

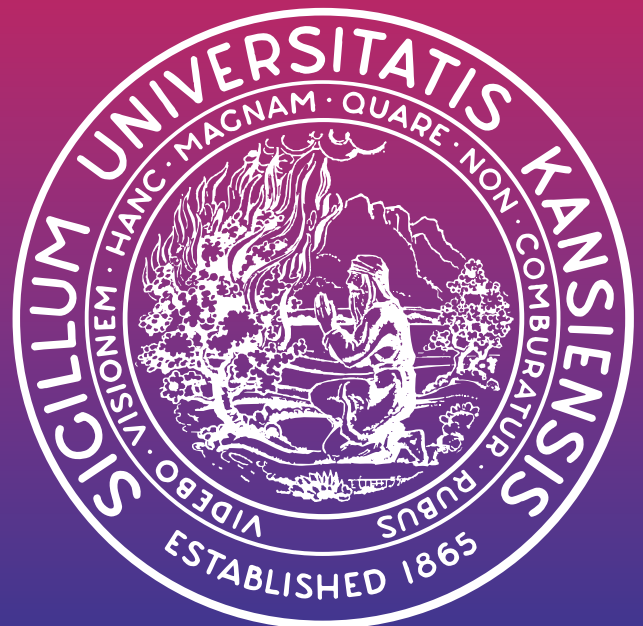


THE CENTER FOR
APPLIED ECONOMICS

Supporting Regional Economic Development through Analysis and Education

ECONOMIC
FACTORS
RELATED
TO THE
DEVELOPMENT
AND
COMMERCIALIZATION
OF
BIOTECHNOLOGIES

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TECHNICAL REPORT 05-0204

February 2005

About the Author

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ECONOMIC FACTORS RELATED TO THE DEVELOPMENT AND COMMERCIALIZATION OF BIOTECHNOLOGIES

I. INTRODUCTION

There is a rich academic literature that identifies both conceptually and empirically economic factors related to the growth of biotechnology activity in the United States. The purpose of this report is to summarize that literature so individual organizations and institutions can use it for planning within the context of a regional economic growth strategy. This literature summary concludes that:

- | The success of biotechnology clusters within several regions in the country has led many other planners to also focus on biotechnology as a key toward stimulating growth in their own regions. To date, the overall success of such an imitative strategy is unclear although there have certainly been success stories.
- | The biotechnology clusters that have achieved visible success have at their core a university(ies) or a research institute(s) where the underlying bioscience base, upon which the biotechnology emanates, is created. Thus, many planners who are seeking to develop a biotechnology cluster are looking toward the creation of a university research park to be the catalyst to the formation and growth of the cluster.
- | Historical circumstances – generally unplanned creative research activities – centered around a bioscience core were key to the success of those clusters that have achieved visible success. Thus, the success of new purposeful efforts to develop biotech-

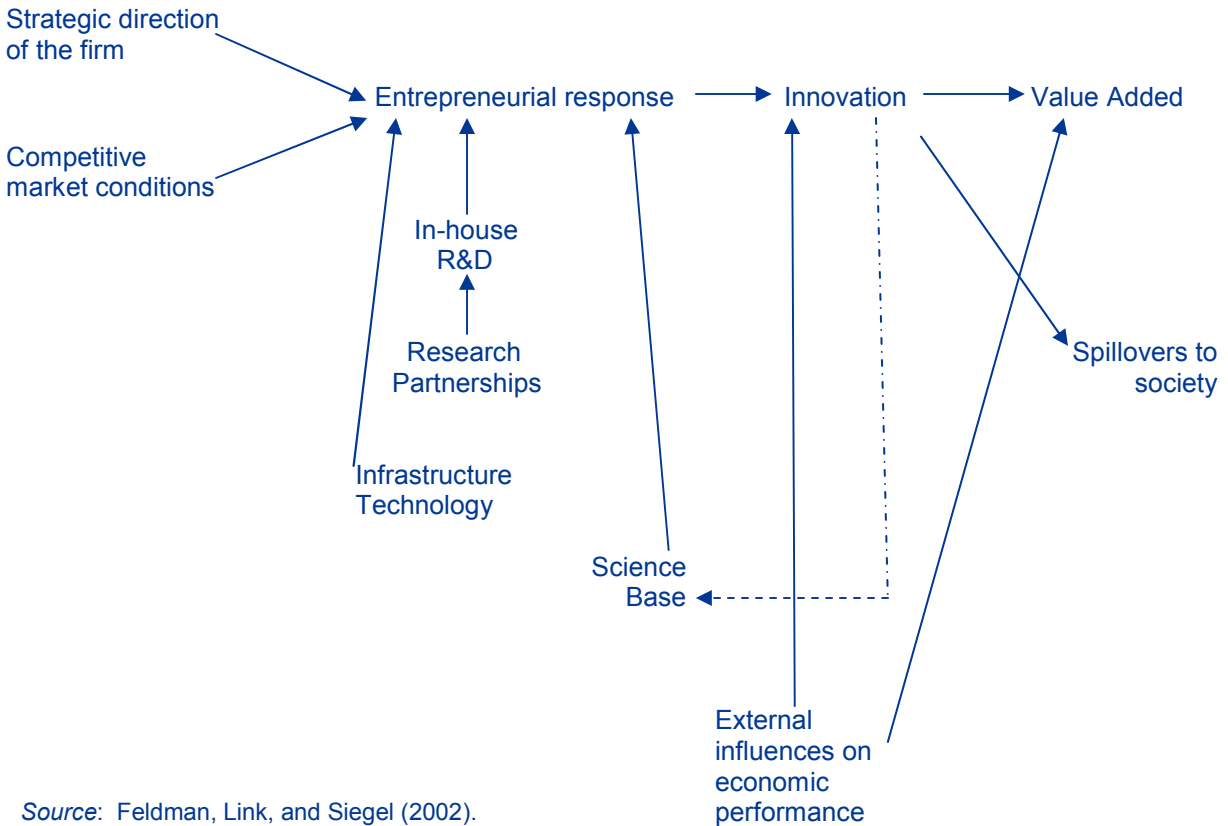
nology clusters could be uncertain unless planners are able to create an environment that spawns similar creative research.

This report begins with a traditional model of technology-based entrepreneurial activity as an effort to bring all readers to a common point of understanding about research, innovation, and economic factors that affect both. The model is traditional in the sense that it applies to manufacturing firms, which have long been engines of economic growth in the United States and in most industrialized nations. Economists have theorized about innovative activity with reference to manufacturing firms, and they have emphasized that innovative activity is a catalyst to economic growth at both the aggregate level as well as the regional level. Thus, this so-called traditional model is a logical starting point. Within this model, which is discussed in Section II, a number of knowledge bases are identified and their relationships to each other and to the growth of the benchmark firm are described.

The biotechnology industry, including an historical overview of bioscience and biotechnology successes and of biotechnology cluster formations, is discussed in Section III.

Using the information from Section III, the traditional model from Section II is recast in Section IV with a specific emphasis on biotechnology. Within this new model of what may be called technology-based entrepreneurial activity applicable to biotechnology firms, the lessons from the history of the biotechnology industry are highlighted in an effort to emphasize to individual organizations and institutions the myriad factors that need to be understood

**Figure 1:
Technology-Based Model of Entrepreneurial Activity**



Source: Feldman, Link, and Siegel (2002).

if successful cluster planning is to occur. Also within the context of this model, the extant literature is reviewed so as to describe the unique nature of biotechnology firms and the role of public policy to foster an environment conducive for cluster formation. That environment will focus on the role of alternative knowledge bases.

Section V discusses several strategic issues for economic development related to the topics of Section III and Section IV. Section VI concludes the report with a summary statement.

II. A TECHNOLOGY-BASED MODEL OF ENTREPRENEURIAL ACTIVITY

Consider the technology-based model of entrepreneurial activity in Figure 1. Within this model, the strategic direction of the firm and the competitive pressures that it faces from market activity motivate an entrepreneurial response. Thinking of entrepreneurship as the perception of opportunity and the ability to act upon that perception (Hébert and Link 1988), the firm, based on its perceptions of competitive market conditions –

domestic and global – and its determined strategic direction, both perceives opportunities for growth and acts upon those perceptions. This action is referred to in the figure as the firms’ “entrepreneurial response.”

From left to right in the upper portion of the figure, the firm evaluates competitive market conditions in light of its own strategic directions, perceives opportunities, and responds to those opportunities through innovation. The results of the innovation process are new or modified products or processes, and they add value to the firm. This is, within the economics and R&D management literatures, a traditional technology-based production process.

A number of activities leverage or enhance the firm’s entrepreneurial response. One activity is in-house research and development (R&D), and that is the focal point of the model. There are other knowledge sources that leverage the response as well, but in-house R&D is the most important. Enhancing the firm’s R&D activity is its relationship with other organizations and with the external environment. One such relationship is the firm’s involvement in research partnerships, with other firms or perhaps with either a university or a federal laboratory.¹ Research partnerships provide a number of advantages to R&D-active firms including reduced research time and less redundant research leading to less R&D costs. Of course, countering these advantages is the possible lack of appropriability of the research results.

Infrastructure technology is also an important factor that leverages a firm’s R&D. It represents what economists call public good technology meaning that no one firm in an industry gains a competitive advantage from using it, but using it increases efficiency. Infrastructure technology emanates from federal laboratories, such as, for example, the National Institute of Standards and Technology (NIST) (Tassey 1992, 1997), or from the environment created by, for example, being located in or near a research park (Link 1995, 2002, 2003; Link and Scott 2003a, 2003b, forth-

coming a, forthcoming b). Examples of infrastructure technology include test methods, measurement standards, and standard reference materials.

Finally, there is the science base, which consists of the stock of knowledge generated from basic research. The science base resides in the public domain – and the public domain is international in scope – generally in the form of scientific journals, but also it is in part embodied in a university’s or institute’s human capital – its researchers, scientists, and students.² It is important to emphasize that in this model the science base provides general knowledge to the firm to enhance its ability to respond to perceived opportunities. In the technology-based model of entrepreneurial activity specific to the biotechnology industry, discussed below, the science base has a different role.

The result of the entrepreneurial process is an innovation. An innovation will generate value added if it is accepted in the marketplace, and it will diffuse into society and generate spillover benefits to other firms both within the industry and in outside industries that ultimately use the innovation.³

The dashed arrow coming back to the science base represents internal feedback. Once an innovation exists, knowledge has been created and it too will then reside in the public domain.

Also influencing the nexus between the firm’s entrepreneurial response and innovation are other external influences such as federal and state science and technology policies. Examples of such include, but are certainly not limited to, federal or state policies to encourage innovation such as changes in patent regulations, or purposeful activities designed to grow a regional biotechnology industry.

The usefulness of this model is as a means to highlight the myriad sources of scientific and technical information that firms rely on to support their innovative activity. Certainly, not all firms rely on each source to the same degree. Public-domain data suggest that larger firms –

manufacturing firms in particular – in competitive environments generally rely more heavily on their in-house R&D than smaller firms. Smaller firms rely more on external sources of technical expertise, but most external sources are based on private-sector R&D. The reason for this pattern is that economies of scale are needed within a firm to conduct R&D efficiently. Regardless of the source of R&D, an important generalization from the model in Figure 1 is that manufacturing innovation and technology development is driven by private R&D.

III. THE EVOLUTION OF THE BIOTECHNOLOGY INDUSTRY

A. Defining Biotechnology

A number of alternative, yet similar, definitions of “biotechnology” appear in the academic (as opposed to the scientific) literature. Several are excerpted below, not in a particular order.

According to the U.S. Department of Commerce (2003, p. 3):

... biotechnology [is] the application of molecular and cellular processes to solve problems, conduct research, and create goods and services.

The hallmark of biotechnology, according to the U.S. Department of Commerce (2003, p. 7) is:

... cellular and genetic techniques that manipulate cellular and subcellular building blocks for applications in various scientific fields and industries such as medicine, animal health, agriculture, marine life, and environmental management.

More simply, the North Carolina Biotechnology Center defines biotechnology as:⁴

A collection of technologies that use living cells and/or biological molecules to solve problems and make useful products.

This is similar to the definition posited by Toole (2003, p. 176):

At the broadest level, biotechnology refers to the use of micro-organisms to make or modify a product or process.

Audretsch (2001, p. 3) defines biotechnology as:

... techniques and technologies that apply the principles of genetics, immunology and molecular, cellular and structural biology to the discovery and development of novel products.

It is important to emphasize that it is not the products and processes associated with biotechnology that are its defining characteristics, but that biotechnology, as similarly stated above, is defined with regard to the techniques or fundamental technologies used to develop the products and processes. According to Paugh and Lafrance (1997, p. 21), for example:

... biotechnology is not defined by its products but by the technologies used to make those products. Biotechnology refers to a set of enabling technologies by a broad array of companies in their research, development, and manufacturing activities.

Cells contain genetic material, DNA that acts like a blueprint for the function and structure of the cell. Through biotechnology, the genetic blueprint can be isolated, copied, and rearranged at the molecular level to alter or manipulate the function and structure of the cell (Paugh and Lafrance 1997).

In all likelihood, current definitions of biotechnology will increasingly be modified as what is now the biotechnology industry becomes embedded within other industries. As well, some have defined biotechnology on the basis of techniques and technologies used, but that may be an arbitrary constraint. Molecular and cellular biology will increasingly be integrated with chemical and computer technology as the process of R&D becomes further automated.

B. Defining the Biotechnology Industry

Definitions aside, the term, “biotechnology industry,” remains somewhat misleading to academics, although the term is casually and widely used by public policy makers as well as the popular press. One possible reason for this is that there is in the United States, as well as in other industrialized nations, no group of homogeneous firms or organizations that clearly defines such an industry (Toole 2003). In the United States, for example, firms that are involved in the technology that resulted from advances in biosciences – biotechnology – are not classified separately for industrial census purposes. One obvious reason for this is that the application of that technology is relatively new. And another obvious reason is that the scope of application of that technology is vast and constantly changing. Accordingly, a number of scholars have argued that one should not think of a biotechnology industry in the traditional sense of products and products produced by similar techniques, but rather in terms of an agglomeration of scientific and product collaborations (Liebeskind 1996; Oliver 2001, 2004; Owen-Smith 2002; Powell 1992, 2002; Weisenfeld 2001; and Zucker 2002).

The U.S. Department of Commerce (2003) recently surveyed a large sample of U.S. firms that identified themselves as “biotech organizations.” These organizations operate in a variety of traditionally-defined industries, thus illustrating the

heterogeneous nature of the application of the underlying technologies. The application industries, along with the percentage (rounded) of respondents in each, are:

- | Basic industries and materials (4.3%);
- | Chemical manufacturers (4.4%);
- | Information and electronics (4.3%);
- | Machinery manufacture (0.6%);
- | Medical substances and devices (32.6%); and
- | Various services (R&D, testing, diagnostic, etc.) (40.9%).

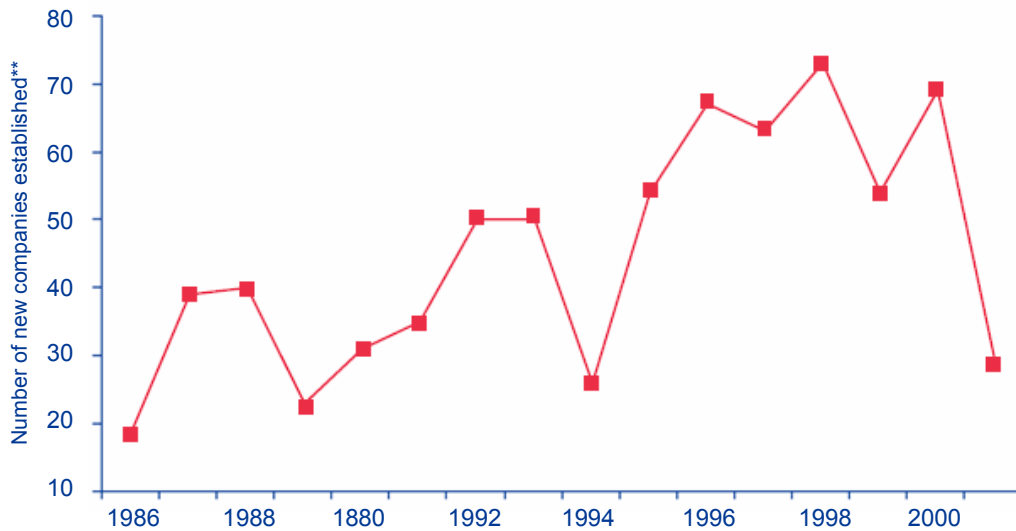
And, 13.0 percent of the respondents could not identify a specific application industry.

Prevezer (1998), among others, conceptualizes the so-called biotechnology industry in terms of the applications that the sector develops:

- | Therapeutics sector – developing therapeutic application (drugs);
- | Diagnostic sector – creates diagnostic applications;
- | Chemicals sector – makes pesticides, insecticides, and new chemicals;
- | Agriculture sector – develops seed, plant, and animal applications;
- | Food and cosmetic sector – formulates enzyme applications;
- | Environmental sector – deals with waste products; and
- Energy sector – seeking biomass energy sources.

Albeit somewhat imprecise and ill-defined from a strict economics definition of an industry, as discussed below, the number of new so-called biotech firms has increased over time in the United States, as shown in Figure 2. The underlying data depicting this irregular trend come from the above-mentioned U.S. Department of Commerce (2003) survey. These data relate to start-ups, and there is no information available regarding the success or failure of such firms. Based on the survey data underlying Figure 2, and accepting an application-based definition of the biotechnology industry, Figure 3 shows the

**Figure 2:
Number of New Biotech Companies by Year: 1996-2001**

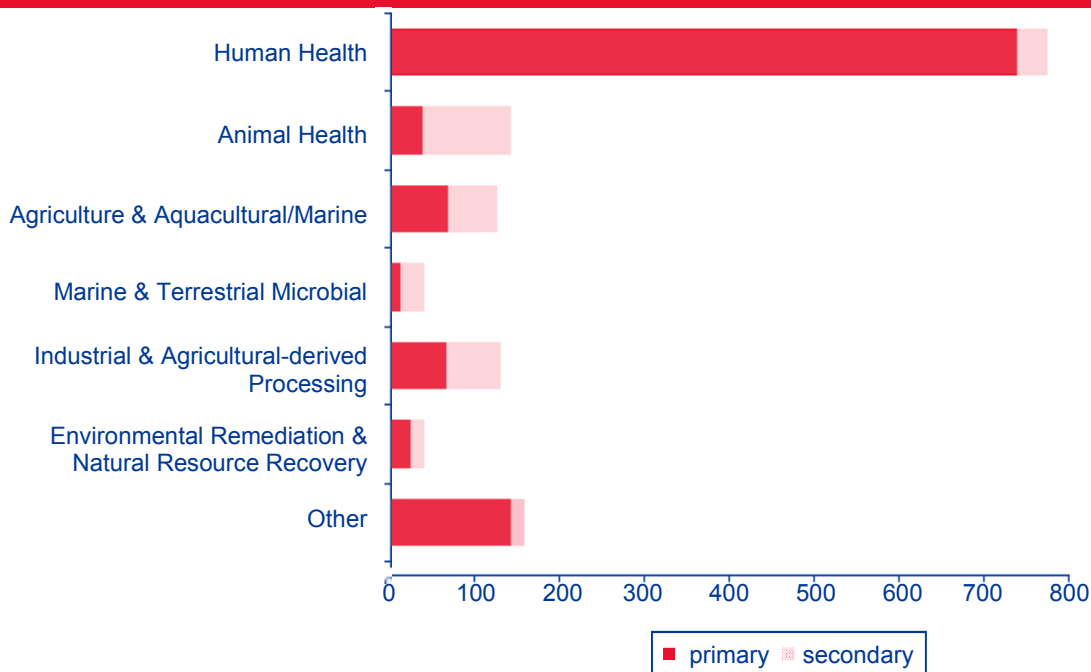


*2002 data are excluded due to difficulty identifying all new firms to receive the survey and because the survey was conducted before the end of 2002; 2001 data may also undercount the number of firms established in that year.

**Based on responses from 722 firms representing 73.1 percent of the 959 respondents that provided establishment data.

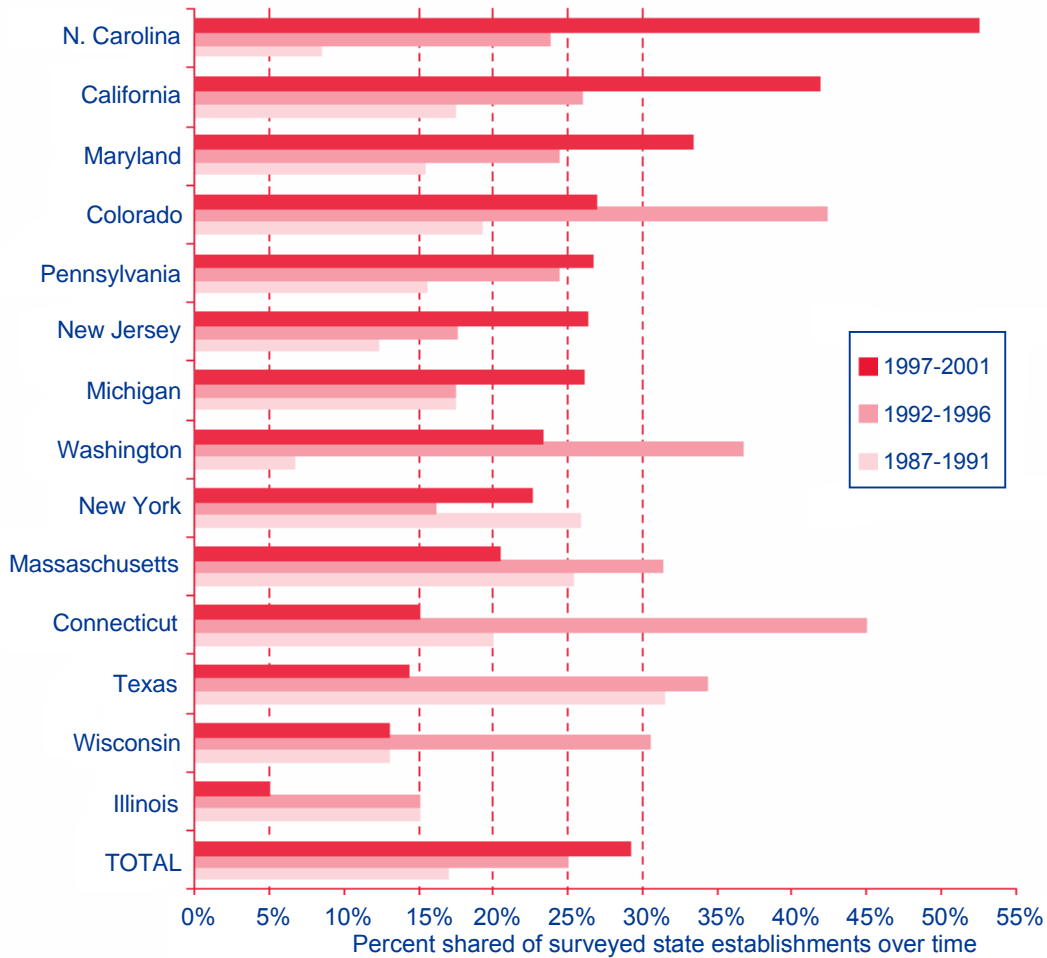
Source: U.S. Department of Commerce (2003).

**Figure 3:
Primary and Secondary Activities by Biotech Applications**



Source: U.S. Department of Commerce (2003).

**Figure 4:
Growth in Biotech Firms, by State and by Years**



*96 percent of responding firms reported establishment dates; data include only states reporting 20 or more firms.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry*, question 1, p.1, August 2002

relative distribution of application areas and Figure 4 shows the growth of new biotech firms by selected time periods and states.

Human health, as an application area, dominates because of pharmaceuticals (Figure 3).⁵ In the most recent years, the growth of biotech firms has been greatest in North Carolina due, in part, to the changing tenant mix of Research Triangle Park, spin-off from those companies, and the success of the state-funded North Carolina Biotechnology Center in building a bioscience and biotechnology industry

in the state (2002). See Figure 4.

Collectively, these three figures suggest that:

- | Since 1996 there has been an upward trend in the birth of new biotechnology companies;
- | These new companies have as their primary application human health; and
- | These new companies are geographically dispersed.

In 2001, self-defined biotech firms accounted for \$50.47 million in revenue, of which nearly 21 percent came from firms with total revenues of \$501 to \$2,500 million, 30.6 percent from firms with total revenues of \$2,501 to \$15,000 million, and 35.1 percent from firms with total revenues exceeding \$15,000 million. Clearly, biotechnology applications are occurring within very large firms, but biotechnology applications represent, on average, less than 10 percent of the total revenue of such firms (U.S. Department of Commerce 2003).⁷

As opposed to defining the biotechnology industry in terms of application industries or areas, one possible alternative is to think about the biotechnology industry in terms of the sectors from which those organizations involved in the overall value added process come. Thus, the biotechnology industry has three distinct segments. Segment one includes universities and research institutes where the underlying bioscience base upon which the technology is created; segment two includes dedicated biotechnology firms (DBFs) which rely on the science base and, using it, develop new technological procedures and techniques; and the third segment includes user firms which apply the technological procedures of DBFs to application areas, and I refer to these firms as biotechnology commercializing firms (BCFs).⁸

According to Lehman (2003), using Ernst & Young proprietary data from 2002, the top five states in terms of the number (in parentheses) of biotechnology companies – DBFs plus BCFs – are: California (410), Massachusetts (210), Maryland (95), North Carolina (87), and Pennsylvania (71).

C. Historical Background about Bioscience and Biotechnology⁹

Science, in a broad sense, is the search for knowledge, and that search is based on observed facts and truths. Thus, science begins with known starting conditions and searches for unknown end

results (Nightingale 1998). Technology, in contrast, is the application of new and unapplied knowledge, learned through science, to known practical problems. Technological change is the rate at which new and unapplied knowledge is diffused and put into use in the economy. Thus, and this distinction is important for understanding the biotechnology industry, bioscience is the search for new knowledge in the biological sciences, and biotechnology is the application of bioscience to new products and processes.

The biotechnology industry began with breakthroughs in the biosciences.¹⁰

- | In 1953, Watson and Crick discovered the double helix structure of DNA.
- | In 1957, Kornberg revealed how DNA is replicated through the discovery of the enzyme DNA polymerase I.
- | In 1973, Cohen and Boyer developed the recombinant DNA (r-DNA) technique.
- | In 1975, the first monoclonal antibodies were discovered.

These above bioscience breakthroughs were used very quickly by DBFs to develop biotechnologies, and, not surprisingly, these DBFs located near the bioscience breakthroughs in San Francisco and nearby Silicon Valley and in Cambridge, MA:

- | In 1976, Genentech (a DBF) was founded in San Francisco by venture capitalist Robert Swanson of Kleiner Perkins and professor Herbert Boyer of the University of California at San Francisco.¹¹ The goal of the new company was to use bioscience to synthesize human insulin. This was accomplished in 1978.
- | In 1978, Biogen (a DBF) was founded in Cambridge, MA, by Harvard professor Walter Gilbert, among others including MIT professor Phillip Sharpe.
- | In 1979, Genentech developed the first synthetic human growth hormone, somatropin.

- In 1980, based on the Nobel Prize winning research of Gilbert in sequencing nucleotides, Biogen agreed to allow pharmaceutical company Schering-Plough (a BCF) to license beta interferon
- In 1982, the Food and Drug Administration (FDA) approved the Genentech – Eli Lilly (a pharmaceutical company and a BCF, as well as a competitor of Schering-Plough) product, Humulin, for commercial use.

There are at least two generalizations that come from these parallel pioneering bioscience and biotechnology histories. First, specialized knowledge – tacit knowledge which requires face-to-face interaction as opposed to codified knowledge – is prerequisite or a necessary condition for the creation of a DBF.¹² Genentech in San Francisco and Biogen in Cambridge, MA, were formed on the basis of tacit bioscience knowledge from the University of California at San Francisco and from Harvard University and MIT, respectively, that transferred through scientists.¹³ Second, DBFs rely on strategic alliances with established companies – pharmaceutical BCFs in these early instances – to bridge the intellectual gap between science and technology, and then technology and commercialized products.¹⁴

D. Biotechnology Clusters

Clusters, according to Porter (1997, p. 78-79):

... are geographic concentrations of interconnected companies and institutions in a particular field. ... A cluster's boundaries are defined by the linkages and complementarities across industries and institutions that are most important to competition. ... Clusters rarely conform to standard industrial classification systems, which fail to capture many important actors and relationships in competition. ... Clusters

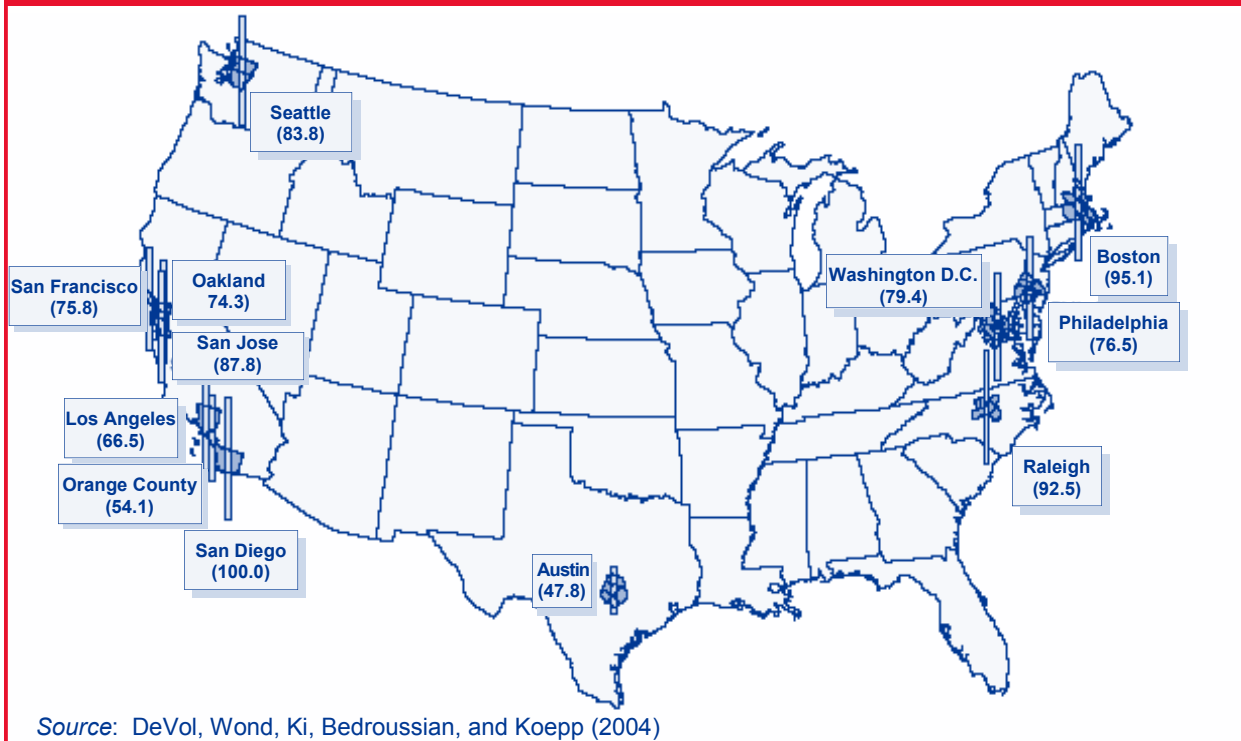
promote both competition and cooperation. ... Clusters represent a kind of new spatial organization form in between arm's-length markets on the one hand and hierarchies, or vertical integration, on the other. A cluster, then, is an alternative way of organizing a value chain

Based on the historical activity surrounding San Francisco and Cambridge, it follows that DBFs would spin-off from universities heavily involved in the biosciences, and these biotechnology firms would be within clusters of each other and of pharmaceutical firms or other application firms. In fact, as shown in Figure 5, this is exactly what happened over time.

Figure 5 is based on the Milken Institute's Biotech Index for 2004 (DeVol et al. 2004). That index, which ranges from 0 to 100, is constructed on five local dimensions: R&D inputs, risk capital and the entrepreneurial infrastructure, biotech human capital investments, biotech workforce, and the biotech current impact based on scale of biotech activity. As seen from the index numbers in the figure, San Diego ranks first and is therefore benchmarked at an index value of 100, followed by Boston with a relative index of 95.1, the research triangle in North Carolina with a relative score of 92.5, and the San Jose region with a relative score of 87.8. These are relative composite index values – Boston's composite index is five percentage points lower than San Diego's meaning that on average its R&D inputs, risk capital, investments in biotech human capital and workforce are about 95 percent of those for San Diego. Of course, the evolution of bioscience and biotechnology since the mid-1960s has seen a number of new university centers of excellence arise, yet the Harvard area and San Jose / San Francisco areas remain dominant.

The San Diego biotechnology area developed similarly to the San Francisco and Cambridge areas. The Salk Institute was founded in 1955, followed by the Scripps Research Institute in 1960 and the

**Figure 5:
Major Biotechnology Centers in the United States, 2004**



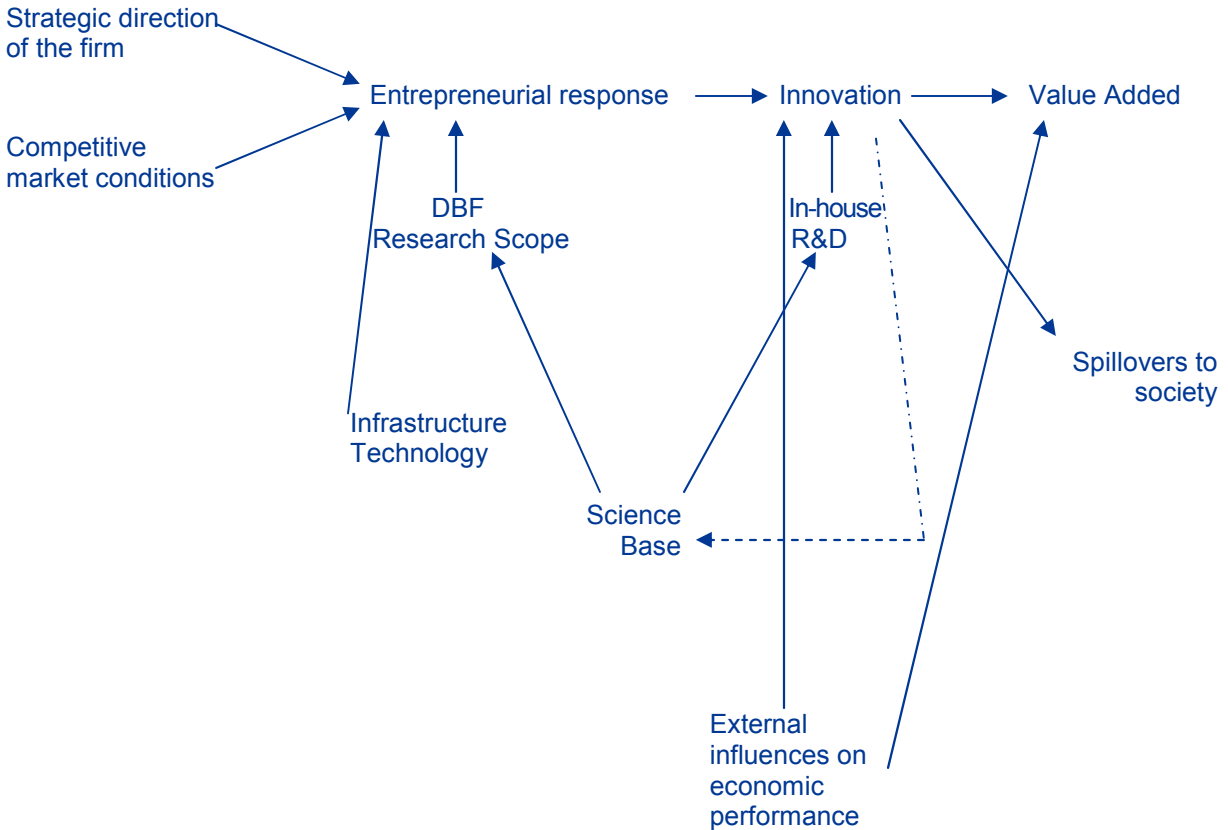
University of California at San Diego (UCSD) in 1964. The Burnham Institute was founded in 1976 by William H. Fishman and his wife Lillian Fishman. Fishman spent his research career at Tufts University School of Medicine. The Foundation originally focused on cancer research but today its focus is much broader. Hybritech was founded in 1978 and was San Diego's first DBF; it was acquired by Eli Lilly in 1986. Hybritech became the anchor firm in the San Diego area (Porter 2001).¹⁶

Aside from these three regional cases, Zucker and Darby (1994, 1997, 1998) and their colleagues – as well as others such as Audretsch and Stephan (1996) using U.S. data and Seller (2001) using European Union data, have demonstrated empirically – using U.S. data, that the timing and location of new DBFs can be explained in large part by the presence of bioscience scientists in a particular location at a particular point in time.

Why do biotechnology firms cluster?¹⁷ From a theoretical perspective, there are both demand and supply forces at work that result in the clustering of DBFs, as well as the clustering of larger application firms with which the DBFs have a strategic alliance relationship. On the demand side, within a cluster there are sophisticated users for the bioscience-based biotechnology of the DBFs.¹⁸ And, search costs for users of the technology are minimized. Of course, there are disadvantages associated with clustering, namely greater competition for the developed technologies.

On the supply side, there are within clusters more skilled and specialized labor, although there is also more competition for that pool of labor. And, clusters provide a greater opportunity for knowledge – tacit knowledge in particular – spillovers. The theory of agglomeration economics emphasizes this latter point (Swann 1998).^{19,20} According to Beaudry and Breschi (2003, p. 326):²¹

**Figure 6:
Technology-Based Model of Entrepreneurial Activity
in the Biotechnology Industry**



Source: Adapted from Feldman, Link, and Siegel (2002).

... transmission of technological knowledge works better within spatial boundaries because this type of knowledge has a tacit and uncoded nature and thus flows through networks of interpersonal communications.

IV. A TECHNOLOGY-BASED MODEL OF ENTREPRENEURIAL ACTIVITY RELATED TO BIOTECHNOLOGY

Figure 6 is slightly different than Figure 1, but the difference is critically important since it defines, to an extent, the economic factors related to the development and commercialization of biotechnologies. First, the driver of the biotechnology commercializing firm (BCF; e.g., a pharmaceutical firm) is the scope of

research of a DBF that is spatially nearby. Underlying innovations occur with DBFs and are then embodied, through strategic alliances or mergers, into BCFs. Biotechnology applications do not necessarily result from in-house R&D as they do in manufacturing firms (see Figure 1). Rather, in-house R&D is important in modifying the DBFs innovations and providing absorptive capacity for the BCF.²²

For the BCF represented in Figure 6, its entrepreneurial response to potential markets for biotechnology products and processes depends on the scope of research of DBFs, and such firms must be spatially close. The BCF, unlike the traditional technology-based manufacturing firm, does not rely on in-house R&D as the driver of its innovations; rather it relies upon the DBFs embodied knowledge base and technological capabilities. The role of in-house R&D for the BCF occurs at the innovation stage when product and process modifications are needed just prior to commercialization.

The science base emanating from universities and research institutions and flowing through scientists is a necessary condition for the success of the DBF, and such knowledge leverages the success of the BCF's in-house R&D.²³

V. BIOTECHNOLOGY, UNIVERSITY PARTNERSHIPS, AND REGIONAL ECONOMIC DEVELOPMENT

There is abundant evidence that regions and localities are looking toward biotechnology as a lever to stimulate economic growth. Many are looking toward universities and other laboratory complexes (e.g., federal laboratories) to develop research parks with a biotechnology focus to stimulate economic growth.

The model in Figure 6 describes a number of necessary conditions associated with cluster formations. In a

successful biotechnology cluster, one that is long-lived – and the data that are available are for long-lived clusters – there must be BCFs since they are major employers and drivers of regional economic growth. But, as shown in the model, fundamental to the success of BCFs is a sub-cluster of DBFs from which inventions emanate. But then again, fundamental to inventive DBFs is the presence of a rich science base driven by university or institute research. At the core of the clustering process, then, is basic and fundamental research.

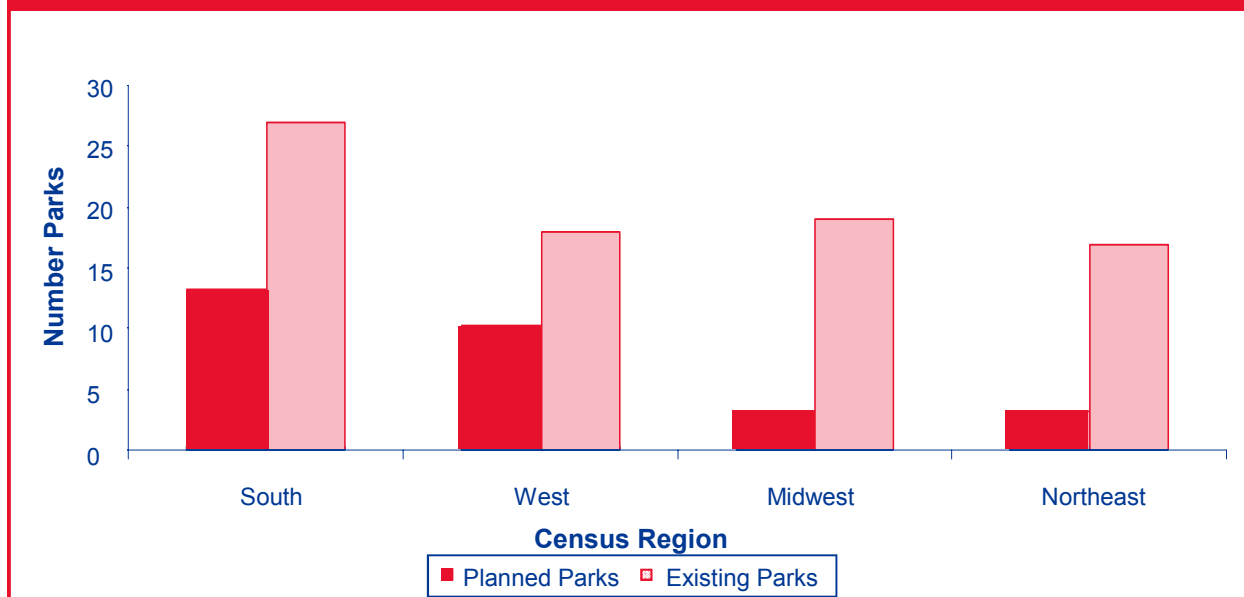
More generally, the benefits to firms from developing a research relationship with universities are well known; specifically, the R&D efficiency of firms increases. These efficiencies are gained through access to complementary activities and research results, and access to key university personnel – star research scientists as well as research faculty and students. As Hall, Link, and Scott (2003, p. 490) note:

Universities are included (invited by industry) in those research projects that involve what we [call] “new” science. Industrial research participants perceive that the university could provide research insight that is anticipatory of future research problems and could be an ombudsman anticipating and translating to all the complex nature of the research being undertaken. Thus, one finds universities purposively involved in projects that are characterized as problematic with regard to the use of basic knowledge.

Relatedly, Link and Scott (forthcoming c) show that bioscience firms are more than 32 percent more likely to partner with a university in a research venture than are firms in other technology areas.

Regarding the university/industry research nexus, Link and Scott (forthcoming a) show that as of year-end 2002 there were 81 university research parks operating in the United States, and there were another 27 in the planning stage. See Figure 7. Of those 27, about 40 percent are to be biotechnology

**Figure 7:
Existing (n=81) and Planned (n=27)
University Research Parks by Census Region**



focused meaning that they are seeing the spin-off DBFs and attract BCFs.

Will these university efforts succeed? Will regional and local efforts to develop technology clusters succeed? According to Cortright and Mayer (2002), both will be difficult tasks. First, the scale of the local knowledge base that is requisite for bioscience research and to stimulate the emergence of DBFs is huge, and the ability of non-established bioscience universities to significantly increase federal research support (e.g., from NIH) is an issue. The academic literature is clear about the role of star scientists in the emergence of DBFs. While many universities certainly have pre-eminent scientists, the likelihood of any one attracting an eminent star is related to the research resource base therein.²⁴ Second, the history of the biotechnology industry is such that it is reasonable to question whether regions or localities can recruit DBFs or BCFs. Rather, such firms have clustered around sources of bioscience. And third, even if excellence in the biosciences could be achieved and if technology breakthroughs were achieved – keeping in

mind that the roots of most clusters in the United States can be traced to historical circumstances – it will take a decade or more for a new cluster to begin to develop. Indeed, it can be a long time from seed to harvest.

VI. SUMMARY REMARKS

In summary, and with an emphasis on individual organizations and institutions involved in planning a biotechnology-based regional economic development strategy, there are lessons from history to learn. The history of the bioscience and biotechnology breakthroughs in the San Francisco and Cambridge areas teach that:

- 1 A necessary condition for the creation of a DBF is tacit knowledge, and tacit knowledge stems from university or institute bioscience research and is shared through professional face-to-face research interactions.

-
- DBFs rely on strategic alliances with established companies – BCFs – capable of commercializing their biotechnologies.

Biotechnology clusters develop, as the history of the San Diego area experience teaches, when:

- University or institute bioscience research is well established and ongoing;

- An anchor DBF emerges in the area; and
- BCFs locate near the DBF to take advantage of its biotechnology and to take advantage of expected new biotechnologies from burgeoning DBFs.

Therefore, a necessary condition, for the implementation of an economic development strategy is a rich science base centered within a university or institute.

V I I . E N D N O T E S

- For a review of the literature on research partnerships, see Hagedoorn, Link, and Vonortas (2000).
- This model of technology-based entrepreneurial activity was first set forth by Link and Tassej (1987), and later elaborated upon in Feldman, Link, and Siegel (2002).
- Following Bozeman and Link (1983, p. 4): “The concepts commonly used in connection with innovation are deceptively simple. *Invention* is the creation of something new. An invention becomes an *innovation* when it is put in use.” Innovations may be new products, new processes, or new organizational methods that are novel and add value to economic activity. Thus, at a general level, invention parallels the concept of science and innovation parallels the concept of technology.
- See, <http://www.ncbiotech.org/biotech101/glossary.cfm#b>
- As an aside, Drucker (1997) argues that the growth of such biomedical inventions was the genesis of university technology transfer efforts.
- Only 14 of 50 states are listed in Figure 4. These are the more biotechnology-intensive states. There has not yet been an inventory of state-based biotechnology centers or state-based biotechnology initiatives to explain the observed cross-state variation in the growth of new biotechnology firms. And, as noted above with reference to Figure 1, no information is available about the success of the firms underlying Figure 4.
- Relatedly, National Science Board (2004) data show that the median sized firm doing biotechnology R&D has between 1,000 and 4,999 employees.
- The term corresponding to DBFs in many European and Asian countries is new technology-based firms (NTBFs) (Lehrer and Asakawa (2004).
- Public support of the biosciences is important but not within the boundaries of this paper. It should be noted, however, that much of the path breaking bioscience research was funded by the National Institutes of Health and the National Cancer Institute, and in 1980 the U.S. Supreme Court in *Diamond v. Chakrabarty* approved the principle of patenting genetically-engineered life forms; in that year, Cohen and Boyer received a patent for gene cloning.

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10. This historical timeline comes from <http://www.ncbiotech.org/biotech101/timeline.cfm> and from Orsenigo (1989). Hall (1987) and Teitelman (1989) also provide excellent documentations of the evolution of the biotechnology industry.
 11. According to Prevezer (2001, p. 26): “The ethos of the early biotechnology firms such as Genetech ... was one of openness and informality, encouraging an academic atmosphere in the hope of attracting high caliber research scientists and encouraging them to maintain their scientific links”
 12. According to Powell et al. (2002, p. 291): “The importance of tacit knowledge, face-to-face contact, and the ability to learn and manage across multiple projects are critical reasons for the continuing importance of geographical propinquity in biotech.”
 13. Using U.S. survey data, Audretsch and Stephan (1999a, 1999b) showed that about 50% of the founders of new biotechnology firms, DBFs, were from universities and about one-third of them retained their university affiliation after the firm was established.
 14. According to Sharp (1991), early-on established pharmaceutical firms did not comprehend the vast applications of biotechnology and accordingly did not establish in-house R&D areas. By the mid-1980s, as market potential was realized, pharmaceutical companies developed in-house expertise – absorptive capacity (Cohen and Levinthal 1989) – and either formed strategic research alliances with DBFs or merged with them. Cooke (2001) demonstrates the importance of the DBF-to-BCF relationship in the U.K.
 15. For more detail see DeVol et al. (2004).
 16. Agrawal and Cockburn (2003) also emphasize the importance of anchor tenants for stimulating regional economic growth, in all industries not just in biotechnology. Anchor tenants because of their size and scope of research activities can more readily absorb university research and stimulate local industrial technology development.
 17. Alfred Marshall (1920, pp. 271-272) noted: “When an industry has chosen a locality for itself it is likely to stay there long, so great are the advantages which people following the same skilled trade get from near neighbourhood to one another ... And presently subsidiary trade grows up in the neighbourhood.”
 18. Orsenigo (2001) claims that Italy failed to develop biotechnology clusters due to an absence of research activity in firms with whom DBFs could collaborate. This is an important finding for those involved in technology-based economic growth. As noted below with reference to Figure 6, and with reference to a component of the Milken Institute index in Figure 5, a necessary condition for DBFs is within the region well established research activity.
 19. See also, Audretsch (1998), Audretsch and Feldman (1996, 1999), Breschi and Lissoin (2001), Jaffe (1989), and Jaffe, Trajtenberg, and Henderson (1993) for empirical support of this agglomeration effect.
 20. Swann, Prevezer, and Stout (1998) argue that incumbent firms in a cluster of similar firms will grow faster than new entrants because the incumbent firms are better placed to take advantage of knowledge spillovers.
 21. Henderson (1986) and Krugman (1991) emphasize conceptually and empirically the importance of location, *per se*. Arthur (1989) and David (1985) emphasize conceptually the related importance

of network externalities. David (1985) also argues in general, but this argument applies particularly well to biotechnology clusters, that chance or historical events (e.g., scientists with a breakthrough discovery) can lock a technology (e.g., an industry in the case of biotechnology) on a particular path of development. See also, Porter (1998). Clustering gives positive feedback to continue the path dependency of the particular technology. This idea has, according to Arrow (2000), its origins in the early writings of Veblen and Cournot. It also can be traced to the evolutionary economic concepts of Nelson and Winter (1982).

22. According to Ramani (2002), in India BCFs rely on strategic alliances with foreign firms rather than on in-house R&D.
23. Pisano (1991) refers to this knowledge flow in terms of the core competencies of DBFs.
24. See U.S. Department of Commerce (2004) for a state-by-state ranking by R&D inputs and patent outputs.

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