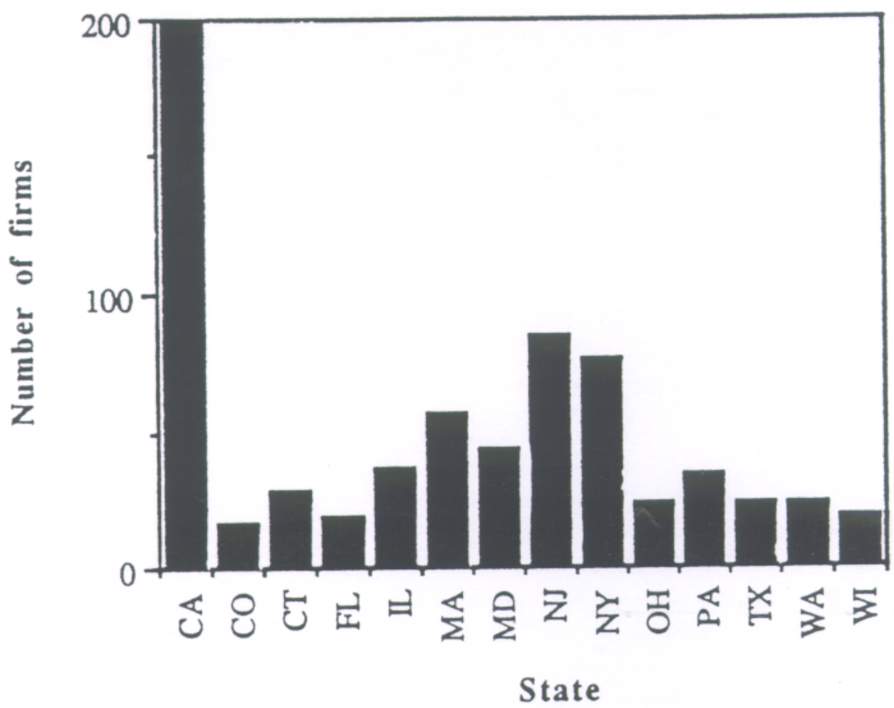

Figure 2. States leading in the formation of new biotechnology firms: 1973-1987.

and development of new firms. Table 1 shows the distribution of DABS and their linkages to firms for 24 universities with the largest number of faculty involved in the commercialization of biology. Thus, from our data base, Harvard has 69 DABS from its Faculty of Arts and Sciences and its Medical School, representing 83 linkages (formal ties) to 43 companies. The higher figure for linkages indicates that some faculty have formal ties to more than one firm. Also, some companies sign up multiple faculty from a given institution.

The closest competitor to Harvard in faculty-industry links is Stanford, with 40 DABS, 51 linkages, and 25 firms. MIT, which does not have a medical school, shows a very commercially active biology department with 35 DABS, 50 linkages, and 27 firms. The ratio of DABS to the total biotechnology faculty of an institution or department is an indicator of university penetration by the new industry. However, the total number of DABS for a given university may be distributed over many departments, some of which may be only marginal to the commercial development of biotechnology. Thus the ratio of DABS to total biomedical faculty is not a

Table 1. Linkages of Biomedical Faculty to Firms

	Number of DABS[a]	*Number of Links*	*Number of Firms*
Harvard	69	83	43
MIT	35	50	27
Stanford	40	51	25
University of California, San Francisco	24	28	14
Yale	22	26	21
University of California, Los Angeles	26	30	19
University of California, Berkeley	22	24	16
University of California, San Diego	22	22	11
Johns Hopkins	20	24	16
Columbia	15	18	15
University of California, Davis	17	17	12
New York University	14	15	12
California Institute of Technology	12	15	11
Baylor	17	18	11
Cornell	20	20	15
University of Texas	21	27	22
University of Wisconsin	24	24	19
University of Washington	21	22	18
University of Colorado	12	15	10
University of Michigan	11	12	12
University of Minnesota	16	16	12
University of Pennsylvania	15	17	11
Rockefeller University	10	12	12
Tufts	11	12	11

a. DABS = Dual-affiliated biotechnology scientists.

useful indicator of the degree to which departments have been affected by commercial affiliations. Instead, we have calculated the percentage of DABS in select departments for 10 universities. The total number of faculty in these key departments was obtained from university catalogs and Peterson's *Guide* (see Table 2). Twenty-three of MIT's 35 DABS are in the Department of Biology, which lists 74 members. The rate of commercialization penetration (de minimis) for this one department at MIT is 31.1%.

In contrast, Stanford and Harvard, with medical schools, have, respectively, four and six commercially active departments with de minimis penetration rates of 19.5% and 19.2%, respectively. At the University of California, Davis; the University of California, San Francisco; and the University of California, San Diego, most of the dual-affiliated faculty are located in one or two departments, with penetration rates between 11% and 15%.

Table 2. Rate of Commercial Penetration into Select University Departments

	Number of Key Departments	Number of Faculty	Number of DABS[a]	% Penetration
MIT[b]	1	74	23	31.1
Stanford[c]	4	82	16	19.5
Harvard[d]	6	156	30	19.2
University of California, Davis[e]	2	38	6	15.8
University of California, San Francisco[f]	1	61	9	14.8
University of California, Berkeley[g]	5	103	14	13.5
University of Washington[h]	2	79	10	12.7
University of California, Los Angeles[i]	4	115	14	12.2
University of California, San Diego[j]	1	77	9	11.7
Yale[k]	4	126	14	11.1

a. DABS = Dual-affiliated biotechnology scientists.
b. Department of Biology.
c. Medical School—Departments of Biological Chemistry, Genetics, Microbiology and Immunology, and Biological Sciences.
d. Arts and Sciences—Departments of Biochemistry and Molecular Biology; Division of Medical Sciences—Departments of Biological Chemistry and Molecular Pharmacology, Cellular and Development Biology, Genetics, Microbiology and Molecular Genetics, and Medicine.
e. Departments of Plant Pathology and Department of Biochemistry and Biophysics.
f. Department of Biochemistry and Biophysics.
g. Departments of Biochemistry, Microbiology and Immunology, Plant Biology, Plant Pathology, and Molecular Biology and Genetics.
h. Medical School—Departments of Biochemistry and Microbiology.
i. College of Letters and Science—Department of Cell and Molecular Biology and Department of Microbiology; School of Medicine—Departments of Biochemistry and Microbiology.
j. Department of Biology.
k. Department of Biology and Department of Molecular Biophysics and Biochemistry. Medical School—Departments of Human Genetics and Cell Biology.

Blumenthal, Gluck, Louis, et al. (1986, 1364) found that biotechnology faculty with industry support were four times as likely to report that trade secrets resulted from their research than other biotechnology faculty were. Another factor that may impede open communication is the number of firms represented within one university or within a single department. In settings where many professors are linked to competing firms, there may be more restrictions on scientific interchange. Table 1 shows the number of firms represented by the DABS at selected high-profile universities. At Harvard, at least 43 independent firms are represented by the formal affiliations of its biomedical faculty. A small percentage of these firms were started by Harvard scientists. At MIT and Stanford the figures are 27 and 25, respectively.

Prospectuses of some firms stipulate proprietary covenants with SAB members. Some may view the diversity of corporate affiliations at a single institution as a positive sign that universities are not subject to the dominance of a single firm. Nevertheless, the magnitude of firm representation within the university helps us to explain the emergence of a new climate in biology in which limited secrecy (Etzkowitz 1983, 198-233) replaced free and open communication.

National Academy of Sciences

Our data show that the new biotechnology industry was actively supported by academic scientists in the nation's leading universities. Participation in the commercial applications of molecular genetics by the nation's elite scientists is reflected in the membership of the National Academy of Sciences (NAS). The academy plays a major consultative role for Congress and other government bodies on a wide range of issues of major concern to society. Academy members frequently serve on panels that issue health and safety recommendations for new products or technologies. The data base was used to determine a lower bound of DABS who were members of the NAS. Of a total of 359 academy members who may be classified as biologists and biomedical scientists (as of 1988), 132 (37%) were identified in the data base with formal ties to companies.

Since membership in the academy is lifelong, the effective percentage of currently active NAS members with industry affiliation may be significantly higher. One NAS member estimated that for active members, the number of DABS is well over 50% (Milunsky and Annas 1985, 67).

Peer Review

Peer review is an essential part of the international system of science. It is difficult to imagine the organization of science as we know it without a peer-review process. Not only does it help improve the quality of published papers, but it also plays an invaluable role in allocating federal research funds.

Reviewers of grant proposals, where innovative ideas germinate, are bound by a code of ethics. A reviewer is expected to protect unique unpublished ideas in a funding proposal from precipitous disclosure and exploitation.

Many of the peer reviewers today have commercial ties. Cutting-edge research may be essential to a firm's competitiveness. Consequently, there is more incentive to circumvent the norms of peer review and channel innovative ideas of grant applicants directly to the commercial sector.

We used the DABS data base to test the relationship of peer reviewership with commercial affiliation of scientists. The National Science Foundation (NSF) provided a complete list of potential and actual peer reviewers for fiscal years 1982 and 1983. The list includes the number of proposals reviewed by each individual. We compared that list with the DABS data base. Forty-nine percent of the dual-affiliated scientists appeared on the NSF peer-review list as potential reviewers in the biomedical sciences. Of the 832 scientists in the data base, 343 (41.2%) reviewed one or more proposals during the two-year period.

It is very difficult to prevent people who are so inclined from pilfering ideas while they serve as peer reviewers. The integrity of the system depends upon the adoption of informal ethical norms by members of the scientific community. Stigmatization and moral opprobrium are important disincentives for violating the norms. But the opportunity to channel innovative ideas in funding proposals to selected commercial enterprises may exacerbate the pilfering of innovative ideas. This may lead some scientists to seek commercial funds for their ideas rather than risk having them stolen through the peer-review process.

Conclusion

In less than a decade, the fields of molecular biology, genetics, and biochemistry in the United States have experienced a dual transformation. First, they have been transformed as basic sciences in the aftermath of the discoveries of gene splicing and gene synthesis. Second, they have been transformed as social institutions as the marriage between academic and industrial science was consummated.

This study has generated the first quantitative map of university-industry linkages across the biological disciplines arising from these transformations. The results indicate that such ties are widespread. U.S. biologists, en masse, have responded to the opportunities of entrepreneurial science. These linkages have appeared rapidly, as university policies have changed and as norms of behavior among biological scientists have shifted. In addition to the overall rate of affiliation, however, the differential location deserves attention. To the extent that these ties are focused on central, elite universities, their consequences are likely to be profound. These institutions not only are the wellspring of future path-breaking discoveries, they also are vital as the training grounds of the next generation of leading scientists and academic faculty. For these reasons, the heavy concentration of faculty-industry ties in first-rank institutions is likely to magnify their possible consequences. Faculty with university and industry affiliation in the biological sciences are becoming the rule rather than the exception in the United States and Canada. Many leaders in the field of molecular biology paved the way to entrepreneurship and serve as role models for younger faculty.

These data focus on relatively enduring forms of corporate involvement. While we have not examined less involving, more transitory associations such as contract research relations, we believe that they will magnify the pattern seen here. Most established large biotechnology firms do not have SABs, but they do have networks of consultants. These relations may also affect the behavior of academic scientists. Therefore, our data understate the full extent of faculty-industry linkages by emphasizing SAB membership or managerial participation, exclusively. The data base of DABS offers the possibility of testing additional hypotheses about the effects of industry associations among academic faculty, particularly the potential influence of commercial affiliation on research agendas, conflicts of interest, and norms of scientific communication.

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