# Inter-Organizational Collaboration in the Biotechnology Industry

by

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This paper examines the key factors that promote inter-organizational collaboration in the biotechnology industry, a field where research breakthroughs are so broadly distributed that no single firm has all the necessary capabilities. The science of biotechnology has brought extensive changes to research universities and multinational pharmaceutical companies, as well as generated hundreds of small science-based entrepreneurial companies, located mostly in the U.S. In this industry there are severe limitations to market transactions and disincentives to vertical integration. Instead, through a combination of mutual need, repeated interaction, and membership in a common technological community, networks of collaborative ventures serve as the primary institutional arrangement governing exchange and production. (JEL: L 23)

## *1. Introduction*

Over the past two decades a new logic of organizing has emerged to challenge mass production. The canonical large corporation, based on the principles of vertical integration, dedicated machinery, a hierarchical structure of management, and a detailed division of labor, is giving way to more flexible forms. Scholars are struggling to understand the etiology and consequences of these ostensibly new modes of governance. Indeed, the varied labels attached to these novel structures – hybrids (WILLIAMSON [1991]), networks (POWELL [1990]; TEUBNER [1991]), symbiotic arrangements (SCHANZE [1991]), or flexible specialization (PIORE and SABEL [1984]) – suggest a lack of consensus about how organizational arrangements that rely on neither market transactions nor hierarchical authority actually work. Indeed, there is considerable debate about whether these modes of governance are actually new, or represent a reemergence of older practices (SABEL [1993]).

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Evidence of a sea change in the prevailing logic of production is seen in many locales: a) in the diversified, interfirm linkages of suppliers, subcontractors, assemblers, and end users that typify the industrial districts of southwestern Germany and north central Italy (BRUSCO [1982]; HERRIGEL [1990]; SABEL [1989]); b) in the Japanese business groups that have long relied on extensive subcontracting, joint learning, diffuse responsibility for technological innovation, and inter-firm cooperation (AOKI [1990]; DORE [1987]; FRUIN [1992]; GERLACH [1992]; SAKO [1992]); and c) in the transformation of large corporations through the launching of all manner of collaborative ventures with former competitors that blur organizational boundaries in profound ways (BADARACCO [1991]; HARRISON [1994]; POWELL and SMITH-DOERR [1994]; SAXENIAN [1994]).

The rapid expansion in corporate "partnering" and the reliance on diverse forms of external collaboration have been widely documented (GULATI [1995]; HAGEDOORN [1990]; HERGERT and MORRIS [1988]; MOWERY [1988]). These varied types of inter-firm alliances are especially pronounced in R & D-intensive sectors (EISENHARDT and SCHOONHOVEN [1996]; FREEMAN [1991]; HAGEDOORN [1995]). In part, this movement toward stronger involvement in external relationships reflects the increasing diversity of institutional sources of innovation. Non-U.S. firms, especially German and Japanese corporations, as well as universities, government laboratories, and nonprofit research institutes now play a vital role in developing new forms of knowledge and new kinds of products (NELSON [1990]). Moreover, when there is a regime of rapid technological development, research breakthroughs are so broadly distributed that no single firm has all the internal capabilities necessary for success. Many groups of competitors are likely to be working on the same targets; the rewards go to the swiftest. Thus, new technologies are both a stimulus to and focus for a variety of collaborative behaviors that seek to reduce the inherent uncertainties associated with novel products or markets.

Although there is ample documentation of the growth in collaborative ventures, knowledge of the governance – institutional ways and means – of these partnerships remains primitve. Are the forces that promote external collaboration period-specific, or unique to a regime of technological change? Are the principles that govern cooperation durable, or easily undermined in the face of failure or environmental changes? In short, has there been a fundamental "change in the technology of institutional design" (SCHANZE [1993, 693])? This paper addresses these questions in the context of inter-organizational relationships in the biotechnology industry, a sector noted for perhaps the most extensive reliance on external collaborations (ARORA and GAMBARDELLA [1990], [1994]; POWELL and BRANTLEY [1992]; POWELL, KOPUT and SMITH-DOERR [1996]). On several key dimensions, the biotech sector appears to be unique. Nevertheless, this research is generalizable in several respects: it heeds COASE'S [1992] call for more fine-grained analysis of the institutional arrangements that

govern exchange and production; and it offers insight into how cooperation can be sustained in competitive circumstances.

## *2. Biotechnology: Origins and Development*

The science underlying biotech has its origins in university laboratories and research institutes. The intellectual origins of the field date back forty years to Watson and Crick's mapping of DNA, but the initial core technologies were developed in the 1970s. Universities and research institutes played a critical role in biotech's emergence, not only as the places where young scientists were educated but also as the sources of breakthrough discoveries and techniques that fostered scientific and technological innovation. Indeed, the science and technology of biotechnology are inextricably intertwined. It is as accurate to say that the new technologies have fostered the new science as the other way around. But biotechnology has also triggered sharp changes in university practices, requiring an interdisciplinary mixing of specialities in a manner, and to an extent, unprecedented in biomedical research. Moreover, biotechnology has largely collapsed the distinction between basic and applied science. Consequently, fundamental research in the biosciences has simultaneously become commercially relevant, with dramatic consequences for a number of parties.

University research is thus an essential contributor to the advance of biotechnology, but the commercialization of the science has been initiated by dedicated biotech firms, founded by the score throughout the 1970s, '80s, and '90s. These small, science-based, entrepreneurial companies have attacted enormous attention from both the financial and research communities. The first companies went public in 1980. In the decade and a half since, hundreds of companies have been created in the U.S. (and many more abroad). Investors of all kinds have poured billions into biotech (by some accounts, more than $ 60 billion by 1993).[1] But these entrepreneurial companies face stiff obstacles. The process of creating new biotech drugs is research-intensive, very protracted, and extraordinarily expensive.[2] Nonetheless, by the close of 1994, more than two dozen biotech drugs and vaccines had been approved by the U.S. Food and Drug Administration, more than 200 medicines are at present in various stages of clinical testing, and some two dozen drugs await FDA approval.[3] Many of the initial medicines, such as those for treatment of kidney failure or heart attack, had sales well in excess of $ 500 million in just a few years. Biotech industry

[1] Figure quoted in "Panic in the Petri Dish," *The Economist*, July 23, 1994, pp. 61f.

[2] The "ballpark" figures commonly cited are 6 to 10 years from discovery to market, at a cost of $ 100–$ 250 million.

[3] Information on U.S. regulatory approvals comes from *Pharmaceutical Manufacturers Association Annual Reports* in 1993 and 1995.

sales reached $ 7.7 billion in 1993, an impressive sum for a young field but still two billion less than the sales of pharmaceutical giant Merck.[4]

The cross-traffic between universities and biotech companies is so extensive and reciprocal that it is approriate to consider them part of a common technological community. University professors take their sabbaticals at biotech firms, and both postdoctoral fellows and senior scientists move back and forth between universities and biotech firms. Biotech scientists at Genentech and Chiron are among the most-cited researchers in molecular biology and genetics.[5] These close relationships are unprecedented in the recent history of high tech. In part, they are due to the industry's closeness to fundamental basic science, but these developments also come at a time when universities face tight budgets and existing sources of federal funding for biomedical research have been stagnant. As a result, biotechnology is reshaping university policy regarding relations between professors and private companies, and altering both the traditional means of funding biomedical research and the opportunity structures for young scientists. A new identity has emerged – the scientist-entrepreneur. What would once have been regarded as inappropriate for a top scientist is now increasingly viewed not just as legitimate but as desirable. This new identity is a combined product of the quality of the science done at commercial firms and the financial exigencies facing universities.

Most biotech firms have been started by scientists, with the assistance of either venture capitalists, law firms specializing in high tech, or ex-pharmaceutical executives. Because their focus was on science, and a firm's reputation was tied to its R & D prowess, the scientists "contracted out" many of the financial and managerial aspects of the business. An organizational model developed in which biotech firms possessed an "open architecture," a fluid structure in which some of the key functions were provided by "outsiders" and key projects were pursued jointly with external collaborators. Figure 1 is an illustration of Biogen, a Cambridge, Massachusetts firm with multiple external collaborators, where a great many more employees work on Biogen projects outside the firm than inside it. Biogen is a successful example of a firm with permeable boundaries, organized on a project team basis. In such an environment, firms quickly develop reputations for whether or not they are good at cooperation, and this news travels rapidly through the technological community. Similarly, professional service firms – lawyers, venture capitalists, consultants, etc. – develop reputations for their expertise. Law firms and venture capitalists have responded by hiring young Ph. D's. in molecular biology and sending them off

[4] Annual sales figures provided by Ernst & Young, reported in *Wall Street Journal*, Medical and Health Report, May 20, 1994.

[5] In a ranking of high-impact publications in molecular biology and genetics over the period 1988–1992, the top five institutions in terms of citations per paper were the Salk Institute, Cold Spring Harbor Laboratories, the Whitehead Institute, Genentech and Chiron. The latter two are dedicated biotech firms. Data provided by the Institute for Scientific Information, reported in *The Scientist*, November 15, 1993, p. 14.

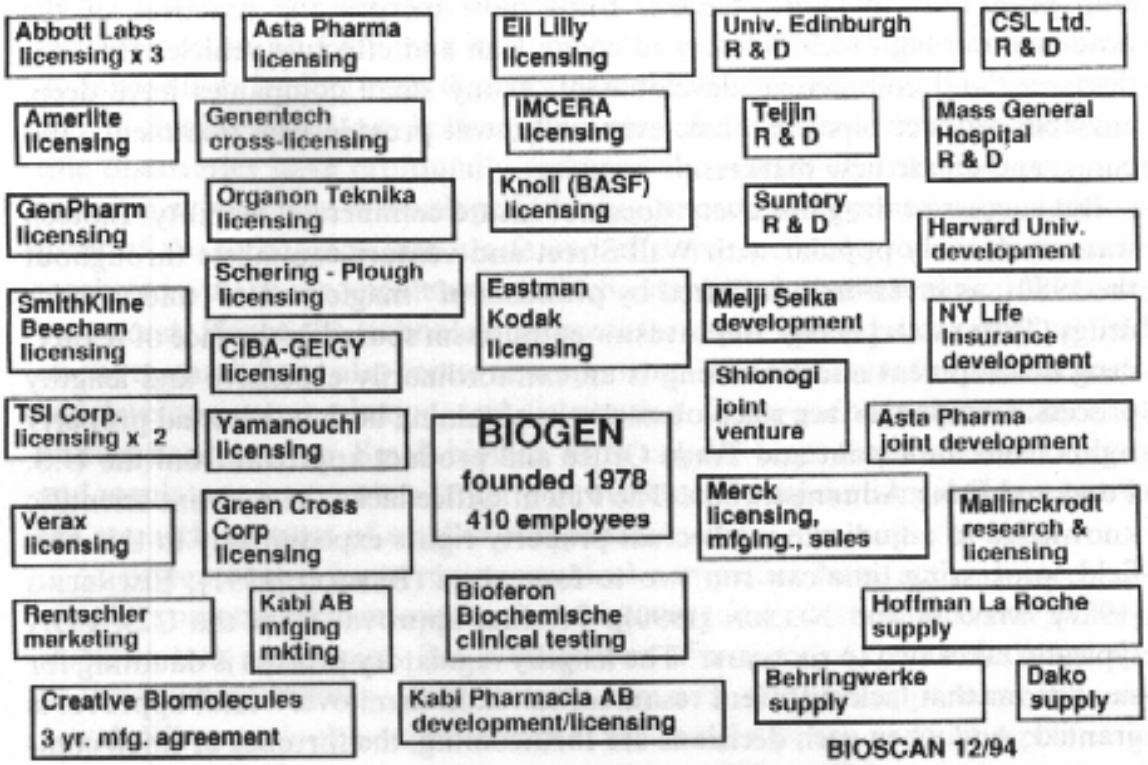


*Figure 1*

for legal or financial training. Law and venture capital firms play a key role as bridging institutions, bringing scientists into contact with sources of managerial expertise, advising firms on patenting strategies and how to structure partnerships, and steering young companies through their early years. New mechanisms for starting and financing science-based companies have been created, and a dense consultative network is in place to provide services and guidance. The incompleteness of financing, that is, every firm needs more funds to sustain costly research programs, produces high-powered incentives inside the firm and encourages firms to look for external partners. Inside a biotech firm, there is keen awareness that if something good happens, all the participants benefit. Externally, partners that perceive correctly what a firm can accomplish are eager to provide a wide range of key organizational functions. (The role of elite law and venture capital firms in creating an industry infrastructure is not limited to biotech; for other high tech industries, see SUCHMAN [1994].)

Internally, biotech companies organize themselves flexibly into overlapping, interdisciplinary project teams. The firms have minimal hierarchy, researchers are given ample time to pursue their own work, and merit pay is commonly tied to publication.[6] Some biotech firms have created their own postdoctoral fellow-

[6] For a useful illustrative account of the "managed chaos" of biotech R & D, see "Amgen, Inc.: Planning the Unplannable," Harvard Business School, case 9-492-052, 1992.

ship programs. In short, biotech firms have merged the practices of the academy and high tech industry to create lean and effective vehicles for drug discovery and commercial development. Many small companies have deep, enviable product pipelines that, eventually, will provide new treatments and cures, and create new markets.

But success at drug discovery does not insure commercial viability. Biotech was enormously popular with Wall Street and venture capitalists throughout the 1980s, as investors were lured by promises of "magic bullets" and wonder drugs (TEITELMAN [1989]). But investor enthusiasm soured in the face of reality; drug development and launching is an extraordinarily expensive and lengthy process. Companies face steep obstacles in obtaining both intellectual property rights from the Patent and Trade Office and product approval from the U.S. Food and Drug Administration. The Patent Office lacks the relevant scientific knowledge to adjudicate intellectual property rights expeditiously in this new field; processing time can run two to four years (BARTON [1991]; EISENBERG [1987]; MERGES and NELSON [1990]). Product approval from the U.S. FDA typically takes two to six years.[7] The lengthy regulatory process is daunting for small firms that lack sufficient resources to "hold them over" until approval is granted. And when such decisions are forthcoming, the fortunes of small companies gyrate, climbing to lofty levels when approval is obtained or going into a tailspin when approval is not granted, often forcing a small company into the arms of a larger partner.

With a great many biotech firms in need of funding to support costly research, as well as short on experience with the regulatory approval process, marketing, and distribution, the balance of power might be expected to shift to the large pharmaceutical corporations. But pharmaceuticals are under stiff pressures from other sources, discussed below, and as the pharmaceutical field restructures, biotech is deeply involved but does not face wholesale absorption.

During the early years of biotechnology's development, most established pharmaceutical companies remained on the sidelines. The global pharmaceutical industry was highly profitable and seemingly buffered from challenge. But biotech proved to be, in Schumpeterian terms, a competence-destroying innovation because it built on a new science base (molecular biology and immunology) that differed significantly from the knowledge base (organic chemistry and its clinical applications) of the mature pharmaceutical industry (SCHUMPETER [1934]; ABERNATHY and CLARK [1985]). Lacking a work force trained in biotechnology, and unable to create an internal environment that was comparable to university or biotech laboratories, pharmaceutical companies found themselves losing out in competition for intellectual talent. Moreover, biotech firms

[7] See POWELL and BRANTLEY [1996] for an account of the product development process for two of the industry's initial "blockbusters:" *tpa* (Activase) developed by Genentech for treatment of heart attacks, and *epo* (ncupogen) developed by Amgen for use in kidney failure and dialysis.

have evinced formidable skill at drug discovery. As the vice president of drug development at Eli Lilly puts it, "The biotech industry has proven that it can do innovative, leading-edge discovery quicker and faster than the big companies."[8] But biotechnology is an unusual case of competence destruction. Scientific discoveries have profoundly reshaped the nature of drug discovery, but once a new medicine is developed, the key uncertainties concern the development of the technology into a safe and effective medical product that can be marketed widely, a competence at which established pharmaceutical firms are very good. Hence the technological breakthroughs that level the playing field on the research front also create new opportunities for mature firms in commercial development, marketing, and distribution. Consequently, circumstances of mutual need develop. Small biotech firms require large firm financial support and regulatory savvy, while larger pharmaceutical corporations desire access to the research prowess of smaller companies.

At present, most large pharmaceutical companies have active biotech research programs of their own and multiple ongoing partnerships with various small biotech companies. But pressures on a number of fronts challenge the pharmaceutical industry, and biotech may well offer an opportunity for renewal. When we look comparatively at the two fields, the product pipelines in pharmaceuticals look thin, with too many derivatives and "me-too" products.[9] In contrast, the biotech pipeline is deep, filled with novel products.[10] Biotech companies are rapidly pursuing such new, albeit highly risky, arenas as gene therapy, genomics, structure-based drug design, and other technologies for speeding discovery and treatment. Pharmaceuticals, meanwhile, face the prospect of the great majority of their top selling drugs going "off patent;" thus they will soon be available as much cheaper generic substitutes. Put differently, pharmaceuticals compete to deliver and market new editions of products while biotechs pursue new approaches to novel products. In this sense, product competition in biotech involves less rivalry and more of a learning race.

[8] Quote by David Thompson, in *Wall Street Journal*, April 6, 1994, p. B4.

[9] A particularly grim assessment of pharmaceutical prospects is offered by Bear Stearns & Co., in its analysis entitled "Purge and Surge," October 15, 1993, New York, NY. See also "Drugmakers are Discovering the High Cost of Cutting Costs," *Business Week*, October 17, 1994, pp. 204ff. The article suggests that the thin product pipeline is due to an early resistance by pharmaceuticals to biotechnology and too much focus on making low-risk improvements to existing drugs.

[10] ZUMBROICH, GADICKE and STEINER [1994] provide data showing that the number of biotech applications submitted to the U.S. FDA now exceeds the number of pharmaceutical industry applications. As a contrast, consider Merck which spent $ 1.1 billion on R & D in 1992, while the entire biotech industry spent about $ 2 billion. Merck now has about 20 products in advanced stage clinical trials, while the biotech field has more than 120 at comparable stage. Testing is not a guide to future sales, of course, but consider that Merck employs more than 47,000 people while Amgen and Genentech, the two largest biotechs, combined have less than 6,000.

The slowing of new pharmaceutical drugs is a twin result of discovery methods and corporate strategy. The focus of pharmaceuticals has been on besting their competition. According to the Boston Consulting Group, 90% of patented drugs have direct competitors; in 15 of the 20 most lucrative therapeutic areas, there are three or more drugs available with similar properties.[11] And as the patents expire on these drugs, generic competition ensues. Moreover, the methods used for finding pharamaceutical drugs are laborious and costly; consequently, by the time a drug reaches the market, its patent life is often well past the mid-point of its seventeen-year license. The standard methodology for pharmaceuticals was to choose a disease that affected a significant population; define a model of the disease; take compounds off the chemists' shelves and screen for efficacy. Through laborious trial and error, an eventual success was achieved, although understanding of the causes of success was often primitive. In contrast, biotechnology, while considerably more complex, offers more pinpoint targeting and a better understanding of causal mechanisms. Biotechnology begins with a more focused target, that is, scientists typically know what it is they are aiming for, thus they attempt to "design" a drug to affect either a target or a biological interaction they wish to alter.

Health care reform and restructuring, reflected in the spread of health maintenance organizations in the U.S. and adoption of utilization controls in Germany, have resulted in mounting efforts at medical cost containment. Health care systems are, in the words of industry analysts ZUMBROICH, GADICKE and STEINER [1994, 18], "unwilling to reward the drug industry at the same high levels as they did in the past, especially for new drugs or therapies that fail to provide substantial improvements over existing treatments." Thus a combination of factors – competition from less expensive generic drugs, more sophisticated biotech products, and cost-effectiveness pressures from healthcare providers – is prompting a significant reshaping of the pharmaceutical industry. To reduce manufacturing and marketing costs, the largest firms are consolidating in a wave of mergers, and at the same time expanding their informational and distributional capabilities in efforts to embrace "disease-state management." To use a cliche, pharmaceuticals now want to sell health, not pills. On the research side, a marketplace that will not reward mediocre or derivative products places a new premium on innovation. Consquently, large companies are "outsourcing" their R&D to the biotech community. Firms such as Ciba-Geigy, Glaxo, Lilly, and Roche each have more than twenty collaborative ventures with biotechs – a recognition that no matter how large their budgets, R&D can no longer be done internally.

[11] Data reported in "Reshaping Things to Come," *The Economist*, August 6, 1994, pp. 65f.

*3. Relevant Assets are not Easily Assembled in a Single Organization*

Clearly, then, the full range of relevant skills needed to develop therapeutic drugs is not readily found under a single roof. While the basic and applied research skills needed to create new products are based in universities, research institutes, and biotech companies, the cash necessary for product development, the experience required in launching extensive clinical trials, and the established, world-wide marketing channels are located in large chemical and pharmaceutical companies. So the participants in this field have turned to joint ventures, research agreements, minority equity investments, licensing, and various kinds of partnerships to make up for their lack of internal capabilities.

Several illustrations can highlight the symbiotic complexity that has emerged. Two recent notable advances have been reported for breast cancer and Alzheimer's disease. The paper identifying a strong candidate for the gene determining susceptibility to breast cancer was written by 45 scientists, located in university departments and medical schools in the U.S. and Canada, a biotech company, a federal laboratory, and a pharmaceutical company (*Science*, October 7, 1994). The development of a mouse model for Alzheimer's disease was authored by 34 scientists, distributed across two biotech companies, a pharmaceutical company, a federal laboratory, and a university department (*Nature*, February 9, 1995). Moving from discovery to the marketplace, Genentech – the biotech with the largest number of biotech medicines on the market has:

- more than 10 marketing and distribution partnerships with such firms as Boehringer Ingelheim, Mitsubishi Chemical, and Kabi AB;
- more than 20 licensing arrangements with partners ranging from small biotechs to the U.S. Commerce Department to Smith Kline Beecham;
- more than 15 formal research collaborations with small partners, seven of whom Genentech helped create with equity investments, NASA, and various large pharmaceuticals, one of whom, Roche, owns more than 60% of Genentech's stock.

My colleagues and I have been tracking these varied collaborations in an effort to explain their pattern, structure, and evolution. We have built a database that covers an eight year period (1988–1995). Our sample includes all dedicated, independently-traded biotech companies (approximately 230) in the human therapeutics field worldwide, and the more than 1,800 partners with whom the biotechs are engaged in collaboration. We have data on the formal contractual agreements between biotechs and their investors and partners.[12] We supplement the statistical data with interviews with biotech scientists and executives, university scientists, and pharmaceutical scientists and executives. In addition,

[12] For a more detailed discussion of our data base, see POWELL, KOPUT and SMITH-DOERR [1996].

we have constructed profiles of the product development process for biotech's initial best-selling drugs (POWELL and BRANTLEY [1996]), and done observational research inside a biotech firm and university laboratory (SMITH-DOERR [1994]).

In focusing on formal agreements, we omit the myriad informal arrangements that are commonplace, especially in research and development. One reaction to a focus on external collaborations might be to question just how critical these activities are to a firm's operations. But recall figure 1, where Biogen had more ongoing activity outside its formal boundaries than inside. Moreover, even a cursory glance at biotech and pharmaceutical annual reports suggests the importance of collaborations. Often, alliances are accorded prominence in statements of corporate aims. Investment houses commonly evaluate biotech firms on the basis of their partners' capabilities. In coding external collaborations, we follow a logic of production, classifying agreements into the following stages; investment, R & D, clinical trials, manufacturing, marketing or licensing, supply or distribution, joint venture, and complex agreements involving multiple steps. We are particularly interested in the range of activities that a firm collaborates on; hence we have developed a measure we refer to as portfolio diversity, which captures the heterogeneity of a firm's partnerships.

### *4. Limits to Contracting*

External collaborations are difficult to set up initially and require considerable skill in sustaining. Such ventures create complicated relations of dependency and obligation, as well as ample opportunities for miscommunication and misinterpretation of intentions. Many parties would probably opt to "go it alone" if that option were available. These symbiotic arrangements are expensive in time and effort. As AOKI [1990] and POWELL and SMITH-DOERR [1994] observe, collaborative ventures pose steep transaction costs. Fears of malfeasance loom large at the outset, and parties are rendered vulnerable to opportunistic behavior. One party may find it difficult to persuade the other to make appropriate investments in the relationship, or property rights disputes may develop over ownership of new discoveries. Even fully committed partners may find it difficult to transfer complex, tacit technological know-how across organzational boundaries. Given such difficulties, what factors best explain patterns of interorganizational agreements?

As a first approximation, several lines of theory and research – transaction cost economics, notably ideas about credible commitments and co-specialized assets (WILLIAMSON [1985]; TEECE [1986]); research in game theory on the evolution of cooperation (AXELROD [1984]; GAMBETTA [1988]; SCHARPF [1993]); and research on the role of networks in fostering learning (COHEN and LEVINTHAL [1989], [1990]; POWELL [1990]; VON HIPPEL [1988]) – seem useful in understanding patterns of collaboration. In our current research, we have

derived hypotheses from these various approaches and tested them with data on inter-organizational agreements (POWELL, KOPUT and SMITH-DOERR [1996]). I sketch these three agreements and the relevant results briefly, then extend our empirical studies with considerations of how cooperation is sustained in competitive circumstances.

Arguments drawn from transaction cost economics would suggest that an organization should prefer to internalize critical stages in the drug development process and turn to external parties only when in-house capability is absent. Consequently, as firms grow larger and mature, thus overcoming liabilities of smallness and newness, they would rely less on external collaboration for tasks that involve a high degree of risk and asset specificity. When such risks are nevertheless necessary, firms would seek to guard against opportunism by establishing some form of control, such as taking an equity position, to mitigate potential hazards.

More broadly, consider TEECE's [1986] ideas about complementary, or co-specialized, assets. His argument is that firms approach collaboration with specific needs and seek partners that can match those needs in return for an asset the seeking firm has. This view opens up the idea that a firm has a set of competencies it seeks to build on through its relationships with various partners. This mode of analysis suggests that a firm approaches collaborative agreements in a way that "fills in" the missing pieces of its own competencies. For example, small firms will contract with partners to provide services they cannot execute. Larger firms will utilize partners for any critical skills they have not mastered or to exploit opportunities to which they cannot devote sufficient time or resources.

An alternative view, developed by AXELROD [1984] and others, stresses that trust and cooperation increase with use. When there is a high probability of future association, parties are not only more likely to cooperate, but they are also increasingly willing to punish defectors. When parties recognize common interests, collaboration more readily ensues. Trust does not imply blind loyalty, however. Cooperation entails risks; thus firms must create governance structures that allow for monitoring and consultation (SABEL [1993]; SCHARPF [1993]). One option is a form of relational contracting that specifies agreed-upon targets, milestone dates, and escalating commitments based on progress toward mutual goals. Another option is to use reputation as a guide to future interaction; hence prior experience at collaboration would predict subsequent efforts.

In our current research, we argue that biotech firms approach collaboration as a means of enhancing their capability for learning (POWELL, KOPUT and SMITH-DOERR [1996]). Thus a firm would be willing to pursue multiple, related, or even overlapping opportunities when they permit it to stay abreast of scientific developments. Rather than viewing partnerships as a means of providing skills a firm has not yet mastered, we view alliances as opportunities to test and expand competencies – as "learning races." Thus, collaboration can be a con-

tinuing strategy rather than a one-shot calculation. Consequently, internal expertise and external collaboration are not substitutes for each other but complementary. Internal capability is indispensable in order to evaluate research done outside, while external collaboration provides access to "news" and resources that cannot be generated internally. In sum, a network of collaborative ventures serves as a locus of innovation because it provides fast access to knowledge and resources that are otherwise unavailable, while also testing internal expertise and learning capabilities.

We find that as biotech firms grow larger, in number of employees, and get older, in chronological years, they do not retreat from external collaboration. Age per se proves unimportant, but number of years of experience with collaboration generates more external ties as firms develop a reputation for, and competence at, cooperation. The extensiveness of a firm's network is a strong predictor of survival. The range of collaborative activities, captured by our measure of the diversity of agreements that a firm pursues, remains relatively constant over the eight year period. Thus firms do not alter their portfolio of ventures as they age. In short, firms do not start out with R & D partnerships, become experienced at this stage, and move on to collaborations at other stages in the development process. Instead, most biotechs pursue multiple agreements for every step in the development process, suggesting that collaboration is not used to compensate for lack of internal capability. The mean number of external ties for the firms in our sample ranges from 7.5 in 1988 to slightly over 10 in 1995.

Several points stand out in our research. Partnerships prove to be interdependent – they are neither one-shot calculations nor strategic remedies to organization deficiencies. Collaboration begets further collaboration. Larger firms have more external ties, but size does not predict number of partnerships. Rather, collaboration generates growth, measured either by number of employees or speed at going public. Put differently, a biotech firm grows by being a player, by becoming connected to benefit-rich networks that provide resources. A firm does not become a player, that is, become visible and well-connected, by growing in size.

Our quantitative analyses offer ample support for the view that dense networks of collaboration are not transitional steps, but rather a set of institutional arrangements that are well-suited to a field fraught with considerable uncertainty, reliant on high-level scientific expertise, and in need of huge sums to support drug discovery and development. Our empirical work is also buttressed by experiential observations. In accounts of the industry from the early and mid-1980s, collaborative arrangements were typically referred to as "deals," as necessary arrangements that a young firm had to pursue on its path to becoming a vertically-integrated company. Then the language of deals became talk of "strategic alliances" and "agreements," and eventually they were called "partnerships" and "collaborations." The contractual language changed as well, with many fewer technology transfers, and more technology and product swaps

and co-promotions. As industry analysts BURRILL and LEE [1993, 23] note, "We see fewer one-dimensional deals, and more deals that are restructured as they progress, that encompass 'what-ifs' and 'what-thens'." In sum, the industry has developed a great variety of collaborative ventures and operating structures that allow organizations to rely on the competencies and resources of other organizations. At the community level, we see a kind of macro-level mutualism, referred to in the industry as "virtual integration."

This community-level mutualism is both self-maintaining and self-enforcing. It is not a "nexus of contracts" but a complex, multiparty web, in which it is exceedingly difficult to pinpoint the center or starting point. The network structure of the field and the open architecture of firms are both mechanisms for generating communication. In the concluding section below, I discuss whether this communication was prompted by *calculative* motives – as a strategic outcome of an iterated chain of contacts in which far-sighted parties recognize the potential benefits of continued interaction; circumstances of *mutual need* – a by-product of the simultaneous restructuring of the pharmaceutical industry and university research, alongside biotech's development; or an emergent process of *increasing returns to learning* – in which networks represent the development of a new macro structure that evolved, perhaps unintentionally, out of hundreds of independent cooperative ventures.

### *5. Sustaining Collaboration – Are Motives Calculative, Symbiotic, or Emergent?*

*Calculation.* One way of accounting for the dense web of collaborative ventures is to see them as part of a strategy of accessing rather than creating resources or capabilities to complete the value chain from discovery to marketplace. Virtual integration, then, is a means for insuring long-term sustainability without incurring steep short-term risks. Such an approach permits accelerated development and affords more effective use of resources, with less exposure.

It is easy to find examples of such opportunistic partnering. Chiron and Genzyme, both among the most successful biotechs, seem to have chosen collaboration in those emerging areas where they are in greatest need of resources, and opted to integrate internally in areas where they have sufficient in-house support. Amgen, the industry leader in sales, makes collaborative overtures to, and even outright acquisitions of, smaller biotechs when such firms receive negative reports from the regulatory approval process. Immunex and American Cyanamid joined together in a complex restructuring of both companies, in which pharmaceutical giant Cyanamid contributed $ 1.3 billion to Immunex's promising product pipeline and spun out its own oncology business to join Immunex. Arrangements such as these are mutually-dependent strategic investments, the products of considerable negotiation and assessment.

But such an argument makes collaboration sound functional when, in important respects, it emerges unexpectedly. Recall that nearly every player in the

industry has multiple relationships with multiple parties. Indeed, these are often multilateral rather than bilateral collaborations, and recent ventures have brought in governments, health maintenance organizations, and insurance companies. Alliances are fluid and take into account changing circumstances. Relationships are routinely renegotiated, not as a sign of failure but in response to the exigencies of science.

Companies enmeshed in a web of alliances are not self-sufficient. While they maintain operating independence, they are involved in ten or more complex linkages with organizations of varying sizes, with different capabilities and varied motives for collaboration. They could not possibly teach themselves what their partners already know. Under such circumstances, calculations of interest and strategy become difficult, because the identity and interests of an organization and its network of partners are intertwined. And because such relations are multiplex and overlapping, that is, a competitor on one project is a valued collaborator on another, the nature of competition has changed in significant ways.

*Symbiosis.* The growth of collaborative ventures in biotech has rendered organizational boundaries permeable, and much of the "action" takes place in joint activities where on-going learning is a sustaining force. Partners learn to rely on one another out of mutual need and an anticipation of the benefits of continued interaction. By taking a long-term view and practicing mutual forbearance, partners overcome suspicion and the tendency to defect from a relationship when the going gets tough or the rewards look too promising to share.

Such a game-theoretic view of an iterative process in which partners practice joint problem-solving seems apt for describing the evolution of the bio-pharmaceutical industry. The conflicting dynamics of the field, in which university scientists and commercial firms are short on funds to support research, and large pharmaceutical companies need to replenish their product pipelines and stay abreast of intellectual breakthroughs that have reshaped their business, have created an unusual context in which the "shadow of the future" is long indeed. The simultaneous restructuring of pharmaceuticals, biotechnology's development, and resource scarcity in the academy have created circumstances in which all the parties come to the table with something to contribute and in need of the others' assistance. All three parties – the academy, biotech, and pharmaceuticals – need partners to reposition themselves in a changed environment.

Because uncertainy is high, parties must rely on reputation to inform their evaluations. Organizations with reputations for being valuable partners will attract higher quality collaborators, thus setting in motion a self-reinforcing dynamic. Collaboration becomes a process of identity construction. A decentralized system of shared incentives promotes goal congruence. A culture of cooperation, necessary for decentralized coordination, is not given a priori, but

develops through ongoing success. Routine contact between parties allows the development of implicit rules to channel, monitor, and when necessary, sanction the behavior of partners. In short, collaboration in the context of interdependence becomes self-maintaining.

*Increasing Returns From Learning*. Arguments based on complementary assets and iterative games are, in some respects, too sophisticated and unnecessary. Biotechnology emerged in universities, and the simplest answer to why the field is rife with collaboration is that is precisely what scientists do in the conduct of their careers. There is ample evidence that most formal collaborations emerge out of pre-existing, informal relationships (SMITH-DOERR [1994]; GULATI [1995]).

Moreover, membership in a common technological/intellectual community creates strong and visible mechanisms for peer-based governance. As well as sharing the larger goal of advancing biomedical knowledge, and reaping the considerable rewards associated with such gains, participation in a research community affords the opportunity to monitor how participants behave in a wide range of settings, to discuss reputations with others, and to read their work in scientific journals. Pressures to publish, and thus reveal the latest advances, are intense in this field. Thus discovery is open to all to evaluate. To reap the advantages of research, participants need to learn fast and collaborate effectively. Members of this community have ample opportunity to observe how individuals and organizations behave and learn about their reputations. The result of such sustained contact is that one's standing in the technological community shapes one's reputation for business practice.

Seen from the vantage point of learning and discovery, collaboration is an admission ticket to an information network (MOWERY and ROSENBERG [1989, 13]). Knowledge in the life sciences is growing explosively. Research breakthroughs are so broadly distributed that no single organization can stay on top of current work. Multiple collaborations form a portfolio of information sources, and diversity among such sources in highly desirable. A cornerstone finding of network research is that non-redundant contacts increase the probability of information acquisition (BOORMAN [1975]; BURT [1992]; GRANOVETTER [1985]). Dense, non-redundant ties generate positive externalities: the larger the network, the greater the value to its members. Thus merger or integration in such a setting seems a weak choice. With a science that is expanding, outright acquisition or going it alone would reduce the flow of information. In a learning race, the goal is not just to produce a specific product but also to be positioned to understand and participate in a platform technology that can lead to multiple discoveries and numerous new products.

The flow of information through R & D collaborations produces certainty for members in the face of technological uncertainty. Because no single organization has all the relevant pieces of information, or can readily access them, a company is faced with doubt about its ability to keep pace. Building on pre-ex-

isting ties of its scientists, a company makes gains through cooperation. VON HIPPEL [1988] contends that industries with free-flowing information trading, such as he observed among engineers in the mini-mill segment of the steel industry, have lower search costs and find that innovation comes easier. Moreover, without such ties, firms find it exceedingly difficult to recruit new scientists. Consequently, the reputations of individuals and organizations are linked. VON HIPPEL [1988] argues that learning by a firm is enhanced by allowing highly-skilled employees to collaborate with like-minded people at ostensibly competing firms. But much of R & D collaboration is not calculative; rather it is emergent. Research and development outcomes can rarely be forecast in advance; much of what emerges from discovery is unanticipated. Such ongoing cooperation changes, in FREEMAN's [1991, 508] words, "the common sense rules of behavior" for scientists and managers. In such a fashion, the "natural" collaboration among members of a technological community and the "unnatural" cooperation among business enterprises are joined.

Taken together, these arguments suggest a process of increasing returns (ARTHUR [1990]) to collaboration. These "small effects" have expanded into large new ones, as collaborative practices become institutionalized. At the core of these developments is a critical need to access relevant knowledge and resources – assets that are widely dispersed and neither easily produced inside the boundaries of a firm nor obtained through market transactions.

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