Knowledge and the Biotechnology Economy: A Case of Mistaken Identity

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Introduction

When analysts write about the 'biotechnology economy', they assume readers know what the 'biotechnology economy' is and what, despite certain differences, it shares with economies generated by other industrial sectors. This is a phrase, however, that could not have been used with such confidence as recently as two decades ago. It was during that period that the word 'biotechnology' first became part of common language and that the "biotechnology economy" was given a market-based frame of reference that established its identity and a certain ideology which overcame discontinuities and internal inconsistencies.

Without a more accurate frame of reference, however, the "biotechnology economy" has had to be a flexible concept that flows outward to include and conform to a set of comparative concepts and paradigms derived from analyses of other, more familiar industrial sectors. In an effort to reduce the lack of fit, for example, analysts have often reduced the biotechnology industry to a mere part (albeit a novel one) of a larger industrial system. The special attributes of biotechnology, however, are precisely those that are most difficult to incorporate into standard economic models. The fact is few industrial developments have borne such sudden and dramatic changes as the new applications of the life sciences through biotechnology firms. Viewed from a position within the biotechnology community, it appears that the flexibility of the term as it is commonly used by many analysts is wearing out. A more expansive view is needed.

The opportunity to create such a view seems to be afforded by considering the biotechnology economy through the lens of the "knowledge economy," as in Professor Foray's paper ("Characterizing the Knowledge Base: Available and Missing Indicators"). While the goal is to develop a new set of accurate and reliable metrics, success will ultimately depend on understanding how the biotechnology industry actually operates, rather than how well it fits current models and theoretical constructs, such as “knowledge blocks,” “knowledge networks,” “tacit knowledge,” and “codified knowledge.”

Understanding the Biotechnology Economy in a Period of Change

To understand the biotechnology economy, it helps to take a step back and consider a wider context that reveals key factors that fuel and restrain innovation and commercialization in biotechnology.

The life sciences have changed more, in the past few decades, than virtually any other field of science or engineering. Until the 1970’s, the goal of most basic research was to generate new knowledge and advance understanding of biological and biochemical processes. Steady, incremental advance of the life sciences bore important medical benefits, particularly through the pharmaceutical industry and greatly enhanced agricultural production systems. In general, though, research was largely focused on the scientific goals of the academic research community.

In the past two and a half decades, the life sciences have become increasingly relevant to commerce and society, catalyzing the development of an entirely new industry – the biotechnology industry. Discoveries derived from basic research undertaken in publicly funded research institutions is now being applied more rapidly and broadly in commercial firms. Basic research institutions are placing greater emphasis on technology transfer and building new administrative and policy infrastructures to support industry relations. Key among the changes in the U.S. is the Bayh-Dole Act which provided universities and other research institutions that receive federal research monies with a mechanism for extending intellectual property rights to companies seeking to commercialize university inventions. University-industry interactions in the life sciences have expanded as intellectual property rights enabled companies to create value in their investments in university research.

The biotechnology industry, itself, has undergone dramatic change. Since its emergence in the 1970’s, it has been marked by a strong tendency towards increasing heterogeneity and novelty (Figure 1). It is most familiar for producing innovative drugs and diagnostics, but in the past decade the industry has expanded into wide ranging applications in agriculture and foods, informatics, new materials, and forensics, among others. As a broader spectrum of new firms and established industries adopt new biotechnologies, the 21st century will see the impact of the life sciences in virtually every aspect of our lives – from health to food production, the environment, and industrial manufacturing. There will be advances that are, yet, to be imagined.

There are other forces of change. In the past few years the financial climate has become less hospitable to entrepreneurial start-up firms. In the late 1970’s and throughout much of the 1980's, venture capital and public markets invested relatively aggressively and generously in biotechnology start-up firms. In the biopharmaceutical sector, for example, many (if not most) business plans envisioned firms growing into drug development and manufacturing businesses. Long product development times and drug approval uncertainties have eroded the enthusiasm of investors. Today, few new firms start with venture capital funds and very few achieve successful initial public offerings. Business plans are changing and goals are moving from drug development to drug discovery, and from vertical integration to horizontal alliances. At the same time, venture capital seems suddenly to be available to agricultural biotechnology start-ups (particularly those focused on gene discovery), which for a long time was the orphan child of the biotechnology industry. There is also a recent trend of giant, traditionally pharmaceutical or agrichemical firms adopting the tools of biotechnology and referring to themselves as "life science companies."

Taken together, analysts can be assured that change will continue in the biotechnology economy. They can also be assured that the forces of change and the remarkably broad and expanding sweep of industrial applications (ranging from healthcare to agriculture and from industrial materials to environmental technologies) will continue to create discontinuities and inconsistencies that undermine simple definitions of the term "biotechnology economy" and the incorporation of biotechnology into standard economic models.

Challenges to Social Institutions

In the U.S., Europe, Japan, Australia, and many developing countries, governments have targeted biotechnology as a critical economic development vector. There is general understanding (although interpretations vary) that success depends upon a strong basic research base, technology transfer and intellectual property rights, and a climate hospitable to the establishment and growth of entrepreneurial R&D firms. Since the mid-1980's, national and state governments have invested large sums in efforts to foster biotechnology start-ups through incubators, venture capital funds, business grants and loans, R&D tax credits, free or heavily subsidized land and construction, and other strategies to attract businesses and investment capital to their communities. Local research universities and governmental research institutions have sometimes received funding for strengthening scientific personnel, research, and graduate education in areas of the life sciences.

At the same time, changes in the life sciences and the emergence of new biotechnologies have shaken the very foundations of certain governmental and legal institutions. The responses of these institutions have consistently held the potential to make or break the commercial prospects of the industry. There has been public controversy over the perceived safety and appropriateness of new genetic technologies and products. Shortly after the development of gene splicing techniques in the early 1970's, the scientific community called a now historic conference – the Asilomar Conference held in Asilomar, California -- to consider safety and social issues. That conference was the subject of widespread and often sensational news coverage. Controversy erupted, again, with the first patent granted for a living organism. In the early 1980's controversy struck, yet again, with the first outdoor trials of a genetically engineered microorganism (Ice Minus or Frostban) in California. Today, Europe is wracked with controversy over genetically engineered foods and plants. Throughout, activists have typically captured the imaginations of journalists and the public by characterizing biotechnology research and products as unpredictable and unsafe – Frankenstein revisited -- despite repeated scientific assessments to the contrary. They generally call for governmental protections.

Pressure generated by industry and legislators in response to the spectre of potentially lost commercial and economic opportunities has compelled governmental and legal institutions to address the new biotechnology. Many have responded by integrating emerging scientific knowledge into their ongoing analyses and operations. A drug-regulation agency that lacks staff expertise in molecular biology and genetics will seriously undermine the potential for useful biotechnology drugs to enter the marketplace, either through rule-making that disadvantages the new products or through ineffective regulatory review. An agriculture agency without staff who can judge the relationship between traditional plant breeding and genetic engineering can delay approvals or erect regulatory requirements that inadvertently act as market entry barriers for biotechnology plants and foods. A government patent office or local law firms lacking understanding of molecular structure, design, and function will be unable to advance decisions on intellectual property issues related to new biotechnology products and tools.

The greater context in which commercial biotechnology has developed in various regions of the world matters. The biotechnology economy has been marked by external forces that have significantly modulated the directions and goals of R&D and business development on a region-by-region basis. Germany's Gene Law had a chilling effect on commercial biotechnology in the 1980's, causing German pharmaceutical firms to move their biotechnology R&D investments to other countries. Investments in local incubators in many U.S. communities have met with mixed success. The absence of intellectual property policies is undermining efforts by developing countries to participate in worldwide markets.

As rapid advances in science and engineering continue to fuel remarkable new opportunities, forces generated in this greater context will continue to affect the character, size, location, and relative stability of biotechnology enterprises. The biotechnology economy presents a moving target. Its component parts are highly changeable, occasionally effervescent, and rapidly evolving in nature. Analysts are wise to seek both fundamental indicators that are likely to be maintained throughout the economy's evolution and more flexible measures that can assess trends and incremental impacts.

Innovation Capacity and the Biotechnology Economy

For the purposes of this paper, emphasis is placed on measurements of the *contributions of people* engaged throughout the biotechnology economy, rather than on more conventional and commonplace metrics focused on products, sales, publications, and patents. It is not the view of an economist, but of a participant in the biotechnology economy. The approach stems from the broader concept of a knowledge-driven biotechnology economy – that is, one that is fueled by research and innovation, but substantially modulated by other knowledge-dependent forces, including government agencies, financial and legal firms, and other such institutions. The function and impact of each is dependent upon knowledge of advances in the life sciences, and that knowledge is applied and adapted to a function that affects the biotechnology economy *by people* working in various sectors. The rapid pace of change in the science, the institutions, and the economy signals that a fluid process involving streams of incremental and interdependent contributions is likely at work.

The pervasiveness of scientific expertise throughout many sectors of the biotechnology economy has created a system of innovation and economic development. Today, it is not at all uncommon to find individuals with advanced training in the life sciences employed as patent lawyers, venture capitalists, legislative staffers, and government regulators. As these institutions have increasingly employed scientists or individuals with advanced education in the sciences, their own operations have become influenced by the same common culture of basic, discovery-oriented research that drives the biotechnology industry. They all share, to some degree, a special ability to develop and utilize rapidly evolving new scientific knowledge about biotechnology. It is this ability that underlies the fluid nature of economic development in biotechnology.

It also provides a different view of the innovation capacity of the biotechnology economy. Innovation capacity is essential for discovery and commercialization of new products and technologies that, in turn, make businesses more competitive and open new markets. At its core, innovation capacity depends upon creative and well directed research, but research is only one critical factor. In combination, various factors set the boundary limits on innovation capacity in the biotechnology economy.

Research breakthroughs derived from publicly funded research are of no importance to the economy if they are not effectively transferred to firms, or if the firms lack the skilled personnel and resources to perform necessary R&D and manufacturing efforts, or if legal protection of market access is not provided through intellectual property, or if regulatory agencies make scientifically unsound decisions about safety and efficacy. Viewed this way, “innovation capacity” is derived from and measured at multiple essential sources: biotechnology firms contribute R&D, formulations, and manufacturing engineering (among other things); universities contribute basic research, faculty consultants, clinical research, intellectual property, and a highly skilled scientific workforce; financial institutions ranging from banks and venture capital firms to “angel” financiers provide funding and often management guidance; government agencies provide research monies, tax policies, and regulatory systems for products, technologies, land use, and patents; and law and accounting firms provide essential expert services.

There are many examples of regions that host world class biomedical research institutions and healthy economies, but lack any noteworthy biotechnology economy. Outstanding science is not sufficient. Some of these regions have launched aggressive economic development efforts to build a biotechnology economy, only to fail. To achieve the needed “critical mass” in innovation capacity, a number of factors are needed. Thus, to be useful, measures of innovation capacity need to consider the broader context and include the knowledge generators and the knowledge users in industry, research institutions, government, and other sectors that supply these factors. The challenge is to come up with a new set of metrics.

Developing New Metrics

The most difficult challenge presented by this model of the biotechnology economy is that it requires measurements of people and characterizations of their various roles, rather than products, sales revenues, publications, or patents. My colleague, Cherisa Yarkin, and I have undertaken a small study which helps to illustrate some of the fundamental components of the biotechnology knowledge economy that can be measured this way. While it does not explore the full spectrum of contributors, it may suggest some potentially reliable metrics for at least two of them. Relevant highlights are briefly described here.

The study focuses on the California biotechnology economy. California presents an interesting case study because it is the birthplace of gene splicing techniques and home to one-third of all U.S. biotechnology firms (Figure 2), including the world’s three largest, Amgen, Genentech, and Chiron. California has the largest capital investments, R&D expenditures, employment, and sales revenues in the nation (Figure 3). Why the state has been a hotbed for launching biotechnology companies is an interesting question.

California is also interesting as it is home to a major collection of basic research institutions recognized for their strengths in the life sciences, including the University of California which, with its nine campuses, accounts for the largest share of federal support for biomedical research (i.e., approximately ten percent of extramural research funding from the U.S. National Institutes of Health), Stanford University, the California Institute of Technology, and the Scripps and Salk Institutes. As a first step, the study traced a variety of linkages between the University of California and California biotechnology companies, and characterized the roles and contributions of people to the innovation capacity of California's biotechnology economy (see Table 1 for a brief description of the methodology and information sources).

The Biotechnology Firm:

Biotechnology firms have adopted and sustained many of the same traditions of the academic basic research laboratory. They conduct research in much the same way and hire generally the same kinds of scientists, although the goals and timelines for research projects are conceived of differently. The similarities have resulted in a certain seamlessness between the two institutions that has facilitated the communication, transfer and adoption of new knowledge from universities to companies.

The study has found that biotechnology firms have engaged people with advanced training in the life sciences in virtually all major operations, including management, business development, legal and regulatory affairs, manufacturing, and sales (Figure 4). This has established a thread of common understanding among various units that enhances communication and teamwork throughout the production pipeline.

Some firms have developed extensive horizontal linkages with other firms and with academic institutions (see, for example, Figure 5; these linkages are extensively studied by others). Linkages play various roles. Firms license their technologies and products to other firms to gain new capital. Alliances can provide resources for R&D, manufacturing, regulatory approvals, and marketing that a small firm could not achieve, alone. As the financial environment has become more difficult, the number, size, and nature of alliances will likely change.

The chilly financial environment is having another effect, as well. Business plans are changing. Instead of the usual plan of a decade ago (i.e., get venture capital and quickly move to a successful initial public offering and then continue to develop a vertically integrated biopharmaceutical business), young firms are now developing plans that include a number of relatively early exit strategies, such as being taken over by another firm.

The Research University/Institution:

California's biotechnology firms are tightly clustered around the state's basic research institutions (Figure 6). In general, strong and aggressive companies depend upon the knowledge generators – in research universities and national laboratories. Proximity matters. Local companies gain access to the scientific leaders, research facilities, and students of neighboring universities.

Moreover, certain research areas, such as drug discovery, present mutual incentives that drive cooperative industry-university research efforts. Often, university and industry researchers can simply accomplish more working together than apart. Companies collaborate with university researchers because collaboration provides an excellent way to leverage limited R&D resources against the more substantial federal and state investments in universities and national labs. The vast majority of biotechnology firms are small businesses. Most simply cannot afford to build the same research capacity in-house. Firms investing in university research have the additional effect of exposing students to their research interests. These students are often subsequently recruited by the firms and continue to carry out research on the project.

The study illustrates that university faculty and students are often simultaneously participating in two sectors of the biotechnology economy – the university and industry – in the course of advancing their basic research programs and attaining their undergraduate and graduate degrees. They conduct industry-sponsored basic research, present scientific seminars, consult, participate in intellectual property transactions, found new firms, serve on scientific advisory boards, and occasionally hold management positions while maintaining faculty appointments (see, for example, Table 2).

In addition to measuring the contributions of individuals, there are other, more common measures, such as publications and patents. Publications and patents play important roles in the innovation capacity of the industry, but their relative contributions are generally more narrowly defined and static. They provide a snapshot from a specific research effort at a particular point in time. They can provide an especially enabling technological enhancement or, as in the way some firms use many patents and licenses, they can be accumulated simply as a mechanism to keep technologies and products out of the reach of other firms.

Compare the contributions of patents and people identified in the study. Of the $75 million received by the University from all licensing revenues in 1997, 74% was earned by only five inventions – out of 716 disclosures, 206 patents, and 130 licenses. While that is not particularly impressive, patents can have an important impact may or may not be readily inferred by eventual commercialization or financial outcomes. For example, one of the revenue-generators reported was the Cohen-Boyer gene splicing patent, which is widely considered to have had a fundamentally enabling effect both within the field of molecular biology and on the entire biotechnology industry. Patents are also used by firms as part of their portfolio in fund raising activities. Intellectual property is used by investors as one measure of the R&D capacity and market access of young firms.

In contrast, one in five California biotechnology firms was founded by a University of California scientist (Table 2). Eighty-five percent of California biotechnology firms employ University-trained scientists in significant research positions (Table 2). In these roles, these scientific leaders and highly skilled researchers make continuous contributions over long periods of time and in a dynamic and adaptive way. There are, of course, also several hundred more informal research relationships underway between University of California scientists and California biotechnology firms at any given time (for a summary, see Table 3). Each is creating and transferring knowledge in one form or another to the R&D efforts of the firms. They are tracked through institutional records on contracts and grants, gifts and endowments, and faculty consulting.

Entrepreneurism, the Local Business Climate, and Infrastructure

Within this small study's limits, its most important finding may be that metrics can be designed to measure a variety of factors that affect the biotechnology economy. For example, within the state of California there are substantial regional differences in the ability to develop a biotechnology economy. For example, Figure 5 shows that, while the San Francisco Bay Area has been a strong spawning ground for biotechnology firms, the Los Angeles Area has not. Figures 5 also shows that the San Diego Area has had great success.

All three areas have outstanding research institutions. The San Francisco Bay Area has Stanford University, UC San Francisco, and UC Berkeley. Los Angeles has The California Institute of Technology, UCLA, and the University of Southern California. San Diego has UC San Diego and the Salk and Scripps Institutes. University of California scientists have been involved in company start-ups in all three regions (Figure 7). Where they differ significantly is in their business infrastructure. The San Francisco Bay Area benefits from a strong and diverse financial, real estate, and business service community that has grown up alongside Silicon Valley and its high tech firms. The region provides fertile ground for all kinds of entrepreneurial high tech and biotech firms.

The Los Angeles Area has suffered in recent decades from downsizing of federal investments in defense contractors. While the region supports a growing multimedia and entertainment industry, those types of firms do not require the same business infrastructure that biotechnology firms need. Added to this, real estate is expensive and there are few developed research industrial parks or incubator facilities available. The study shows that UCLA faculty and students are involved in biotechnology firms throughout the state (Figure 8), but the local opportunities have been limited.

The San Diego Area presents the most interesting case. The region was economically devastated by defense downsizing and lacked any sizeable industry or business infrastructure of any type after the defense contractors were lost. Nonetheless, the region now enjoys strong business and employment growth, and ranks among national leaders in attracting venture capital investments. Through a concerted decade-long effort involving local economic development organizations, businesses, and UC San Diego CONNECT the needed business infrastructure was created *de novo* to nurture entrepreneurial explorations. A glance at the regional map of biotechnology firms (Figure 9) illustrates how intimately connected UC San Diego's research and education has become to the local economy.

Because the study is building a longitudinal database, it will eventually provide a view of regional biotechnology economies over time. For example, as has been shown by a study conducted by UC San Diego CONNECT (Figure 10), local entrepreneurs often engage in repeated cycles of founding and developing new businesses. Their economic impact becomes amplified over time through the firms they launched (if they continue to do business) and, most importantly, through the experienced biotechnology managers that move on from one firm to another. Each cycle generates incrementally greater "entrepreneurial experience" in the local economy. In the San Francisco Bay and San Diego Areas entrepreneurs seem to stay in the regions.

Finally, the study helps to show that the absence of a local biotechnology economy does not necessarily mean that local research institutions are somehow failing. It is likely that strong scientists are contributing to biotechnology economies in other regions. In the three regional examples presented here, the critical factor was the local business climate and infrastructure. Other factors are essentially equivalent in these regions because they all have strong research institutions and all are located in the same state and subject to the same general governmental policies.

Summary and Conclusions

The "biotechnology economy" has been a much used and little understood term. Yet, with such rapid and important changes in the relevance of the life sciences and their impact in commerce comes a need to help governments and business communities understand the economic dynamics better. The challenge lies in developing metrics that measure useful features of the biotechnology economy. As for other knowledge-based economies, the economic drivers are embodied in the skills, knowledge, problem-solving, and adaptability of highly trained personnel. The process by which they contribute to the economy is a dynamic and fluid one. The speed and impact of basic research advances make the economy highly changeable and expansive, in terms of technologies, products, market sectors, and kinds of participating businesses. A final layer of complexity is added by the strong influence that other sectors, including government, law, finance, and business services, exert.

To measure effectively how knowledge is transformed into a biotechnology economy, metrics need to address these essential sources of impact. Among the most useful and reliable over time will likely be those that characterize roles and contributions of highly skilled personnel, as knowledge-driven economies are fundamentally driven by people. Without understanding the frameworks and processes that enable people to make their contributions, however, economic analysts will be left in a situation much like the blind men and the elephant.