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# Where Science Comes to Life: University Bioscience, Commercial Spin-offs, and Regional Economic Development

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*Abstract*

Biotechnology, rather than being defined as a distinct industry like steelmaking or shipbuilding, is instead a scientific knowledge base—a rapidly evolving technology—that has economically valuable applications in such diverse industries as pharmaceuticals, medical diagnostics, agriculture, bioenvironmental remediation, and chemical processing. Biotechnology has captured the imagination of ambitious scientific investigators and investors seeking high rates of return, as well as state economic development officials who hope to anchor the industry in their locality and reap the industry's economic and employment rewards. Biotech is still at an early stage of its development, and there are many competing hypotheses about its future development. Most importantly, biotechnology involves the commercialization of science resources in which the federal and state governments have made substantial investment. One key question is how to leverage this investment for future economic growth. This article explores the policy issue related to the commercialization of biotechnology, its role as an engine of economic development, and the appropriate public policy response.

*The late twentieth century has witnessed a scientific gold rush of astonishing proportions: the headlong and furious haste to commercialize genetic engineering. This enterprise has proceeded so rapidly—with so little outside commentary—that its dimensions and implications are hardly understood at all.*

Michael Crichton, Introduction to *Jurassic Park*

## Introduction

Science-based activity is at the heart of new theories of economic development, technological change, and industrial evolution (Romer, 1986, 1990; Lucas, 1993; Krugman, 1991a, 1991b). Increasingly, it is recognized that the engines of national economic performance are subnational technology districts that are characterized by strong ties between regional actors (Storper, 1995; Scott, 1993). This work is complemented by empirical research that finds that knowledge spillovers from science-based activities are localized and contribute to higher rates of innovation, increased entrepreneurial activity, and increased productivity within geographically bound areas.[1] How exactly to capture the benefits of a science-based industrial activity is an important economic development issue for places that have the relevant science-based assets.

This article focuses on innovative activity in bioscience,[2] an activity that is very knowledge intensive and in which academic science is directly relevant. The article draws from some recent research projects on the development of the bioscience industry. The intention is to explore patterns that have been uncovered and that deserve further investigation. The pattern of commercialization in bioscience favors the spin-off of new firms from university departments. This article provides an outline of some considerations that affect the commercialization of a university-based science. The analysis is inherently geographic, and the intent is to understand how bioscience activity may influence the landscape of economic development and what the appropriate role of public policy might be in promoting this type of economic development. This article begins with background on biosciences. We have chosen to focus on one important, emerging technology in order to consider the organization of science-based innovative industrial activity and the relationship between scientific activity, commercial activity, and economic growth. Overall, the objective is to add to our understanding of the organization of scientific and technical activity and the role of scientific resources in generating and sustaining regional commercial competitive advantage. Ultimately, this understanding may aid in the design of effective regional economic development policies.

## Background on bioscience

Bioscience presents a unique opportunity to study the emergence and development of a radical new technology that has a strong science base and great commercial potential. Modern bioscience traces its origins to the discovery of the molecular structure of the basic building block of genetic material, deoxyribonucleic acid or DNA, by James Watson and Francis Crick in the 1950s. This work made it possible to identify the genes that make specific proteins.[3] The scientific basis of the discipline is grounded in biology, chemistry, medicine, molecular biology, and biochemistry, and its technical advance is driven by basic scientific research conducted at universities and research institutes.

Commercial bioscience activity began with the Cohen–Boyer patent application in 1974. This work provided the means to manipulate or recombine genetic material into useful, commercial products that are more naturally acceptable to the human body and its environment than synthetic chemical products. Indeed, we can date the beginning of the modern bioscience industry with the Cohen–Boyer patent. The patent created propriety value for bioscience intellectual property that, in turn, enabled the formation of new firms and the financing of profit-oriented endeavors.

Bioscience provides the technological underpinning of many new start-up firms (Zucker and Darby, 1996). The commercial potential of biotechnology was established in 1982 when the California company Genentech introduced recombinant human insulin,[4] the first pharmaceutical product using biotechnology. One recent estimate is that there are currently over 1400 dedicated bioscience companies nationally. The majority of these are new entrepreneurial start-ups. Powell and Brantley (1992) argue that the commercialization of biotechnology requires the formation of new firms. Biotech originates from a radically new scientific knowledge base that does not fit with the existing technological practices of established firms in comparable industries such as pharmaceuticals and chemicals. In this way, entrepreneurial start-ups are a vehicle to commercialize new ideas; radical, competency-destroying scientific discoveries are taken out of the laboratory and to the marketplace.

## Clusters of distinct expertise

The importance of new scientific information to the development of a technologically intensive industry leads to geographic clustering in that industry (Audretsch and Feldman, 1996). Bioscience activity clusters spatially in Boston, the San Francisco Bay area, the Baltimore–Washington corridor, and a few other centers (Lee and Burrill, 1996; Prevezer, 1997). Reasons behind this clustering are complex and multifaceted. Agglomeration takes place so that companies can realize economies of scale and benefit from technological exchanges. But this description begs the question of how the process begins and how the industry becomes anchored.

While the term *biotechnology* is popularly used to describe an entire industry; it is really a set of many different technologies, such as large-scale cell culture, fermentation, protein engineering, and combinatorial chemistry, and of different product applications, such as vaccines and environmental reclamation. In early discussions of the computer industry, there was similar aggregation, since mainframes and personal computers were considered to be the same industry; yet there was substantial regional differentiation between mainframes and PC, and these two industries manifested widely different regional fortunes. The divergence of the economic fortunes of Route 128 and Silicon Valley provides insights into the comparative importance of technology and industrial structure for regional growth and raises questions of how scientific resources and institutional relationships contribute to the development of regional technological specialization (Saxenian, 1994).

Evidence of regional specialization in bioscience products and technological subfields suggests that there are unique and regionally defined centers of expertise. Results, based on the Institute for Biotechnology Information (IBI) company database, suggest that the industry is developing differentiated and unique capabilities in specific locations[5] (the appendix). Of course, this expertise reflects differentiated underlying regional capabilities based on scientific competencies.

The correlation between university research funding and patents and company start-ups is a weak relationship and not statistically significant (cf. Barnes, Mowery, and Ziedonis, 1997; Geiger and Feller, 1995; Nelson, 2001; Raider, 1998). This finding suggests that there are some underlying reasons why regions are not able to capture the benefits of their local science base.

### The entrepreneurial university

U.S. universities have become the de facto, worldwide template for what Clark (1998) has termed *entrepreneurial universities.* Manifest changes in legal, economic, and policy environments aimed at accelerating the translation of academic research into commercial products have created a new environment in which universities actively seek to transfer scientific and technical knowledge (Feldman et al., 2001). Federal legislation passed in the 1980s and 1990s reflects a new interpretation of the federal role in supporting high-tech R&D, an interpretation based on the belief that the commercialization of high tech will increase America's competitiveness and raise the standard of living for Americans (Bowen, 1997). The Bayh-Dole Act of 1980 provided a mechanism for universities to retain title to federally funded intellectual property and resulted in an increase in university patenting (Henderson, Jaffe, and Trajtenberg, 1998) and in technology transfer activities in general (AUTM, 1997).

Conventional wisdom concerning state and local economic development holds that a research university is one of the important conditions for economic restructuring toward a technology-intensive industrial base (Raymond, 1996). Research universities provide scientific knowledge, technical information, and skilled workers—the basic raw materials for high-technology industries. The prominent examples of new industrial growth complexes such as Silicon Valley in California, Route 128 in Massachusetts, and the Research Triangle area in North Carolina are all closely connected to major research universities, and this fact has been perceived as instrumental in positioning these regions on new, technology-intensive growth trajectories. A substantial body of evidence suggests that knowledge spillovers from universities are geographically localized, although the specific factors that condition geographic localization are not well understood (Feldman, in press).

Yet not all research universities have been able to generate local economic effects (Feller, 1990). We may note that although university rhetoric promotes economic development goals, there is often a divergence with what the university culture and reward systems support. There is often a tension in the interpretation of the universities' mission between the search for basic truths in science and the search for ideas with potential commercial or practical application (Wade, 1984). Often the basic search is considered the legitimate function, while commercial activity is regarded as an inappropriate focus. This situation is reflected in the academic incentive and reward systems that govern tenure and advancement.

Even those universities and university departments that do not believe that their role lies in promoting commercial activities are caught up in the recent contagion of entrepreneurial spirit in the biosciences. For scientists, starting a company serves the purpose of appropriating the value of their intellectual property as well as providing access to additional funding mechanisms to further the scientists' research agenda. The potential financial rewards coupled with tight university budgets and competition for the relatively fixed pool of federal biomedical funding create incentives for scientists to engage in entrepreneurial activity (Powell and Owen-Smith, 1998). It is not uncommon for a new faculty recruit at Johns Hopkins University to ask to interview with the Office of Technology Transfer as a part of his or her recruitment process. Faculty at leading institutions are involved in networks that provide information about practices and policies at other universities. In order to compete for the best scientists, universities must play the commercialization game. Clark (1983) notes that the evolution of academic institutions is mimetic, and changes and procedures at prestigious institutions diffuse through the system. Indeed, the opportunities provided by the changes in the legislation and the corresponding changes in university culture provide a natural experiment that allows us to examine how entrepreneurship takes place in regions that previously lacked that tradition (Feldman, 1994, 1999).

Louis et al. (1989) distinguish five types of entrepreneurship in the life sciences: (1) engaging in large-scale, externally funded research projects; (2) earning supplemental income through consulting, directorships, or royalties from licenses; (3) gaining industry support for university research; (4) obtaining patents; and (5) forming or holding equity in private companies based on a faculty member's research. The fifth type of entrepreneurship promises the most impact for local economic development activity, but it is also the most risky. Zucker and Darby (1996) find a strong colocation of university star scientists and start-up firms in biotechnology. A *star scientist* is defined in this work as one with a high rate of publication citations. However, in general, we know that more established scientists with tenure and high rates of publication are most likely to engage in commercial activities (Zuckerman and Merton, 1972).

There appears to be a common pattern of development, with entrepreneurial faculty building larger and larger research groups based on the securing of external funding from grants and sponsored research. Gradually, the research group becomes semiautonomous. Knowledge development typically outruns resources, and forming a new firm opens additional new funding sources. In this way, the classification scheme proposed by Louis et al. (1989) may represent a continuum of activity, with scientists gaining more commercial experience until they ultimately start a company. Etzkowitz (1983) finds that managing large-scale science projects provides faculty members with management skills that permit easier entry into the private sector.

Our interviews suggest that faculty members are interested in advancing their research agenda and that starting a company provides access to new sources of funding, such as Small Business Innovation Research (SBIR) grants and a plethora of other federal, state, local, and private sources (Feldman, 1999). Commercial activity provides a complement to the scientist's academic research. Indeed, faculty move fluidly between the university and the company lab. There are concerns that faculty loyalties may shift and intellectual property developed at the university may not move through the appropriate technology transfer mechanisms but rather may go directly to the company.

The motivation for starting companies appears to fly in the face of the typical assumption of a profit motive. Often scientists are frustrated with university bureaucracy, the demands of grant writing, and the vagaries of university politics. Starting a company may serve such diverse motives as reducing overhead rates, creating the basis to move faster on research, or keeping a research group together. University start-up companies typically employ graduate students and postdocs. When tenured positions become scarce, working at a start-up company becomes more attractive as a career option (Ruedig, 1996).

The role of the university in local economic development seems to follow the pattern of seeding a barren field. Entrepreneurial researchers capitalize on discoveries made while working at academic institutions in order to form new biotech companies. As a new spin-off company takes root, it in turn will generate more spin-offs. In tracing technology family trees in Baltimore–Washington, we found that new spin-off subsidiaries were formed for three primary reasons: first, to apply a broad-based platform technology to a new application or product area, thereby not risking the going concern; second, to retain "star" graduate students by giving them more autonomous opportunities and an equity interest; and, finally, to keep research groups small and focused (Feldman, 1999).

The activity of informal networks of colleagues, clients, students, and others is an important source of information on new technologies and innovations and creates an entrepreneurial environment. For example, Delaney (1993) found that biotechs use local information sources (within a 50-mile radius of the firm) and also documented that start-ups "tend to be formed in the same geographical region as the parent firm or incubator." Such an environment, in turn, attracts the attention of management types interested in commercializing the technology, financiers and other firms may find the environment attractive. Thus there is a natural feedback loop to the geographic clustering: established regions grow stronger through continued endogenous start-up activity and attracting nonlocal new firms.

### What is the role of policy?

Biotechnology has captured the imagination of ambitious scientific investigators who seek fame and fortune and of investors who seek high rates of return. Not surprisingly, the growth potential of industries such as biotech has also captured the imagination of economic development officials who hope to anchor the industry in their locality and reap the industry's economic and employment rewards. Companies, especially promising high-tech companies, can be demanding. There is a precedent for company-specific state support, and companies expect special incentives. Bidding wars result.

Bidding wars are high-profile events. They capture media attention, and there are clear winners and losers. Because an industry is a constellation of individual firms, one regional economic development strategy is to build an industry by investing in one company at a time. But such a strategy creates a perception that government investment should be viewed with the same lens through which myopic private-sector investment is evaluated, with the return to investment in mind—most typically, the number of jobs per government expenditure. States work in partnership with federal government programs to support local awardees and independently assist local companies. This support runs the gamut from enhancing general infrastructure, which benefits all industries, to providing assistance, often financial, to specific companies that promise to bring future economic growth within their borders.

The gold-rush mentality that surrounds new-technology companies creates unrealistic expectations on the part of public officials. There is a disturbing trend towards the adoption of private-sector constructs, such as return on investment, that do not reflect the type of public-sector commitment that is required to bring long-term investments in these companies to fruition. By contrast, Link (1995) writes in *A Generosity of Spirit* about the worldview that led to the development of Research Triangle Park—a view that public policy should serve larger and longer-range goals. Specifically, we may argue that public policy should be concerned with infrastructure building—intellectual infrastructure as well as physical infrastructure. It is not uncommon for economic development officials to talk about the potential of new start-up firms to grow to be the next Microsoft (or Genentech). It seems that there is an emphasis on what might be called the Microsoft Paradigm; firms are expected to grow very large. Policy initiatives based on this model have serious limitations.

There are three lessons for regional economic development that we have gleaned from our work that we would like to discuss next. These are the importance of small, sustained actions, the importance of failure, and the importance of the local in the global economy. Each of these will be discussed briefly.

### The importance of small, sustained actions

There are many reasons for starting a firm, and becoming the next Microsoft may not be a goal for many entrepreneurs, especially if they are working in science-based technologies that are far removed from the market. Many niches may be profitable for small firms that would be ignored by a larger company. Biotech firms tend to pursue differentiated niche markets. Many biotech start-ups survive by providing specialized services, supplies, or test kits that maintain a revenue stream to help offset the cost of developing a new product (Feldman and Ronzio, 2001). These products, expensive and technology dependent, rely on an appreciation for what consumers need and for shortcomings in current pharmaceutical regimens or surgical procedures. A vibrant regional economy may be built upon the base of successful small and medium-sized firms that can serve the specialized niches that their larger counterparts would not find attractive.

Bioscience companies traditionally have long development cycles for major products. In the interim, entrepreneurs describe two survival strategies. The first is "taking in other people's laundry" —that is, subcontracting or doing small jobs for other companies, or making "bread and butter products" such as test kits or reagents that can easily be sold. These strategies keep the companies afloat and also provide resources to work on the development of an R&D-intensive product (Feldman and Pfirrmann, 1998). Economic development policy stresses the importance of venture capital, however, it appears that many small start-ups eschew venture capital and prefer to go it alone. Nationally, venture funds are noted to back only 1% of the technology-oriented start-ups that submit business plans to them each year (Fenn, Liang, and Prowse, 1995).

Many enumerations of bioscience firms overlook small companies that focus on selling services or products with small commercial potential (Lee and Burrill, 1995). These companies simply lack glamour, and they typically do not promote themselves, as firms looking for investors or venture capital are more likely to do. We note that two early supplier firms to the National Institutes of Health (NIH) in Baltimore–Washington have moved into product development. In addition, these firms have also been the progenitors of subsequent spin-offs (Connolly et al., 1998).

The existence of a field of small firms creates a fertile environment. As scientists observe other scientist-entrepreneurs making a go of it, risk perceptions change, and entrepreneurial spirit appears to spread like a contagion through a university community. A repeated theme in our interviews with entrepreneurs is the idea that if acquaintances, department members, and competitors could make a go of it commercially, then why not try starting a company? Norms of behavior change slowly, especially in universities, but they do change (Etzkowitz, 1989). In general, the consensus is that an entrepreneurial environment is important to regional economic development and that through small, sustained actions, such an environment may be created.

## The importance of failure

Not only may small, sustainable actions be desirable but also failing may have more merit to it than we usually ascribe. Within technology-intensive industries, there is a high degree of industrial turbulence since many start-ups do not survive and the pattern of successful entrepreneurship may involve multiple tries. In a local region, attempts to start companies may be viewed as multiple experiments, and local learning and expertise will develop as potential entrepreneurs witness the outcomes. There seems to be a tendency to view the outcomes of the entrepreneurial process without an appreciation of the lessons learned by the process. Failure provides experience with what does not work, what needs to be more refined, or what was simply bad timing. Nothing teaches like failure. Saxenian (1994), discussing start-up firms in Silicon Valley, notes,

> Not only was risk-taking glorified, but . . . there was little embarrassment or shame associated with business failure. One 1988 study found that of 250 Silicon Valley firms started during the 1960s, 50 percent had failed, 32 percent had merged or been acquired and 18 percent had survived as independent businesses. . . . In fact, the list of individuals who failed, even repeatedly, only to succeed later, was well known within the region (p. 39, endnote 29).

Sitkin (1992) introduces the idea of "learning through failure." Failure promotes resilience, which is important to long-run success. Some of the benefits of failure include attention to and deeper processing of information about potential problems, an increased search for solutions, motivation to adapt, and increased risk tolerance.

There is another phenomenon associated with failure that promotes subsequent rounds of local entrepreneurship and new firm formation. We have observed that when a company fails, its assets, including intellectual property, specialized wet-lab facilities, and clean spaces, are sold at fire-sale prices. This lowers the start-up costs for the next round of entrepreneurs and, we can hypothesize, may subsequently increase the likelihood of their success. In addition, just as assets are recycled, people are also recycled, and locational inertia dictates that they will stay in the same location.

Local economic development policy or university procedures that penalize failure in start-up activity and commercialization will result in a reluctance to take the risks that are a prerequisite to success. This approach will only impede the ultimate desired outcome of encouraging entrepreneurial activity and economic growth.

### The importance of the local in the global economy

In interviews, we ask scientists where they would like to set up shop if they could locate anywhere in the world. The response is that even though they are part of global networks, have international opportunities, and easily could locate anywhere and still stay connected with new telecommunications technologies, they typically want to stay where they are. Working spouses, children, and familiar surroundings, among other factors, create what may be termed *locational inertia*—people simply like to stay put. This seems especially true if they are going to start a new company. Staying in a location that one knows minimizes the disruption and uncertainty that result from adapting to a new environment.

Most importantly, local networks and resources provided the catalyst for the start-up. And it is these resources that the start-up attempts to leverage and build upon.

Our locational models are based on the premise of the footloose actor surveying the landscape for the optimal location. Indeed, as was previously mentioned, this model underlies the bidding wars in which states engage. It seems that policy based on a model of endogenous growth would be more appropriate. Under this model, state and local government policy has an important role in creating an environment that will be conducive to creating and retaining science-based firms. Policy should be predicated on an understanding of the area's scientific resources and industrial mix. Policy should reflect the region's emerging expertise and should be patient. Indeed, the very nature of the process precludes short-run returns, but it promises to yield long-term competitiveness in modern markets.

### Reflective Conclusions

Developing, or fine-tuning, the role of state government in growing a technology-intensive industry requires an understanding of how firms develop. Different technology-intensive industries have unique patterns of development; however, there are some underlying similarities. Most notably, industries appear to cluster geographically in a few sites in the early stages of development. As the industry matures, the typical pattern is that one or two sites will become dominant. The economic development question is how may policy best anchor an industry in a region.

Communities differ widely, however, in their apparent ability to benefit from the science-driven model of economic development. The question of how and why some regions capture the benefits of new technology and thrive while other regions do not is a question of great practical importance. There appear to be important distinctions between a region's ability to generate commercial start-ups and to grow them into larger, more successful companies. In addition, there is a distinction between growing a company and growing an industry. While the success, or failure, of an individual company is easier to track, the best result for economic development would be a well-developed local industry.

### Appendix: Is there geographic specialization in biotech?

The term *biotechnology* is used to describe an entire industry; however, it is really a set of many different technologies. To explore regional specialization, we analyze biotech products and processes by state in Tables 1 and 2. For this analysis, we use a national database of biotechnology companies compiled by the Institute for Biotechnology Information (IBI). IBI categorizes biotech activity by products and processes, and to maintain consistency with the data, these categories are retained in our analyses and presented in the

*Table 1.* Location quotients by state for various biotech products.

| State | Location quotients | Percent of state industry | Number of companies (total in state) |
|---|---|---|---|
| Agriculture, Animal 93 companies, or 6.7% of the biotech industry | | | |
| Iowa | 614.93 | 41.2% | 7 (17) |
| Missouri | 426.87 | 28.6% | 6 (21) |
| Aquaculture 31 companies, or 2.2% of national industry | | | |
| Maryland | 190.91 | 4.2% | 3 (72) |
| Bioelectronics 35 companies, or 2.5% of national industry | | | |
| Minnesota | 552.00 | 13.8% | 4 (29) |
| Pennsylvania | 308.00 | 7.7% | 5 (65) |
| Diagnostics, Clinical Human 387 companies, or 28% of national industry | | | |
| Maine | 130.00 | 36.4% | 4 (11) |
| Ohio | 130.00 | 36.4% | 12 (33) |
| California | 126.43 | 35.4% | 104 (294) |
| Immunological Products 151 companies, or 10.9% of national industry | | | |
| Maryland | 153.21 | 16.7% | 12 (72) |
| Virginia | 190.83 | 20.8% | 5 (24) |
| Therapeutics 561 companies, or 40.5% of national industry | | | |
| Massachusetts | 137.28 | 55.6% | 75 (135) |
| Washington | 136.54 | 55.3% | 21 (38) |
| Vaccines 112 companies, or 8.1% of national industry | | | |
| Maryland | 154.32 | 12.5% | 9 (72) |
| Pennsylvania | 151.85 | 12.3% | 8 (65) |
| Agriculture, Plant 145 companies, or 10.5% of biotech industry | | | |
| Iowa | 336.19 | 35.3% | 6 (17) |
| Utah | 254.29 | 26.7% | 4 (15) |
| Energy 16 companies, 1.2% of national industry | | | |
| California | 116.67 | 1.4% | 4 (294) |
| Bioseparations 67 companies, or 4.8% of national industry | | | |
| Maryland | 143.75 | 6.9% | 5 (72) |
| North Carolina | 112.50 | 5.4% | 4 (74) |
| New Jersey | 112.50 | 5.4% | 5 (93) |
| Environmental 107 companies, or 7.7% of national industry | | | |
| Michigan | 171.43 | 13.2% | 5 (38) |
| Oregon | 294.81 | 22.7% | 5 (22) |

(*Continued on next page.*)

*Table 1.* (Continued).

| State | Location quotients | Percent of state industry | Number of companies (total in state) |
|---|---|---|---|
| Reagents 384 companies, or 27.7% of national industry | | | |
| Ohio | 153.07 | 42.4% | 14 (33) |
| Oregon | 164.26 | 45.5% | 10 (22) |
| Veterinary 116 companies, or 8.4% of national industry | | | |
| Iowa | 279.76 | 23.5% | 4 (17) |
| Kansas | 679.76 | 57.1% | 4 (7) |

tables. IBI identifies companies by regularly surveying IBI member firms and through systematic reviews of trade journals and other publications. In order to provide more detail on the industry, IBI collects data on areas of product development activity.[6] Prevezer (1997) used this source to demonstrate the existence of geographic clustering in biotechnology but did not explore regional specialization.

We found 13 biotechnology product groups with at least 1% of the nation's biotechnology industry. We analyzed the regional concentration of these 13 product categories by state; each state included in the analysis had at least four companies within the specified product category. These are shown in Table 1. The product areas of specialization include Agriculture, Animal; Agriculture, Plant; Aquaculture; Bioelectronics, Bioseparations; Diagnostics, Clinical Human; Energy; Environmental; Immunological Products; Reagents; Therapeutics; Vaccines; and Veterinary. Table 2 details state specialization by various biotech processes. These are the technologies in which biotech companies claim (in the IBI company survey) a specialty. The processes are Combinatorial Chemistry, Fermentation, Gene Therapy, Genetic Engineering, Hybridoma, Large-Scale Cell Culture, Liposomes, Oligonucleotides, Protein Engineering, Tissue Culture, Transgenics, and "Other." We are interested in regional specialization by process as well as product because knowledge spillovers, which create regional agglomeration, can be in the form of a technology or a specific product.

The significant share of a particular product or process category is measured by a location quotient, a ratio of the percentage of the state's biotech industry to the percentage of the nation's biotech industry. A location quotient measures the state's specialization in comparison to the rest of the country. A location quotient of 100 means that the state has the same proportion of companies specializing in a certain product category as the nation has. Areas of specialization are important to identify because, according to the observed patterns of biotech agglomeration, company founders will establish their companies in areas where they perceive a regional competitive advantage. We report the states with the top two location quotients for each product and process category.

*Table 2.* Location quotients by state for various biotech processes.

| State | Location quotients | Percent of state industry | Number of companies using (total in state) |
|---|---|---|---|
| Combinatorial Chemistry 55 companies, or 4.0% of the national biotech industry | | | |
| California | 128.33 | 5.1% | 15 (294) |
| Gene Therapy 55 companies, or 4.0% of the national biotech industry | | | |
| Pennsylvania | 196.28 | 7.8% | 5 (65) |
| Texas | 201.31 | 8.0% | 4 (50) |
| Hybridoma 364 Companies, or 26.3% of the national biotech industry | | | |
| Indiana | 221.79 | 58.3% | 7 (12) |
| Maryland | 147.86 | 38.9% | 28 (72) |
| Liposomes 80 Companies, or 5.8% of the national biotech industry | | | |
| Colorado | 256.30 | 14.8% | 4 (27) |
| New Jersey | 241.83 | 14.0% | 13 (93) |
| Protein Engineering 327 companies, or 23.6% of the national biotech industry | | | |
| Maryland | 141.08 | 33.3% | 24 (72) |
| Ohio | 141.08 | 33.3% | 11 (33) |
| Washington | 144.79 | 34.2% | 13 (38) |
| Transgenics 31 companies,or 2.2% of the national biotech industry | | | |
| Massachusetts | 165.35 | 3.7% | 5 (135) |
| Fermentation 375 companies, or 27.1% of the national biotech industry | | | |
| Iowa | 238.81 | 64.7% | 11 (17) |
| Louisiana | 246.04 | 66.7% | 4 (6) |
| Genetic Engineering 465 companies, or 33.6% of the national biotech industry | | | |
| Connecticut | 210.09 | 70.6% | 12 (17) |
| New York | 146.38 | 49.2% | 30 (61) |
| Large-Scale Cell Culture 515 companies, or 37.2% of the national biotech industry | | | |
| Maryland | 134.40 | 50% | 36 (72) |
| Ohio | 138.40 | 51.5% | 17 (33) |
| Oligonucleotides 42 companies, or 3.0% of the national biotech industry | | | |
| Texas | 329.52 | 10% | 5 (50) |
| Tissue Culture 412 companies, or 29.8% of the national biotech industry | | | |
| Delaware | 268.74 | 80% | 4 (5) |
| Kansas | 191.96 | 57.1% | 4 (7) |
| Other 225 companies; or 16.3% of the national biotech industry | | | |
| Georgia | 161.87 | 26.3% | 5 (19) |
| Texas | 141.11 | 26% | 13 (50) |

Several states rank in the top two location quotients for more than one product and process category. Iowa shows specialization in several agriculturally oriented fields: in fermentation (238.81), animal agriculture (614.93),[7] veterinary products (279.76), and plant agriculture (336.19). Maryland has concentrations in various fields signifying diversified companies and local industry: hybridoma technology (147.86), protein engineering (141.08), large-scale cell culture (134.40), aquaculture products (190.91), vaccines (154.32), bioseparations (143.75), and immunological products (153.21) are concentrated there. Such a diversity in Maryland argues against a trend in regional specialization; however, the large-scale cell culture and bioseparation focus could have grown out of supplying the national science and research institutions in the state and suggests a specialization in the development of intermediary biotech processes. The other areas, with the exception of aquaculture, are human applications, which also could have developed from the concentration of human science at the National Institutes of Health and related institutions. Maryland is the only state that has a significant share of the nation's aquaculture biotechs, with a location quotient of 190.90. While it is premature to suggest causal relationships between the environment and the number of firms, we note that Maryland has resources that could attract aquaculture biotechs. The Center of Marine Biotechnology (COMB) is a marine research institute in downtown Baltimore and is one of the University of Maryland Biotechnology Institute's four centers of biotechnology research.

Massachusetts exhibits regional specialization in therapeutics (137.28) and transgenics (165.35). Ohio firms have specializations in protein engineering (141.08), large-scale cell culture (138.40), and reagents (153.07). Oregon shows specialization in environmental products (294.81) and reagents (164.26). Pennsylvania firms specialize in gene therapy (196.28), bioelectronics (308.00), and vaccines (151.85). Surprisingly, two states with a large number of companies, California and New Jersey, rarely have location quotients over 100 (although California shows a regional advantage in two areas: combinatorial chemistry [a process], with a location quotient of 128.33, and energy products, with a location quotient of 116.67). We believe that this is because the diverse product focus of their numerous biotechs approaches the distribution of national firms.

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## Notes

1. Jaffe and Trajtenberg (1996) find that knowledge spillovers, as measured by citations to prior patents, are more important than traditional factors such as taxes and wages in determining the location of start-up activity. Studies by Jaffe (1989), Feldman and Florida (1994), and Jaffe, Trajtenberg, and Henderson (1993) find that knowledge spillovers generated by universities are geographically mediated. Zucker, Darby, and Brewer (1997) link knowledge spillovers to the location of new firm start-ups in the emerging biotechnology industry. Audretsch and Feldman (1996) demonstrate the tendency for industries in which new knowledge is important to cluster spatially. This work is reviewed in Feldman (1999).
2. *Biotechnology* may be narrowly defined as the use of recombinant DNA methods or broadly defined as anything related to life sciences. The term *biosciences* is used to be broadly inclusive of the spectrum of disciplines that utilize modern biology in their work. *Bioscience* is defined as any activity that substantially involves research, development, or manufacture of (1) biologically active molecules, (2) devices that employ or affect biological processes, or (3) devices and software for production or management of biological information. This term is used instead of the more popularly used, and misused, term *biotechnology.*
3. James Watson and Francis Crick were awarded the Nobel Prize in Medicine in 1962 for this work. See Watson (1981) for an account of the discovery process.
4. Source: http://outcast.gene.com/Company/timeline.html.
5. These data are limited to a cross section and are further limited as firms report their research and product development areas. There is no measure of firm effort or success in these fields.
6. The IBI database has been used by other researchers (cf. Greis et al., 1995) but has not been formally validated. We cross-referenced companies in Maryland identified by IBI with those identified by our other sources. IBI missed a total of 55 companies that were identified by the Corp Tech Directory and Maryland Technology Resource Council. However, IBI identified 20 companies that the other two references missed.
7. The very high location quotients are in the product and process categories that comprise a small percent of the nation's biotech industry. For example, animal agriculture is only 6.7% of the nation's biotech industry, or 93 companies nationwide.

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