The Marketplace for Ideas: Can Los Angeles Build a Successful Biotechnology Cluster?

A Report to the John Randolph Haynes Foundation

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Introduction

Los Angeles brands itself as the "creative capital of the world." While a leader in a variety of innovative industries, this leadership has not extended to biotechnology, an entrepreneurial industry responsible for generating dozens of innovative new medicines aimed at curing debilitating disease. This report argues that the Los Angeles region has failed because it has not generated a sufficient *marketplace for ideas* needed to support the activities of entrepreneurs, scientists, and investors within the highly collaborative and failure prone biotechnology industry. This claim is substantiated through comparing the organization of several elements of the marketplace for ideas in Los Angeles with two highly successful biotechnology clusters in California, San Francisco and San Diego. Using descriptive statistics and social network tools, the report will show that vibrant social networks linking managers and founders, scientists and inventors, and investors have emerged in the successful San Francisco and San Diego biotechnology clusters, but not in Los Angeles. Aimed at informing policy debates within the Los Angeles region, the report also explores scenarios by which a more vibrant idea marketplace could emerge within the region. While it is unlikely that policy can directly orchestrate a successful biotechnology cluster in the Los Angeles region, policies can take steps to hasten the development of a more effective biotechnology marketplace.

How poorly has the Los Angeles region performed in biotechnology? Data on independently owned California biotechnology companies focusing on human therapeutics and molecular diagnostics were collected from the origins of biotechnology in 1976 up through 2005.[1] Figure 1 displays data on the number of companies active in the greater Los Angeles region, including Orange, San Bernardino, and Ventura Counties, the San Francisco Bay Area, and the San Diego region. Between 1976 and 2005, there were at least 214 biotechnology firms founded in the San Francisco region and 189 firms active in San Diego. About 40% of companies (78 in San Francisco, 77 in San Diego) have failed in each region. In the greater Los Angeles

[1] A variety of sources were used to locate companies. Companies active in 2005 were located through Rich's Guide to California Bioscience and confirmed as independently owned biotechnology companies through web-searches. Combined 176 firms that had been acquired or failed through bankruptcy and were thus no longer independent firms were also identified. Most of the older companies were identified through career histories of senior managers that were developed for the social network analysis part of this project, described below. Information on companies was then gathered through searches on web-archives (to find old web-pages for companies), SEC filings, the VentureExpert venture capital database, and more general Internet searches using Google. This methodology creates a bias towards finding information on larger companies, and especially companies that have received venture capital investments. It is likely that many small, short-lied companies that failed due to an inability to attract funding were not included in this database.

region, only 55 companies had been founded during the 1976-2005 period, and 11 have failed. One of the key indicators of success for most biotechnology firms is achieving sufficient progress in their drug development research to take a listing on a stock exchange through an initial public offering (IPO). About 30% of companies founded in San Francisco and San Diego (64 and 58 respectively) achieved the IPO threshold. Only 3 companies in the Los Angeles region, less than 5%, have obtained IPOs. San Francisco and San Diego have developed vibrant biotechnology clusters, while the Los Angeles region has not.

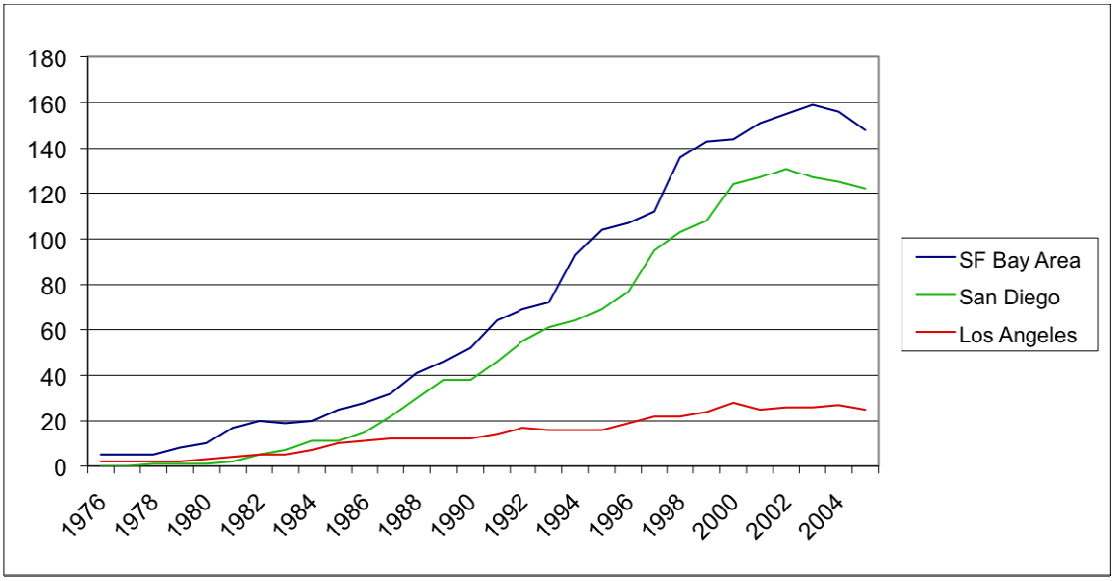

Figure 1: Number of biotechnology companies within the Los Angeles, San Francisco Bay Area, and San Diego regions by year, 1976-2005.

Is Los Angeles's failure in biotechnology surprising? Given the success of San Francisco and San Diego, one might think that it is. The Los Angeles region has similar starting conditions for biotechnology as these other regions. It is commonly assumed that regions succeed in industries for which it has strong factor endowments (for overviews see Krugman 2001; Baldwin et. al. 2001). Most biotechnology firms are founded on the basis of discoveries made within universities. Social scientists at UCLA have shown strong support for what is known as the "star scientist" hypothesis: biotechnology companies with links to eminent life science researchers are more likely to find the success needed to take a listing on stock markets (Zucker et. al. 1988). While the star scientist research focused on individuals, it is a small step to broaden out the argument. Regions with strong universities, containing numerous research stars, are more likely to succeed in biotechnology.

San Francisco and San Diego each have numerous world-class universities and specialized institutes focused on the life sciences. This list includes, Stanford, UCSF, and UC Berkeley in the San Francisco Region, and UCSD, Scripps, and the Salk Institute in San Diego. But

Los Angeles also has a strong collection of universities and teaching hospitals active in the life sciences. The region is home to the California Institute of Technology, one of the leading scientific research institutions in the world. The greater Los Angeles area also contains three large campuses of the University of California, each of which has strong departments in biology, chemistry, bioengineering, and other disciplines impacting the life sciences. The area is also home to large medical schools attached to UCLA and UC Irvine, as well as several research-focused hospitals, such as the City of Hope and the Children's Hospital of Los Angeles. In 2007 biomedical research laboratories in the Los Angeles area received $880 million in funding NIH, a number of that compares favorably with San Diego, which received $602 million, and the San Francisco region, which received $1.05 billion. Scientific factor endowments in Los Angeles fare well with other regions in California.

Moreover, scientific research organizations within the Los Angeles region were active during the formation of the biotechnology industry during the late 1970s and 1980s, and invented several key early technologies. Developing a presence at the formation of a major new industry is often important in establishing the foundations for regional success. Early entrants might be able to capture "low hanging fruit" within a new industry, key technologies or applied discoveries that can allow early firms to establish a market lead. In the biotechnology industry, early protein based drugs, such as synthetic insulin and human growth hormone, were based on well understood science, had proven markets, and would face less complicated regulatory hurdles compared to later drug candidates based on more novel science and with unproven therapeutic effects. Moreover, the existence of early entrants could lead to first mover advantages for a region. Early success stories within a region could spur other entrepreneurs to start companies, creating a critical mass of companies needed to develop a sufficient labor market of scientists and managers as well as spur entry of venture capitalists, specialized law firms, and other service providers. Through these mechanisms agglomeration effects could occur, creating cost advantages for companies located in the region that other regions might not be able to match.

Scientists within Los Angeles were among the more active inventors at the dawn of the biotechnology industry, developing at least three major discoveries that helped establish the industry. Two researchers at the City of Hope, Art Riggs and Keiichi Itakura, were in 1976 the first team to demonstrate that strands of DNA could be created synthetically. This technology was licensed by the San Francisco biotechnology pioneer Genentech and used to successfully clone human insulin, one of the formative events in the development of genetic engineering (see Hall 1987). A second Los Angeles based invention was the sequencing and cloning of human erythropoietin in 1985 by Fu Kuen Lin, a scientist at one of the only early Los Angeles based biotechnology start-ups, Amgen. Lin 's team was the first to successfully clone a human protein whose genetic sequence wasn't previously known. Epogen and Neupogen, two drugs based on erythropoietin, would generate billions of dollars in revenue for Amgen, transforming the tiny start-up into arguably the most successful company in the biotechnology sector (see Binder and Bashe 2008; Pisano 2006). A final early technology invented in Los Angeles is the automatic gene sequencer, invented in 1986 by Leroy Hood with colleagues Michal Hunkapiller and Lloyd

Smith. The company founded to commercialize the technology, Applied Biosystems, was again located in San Francisco.

Despite these early successes, the Los Angeles region did not develop an early advantage in biotechnology. Aside from the success of one company, Amgen, the region has never developed a sizeable industry. One of the reasons for this failure, noted above with the migration of the synthetic DNA and gene sequencing technologies to San Francisco, is that several new technologies invented in the region were commercialized elsewhere. However, this is a likely symptom of broader failings in the Los Angeles biotechnology marketplace, not a cause.

Within a broader context, however, it may be not at all surprising that Los Angeles has failed to succeed in biotechnology. Very few regions have developed sizeable biotechnology clusters. Worldwide, only three regions, San Francisco, San Diego, and Boston, have created large clusters containing over a hundred biotechnology firms active in therapeutic research. While dozens of regions across the world have attempted to develop biotechnology clusters, none has replicated the success of the three large clusters. Other large metropolitan regions in the United States, such as Chicago and New York City, enjoy abundant endowments of university science oriented towards the biosciences, but have also failed to develop a biotechnology clusters. Moreover, first mover advantages probably do not lead to a regional advantage in biotechnology. A recent study by Romaneli and Feldman (2006) traced the history of 12 metropolitan clusters that developed at least one biotechnology firm before the end of 1980. While San Francisco, San Diego, and Boston were in this group, none of the other nine regions were able to develop a critical mass in biotechnology. As Amgen was founded in 1981, Los Angeles was not included in this study. However, this study shows that Los Angeles's failure to develop a sizeable biotechnology cluster is not unusual; in fact the region's failure is typical.

Creating a successful biotechnology cluster: Establishing a marketplace for ideas.

The mechanisms by which technology clusters emerge and become sustainable are complex, and very few regions have succeeded. The key argument advanced in this report is that successful clusters develop a well-functioning "marketplace for ideas" (Casper and Murray 2003). *The marketplace for ideas is the social context in which ideas are brought together with human and financial capital to build a vibrant cluster.* In asking why some clusters develop superior capabilities to commercialize science compared to others, the marketplace for ideas concept provides a framework to understand the missing link between the existence of world class scientific research facilities and the development of well performing biotechnology clusters. If we understand this missing link, then we are in a strong position to take policy action that will promote better economic performance of biotechnology in Los Angeles.

Figure 2 displays the key elements of a well-functioning marketplace for ideas. Los Angeles, like many large metropolitan regions, has an outstanding supply of science. Moreover, there is an international marketplace for new technologies, and in particular new drug candidates, which large pharmaceutical companies actively in-license. In other words, the supply of basic science and the demand for innovative new products is strong. The key

challenge facing regions is developing a well-functioning marketplace linking scientists, founders and other experienced managers who can effectively lead companies, and venture capitalists and other financiers who can invest and effectively govern high-risk biotech start-ups. A well-functioning marketplace for ideas needs more than just having these key elements in place. The *social organization* underpinning the marketplace is crucial for its success. Well-functioning marketplaces have dense social networks linking scientists, founders and managers, and investors. Social networks have been shown, among other things, to increase the innovative capacity of local companies and aid the creation of effective labor markets linking founders and key employees of companies.

Figure 1: Elements of a well-functioning marketplace for ideas. Source: Fiona Murray.

Research linking social networks to the performance of regional high technology clusters was pioneered by UC Berkeley social scientist AnnaLee Saxenian (1994) through a comparison of the Silicon Valley and Boston regional semiconductor industries during the 1970s and 1980s. Saxenian demonstrated that Silicon Valley had developed strong networks linking scientists, managers and entrepreneurs across local companies. She argues that these social networks were created by very high patterns of inter-firm labor market mobility, and sustained by the existence of norms legitimizing frequent contact between scientists, engineers, and managers working within area firms. Firms in the Boston region, by contrast, had developed more insular or autarchic human resource practices that limited the development of strong social networks across firms.

Social networks form the backbone of a well-functioning marketplace for ideas, creating two specific advantages that they create for high-technology firms. First, networks linking scientist and engineers can increase the innovative capacity of companies through creating an information advantage, allowing companies to react more quickly to changing technologies within volatile industries such as biotechnology. Second, a firm's embeddedness in a region

with high labor market mobility can increase its human capital flexibility in reacting to market and technology changes, while diminishing career risks for talented individuals contemplating careers in a high-risk firm. Both of these network effects are discussed in more detail below. Combined, these benefits create what Saxenian calls a "regional advantage" for firms located in clusters with strong social networks.

This report is designed to help answer the following question: *Does the Los Angeles biotechnology marketplace have a social structure promoting innovation and risk-taking by individuals within high-risk companies?* Special attention is paid to two elements of this marketplace that are particularly salient within the biotechnology industry:

1. Can universities and other non-market participants in Los Angeles function effectively in the biotechnology marketplace? Are there networks of inventors that can effectively commercialize university technology?
2. Are there well well-organized teams of entrepreneurial managers and company founders in the regions? Is there an active marketplace of investors willing to finance high-risk start-ups in the region?

To help answer these questions, an extensive dataset containing information about social ties linking scientists, inventors, managers, founders, and investors within California biotechnology firms over the 1976-2005 was compiled. This evidence shows conclusively that Los Angeles lacks a vibrant marketplace for ideas, while both San Francisco and San Diego have one. Examining this data is also useful to understand the mechanisms by which San Francisco and San Diego developed their successful clusters, and particularly the social ties linking its participants. This information will be used in the latter part of this report to explore scenarios by which Los Angeles might develop a better performing cluster.

Elements of a marketplace for ideas: The role of universities and co-inventor networks

Los Angeles has a strong supply of biomedical science. However, in order for discoveries made within the region to percolate into services and products, effective commercialization processes are needed. This section assesses whether the LA area has developed strong networks linking scientists and other inventors in the region. We will examine two elements of the scientific marketplace. A first factor is the role of universities in the region. Within the biotechnology industry universities typically provide an anchor to local scientific communities. Have universities within the Los Angeles region created effective mechanisms for commercializing science? A second factor is whether networks exist linking scientists in the region. Within biotechnology these networks typically include university researchers and the community of scientists working within local industry. Do networks of scientists and inventors exist in Los Angeles exist, such that they can be effectively tapped by entrepreneurs interested in commercializing science?

The research reported on in this section draws primarily from a detailed analysis of close to 20,000 biomedical patents filed by inventors residing in California between 1970 and 2000.[2] This data will be used to compare the effectiveness by which universities across the Los Angeles, San Diego, and San Francisco participate within their regional marketplace for ideas. As the database includes patents with inventors from both the public and private sector across a 30 year time period, it is also possible to examine the emergence of networks linking inventors in each region. This data will reveal significant differences across the three regions, differences that unfortunately point to shortcomings in the ability of Los Angeles area universities to effectively commercialize science or help anchor the development of meaningful co-inventor networks.

University commercialization processes

Though some universities have long been active in commercialization processes, widespread efforts to commercialize research began after the passage, in 1980, of the Bayh Dole Act by the United States Congress (for an overview, see Mowery et. al. 2004). This legislation established property rights over all federally funded research and, in most cases, transferred ownership to universities. In exchange for receiving ownership of federally funded research, universities are expected to steward this intellectual property and guide its effective commercialization. Most universities responded to the passage of Bayh-Dole by developing technology transfer offices (TLOs), which assumed responsibility over commercialization processes. Typical duties of TLOs include working with faculty in creating invention disclosures that form the basis for patent applications, filing applications, and then licensing the resulting intellectual property to either existing companies or to start-up companies that are "spun off" from the university.

While all major universities within California have established TLOs, these offices vary widely in their ability translate basic research discoveries into intellectual property. Figure 3 displays aggregate patenting by universities on a regional level between 1970 and 2000. This data shows the strong increase in university patenting activity following the 1980 passage of Bayh-Dole. Biotechnology related patenting across all California universities increased from 27 patents in 1980 to 305 in 2000.[3] San Francisco universities have been the most active in commercialization biotechnology, developing 1979 patents between 1970 and 2000, more than twice the number of the 860 patents developed by San Diego universities, and close to four times the 543 patents developed in Los Angeles.

[2] The decision to use 2000 as a cut-off date was influenced by the 3-5 year time frame in which it takes the US Patent Office to review and issue most patents. Moreover, at the time of research for this part of the project (early 2008) the US government database of US patents commonly used by social scientists for research was only updated up until 2005.

[3] The spike in patent applications for 1995 was precipitated by a change in patent rules introduced that year as part of the Uruguay Round international trade agreement, shifting the length of patent exclusivity from a variable system determined in part by the date of issue to a fixed system of 20 years since application.

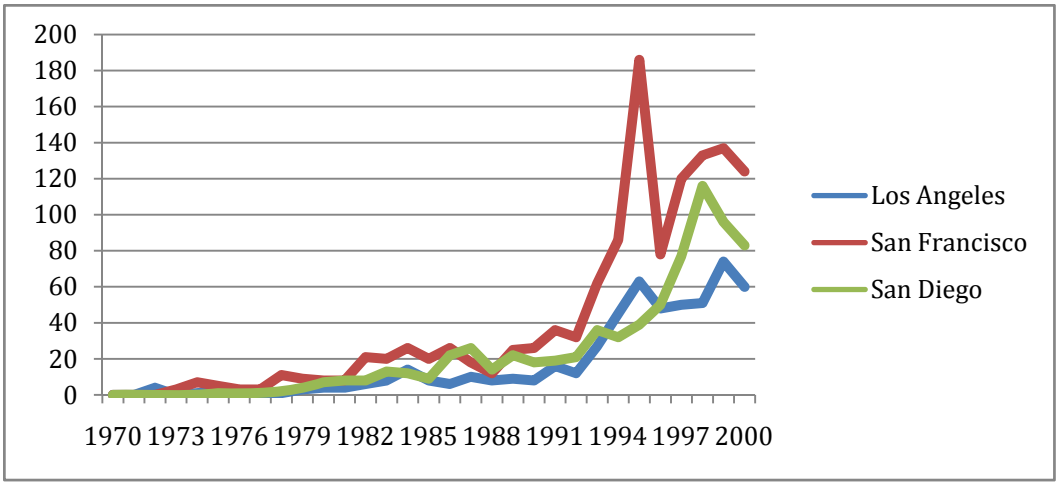

Figure 3: University patents in biotechnology, 1970-2000, by California region

Figure 4 displays aggregate patenting by major universities or research institutes in each region. Stanford and UC San Francisco have each accumulated over 400 patents, twice as many as the 200 patents developed by UCLA. The Salk Institute and the Scripps Research Institute, both relatively small biomedical research facilities in La Jolla, have each developed more patents than UCLA, Caltech, or UC Irvine. Combined, figures 3 and 4 demonstrate that Los Angeles area universities have collectively commercialized far less research than their peers in other parts of California.

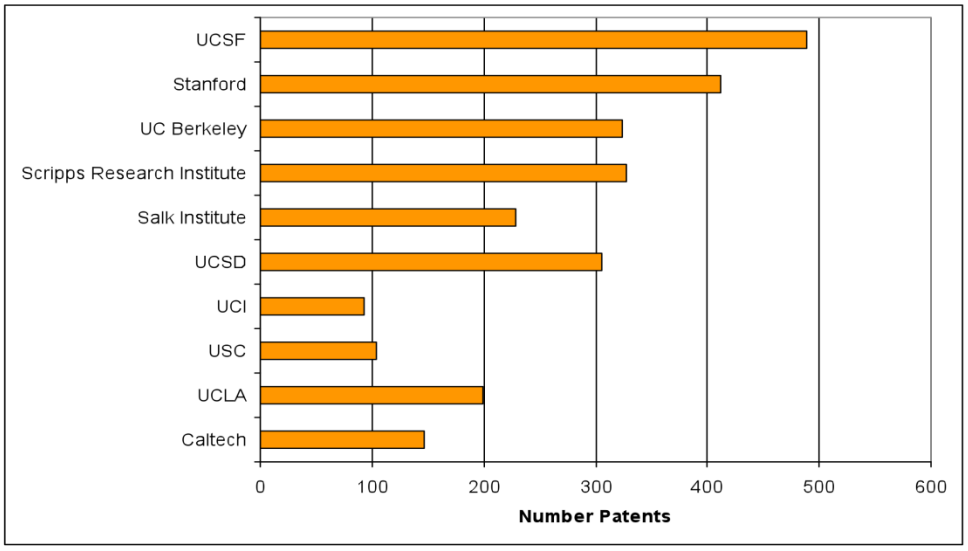

Figure 4: Aggregate biotechnology related patenting by major California universities and biomedical research institutes, 1970-2000

Limited commercialization activities by Los Angeles universities directly impacts the vibrancy of the local marketplace for ideas. Over the 1970-2000 period the ability of universities in the Los Angeles region to develop intellectual property from discoveries that can fuel the local

marketplace for ideas has been substantially weaker compared to San Diego and especially the San Francisco Bay Area.

The impact of university commercialization can be seen most directly by comparing the number of so-called spin-off companies developed by university faculty in each region. While most university patents are licensed to existing firms, intellectual property licensed to spin-off companies are especially important within new technology industries such as biotechnology. The commercialization of many scientific methods emerging from university labs often requires close collaboration between spin-out companies and university labs to develop the instrumentation and necessary proof of principles to prove their worth – spin-offs are often a more appropriate vehicle. Moreover, in exchange for licensing intellectual property, universities usually chose to receive an equity stake in the new venture. If the new company proves successful, equity stakes can create huge financial windfalls for universities.

Figure 5 contains an estimate the number of spin-offs attributed to faculty at universities in San Diego and Los Angeles between 1980 and 2004 that are located within the region (spin-outs that leave the local region are excluded).[4] These estimates were drawn from a database of company founders developed for this project, and thus only include companies where the scientific founder from a local university could be identified, usually through membership on company scientific advisory boards. It is almost certain that this data misses many university spin-offs in which faculty chose not to advise the new company or for old companies for which early scientific advisory board data is unavilable.[5] Nevertheless, the results are striking. During the 1980 to 2005 period at least 51 biotechnology companies located in San Diego can trace their origins to local university science. Only 10 Los Angeles region biotechnology companies could be linked to local university science.

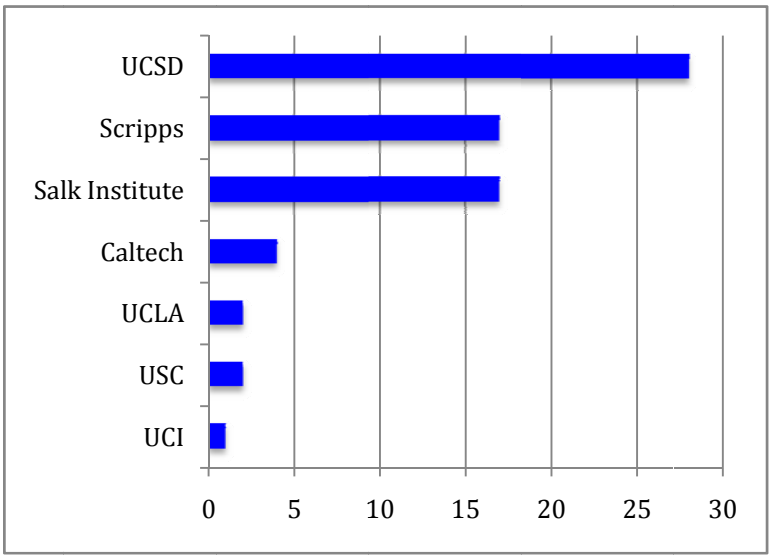

Figure 5: Number of university spin-outs, San Diego and Los Angeles, 1980-2005

[4] San Francisco was excluded as scientific founders could not be found for a majority of companies.

[5] During interviews conducted for this project, TLO officers at one LA area university informed me that confidentiality agreements prevented the disclosure of university links to at least one spin-out.

What explains the inability of Los Angeles area universities to effectively commercialization biomedical science? Both "push" and "pull" explanations factor into Los Angel's poor performance. Push explanations focus on the varying capacity of universities to develop and license intellectual property, while pull explanations draw attention to the broader organization of the marketplace for ideas within a local economy, and the ability of this marketplace to effectively create the networks and incentives needed to entice university scientists into commercialization activities.

The wide variation in university patenting seen in figures 3 and 4 must in part be explained by differences in the effectiveness of university TLOs. Technology transfer is a complex and expensive activity. Modern TLOs are typically staffed by teams of individuals that ideally possess the scientific knowledge needed to evaluate research, legal skills needed to participate in the patenting process, and sector specific business knowledge needed to broker licensing deals with existing or start-up companies. Universities must also finance initial legal costs to develop patents, which can cost several thousand dollars for initial US filings, but up to $50,000 to eventually file internationally. While many university TLOs have become profitable, achieving profitability can take many years and is idiosyncratic. Moreover, while many patents are eventually licensed, patents capable of generating huge windfalls for universities are extremely rare (see again Mowery et. al 2004). As a result, universities differ in their willingness to commit financial resources, which often must come from endowment pools, into expensive TLO operations. Universities must also develop broader guidelines governing the distribution of revenues generated from licensing activity (typically split between the university, academic department of the inventor, and faculty inventors). Finally, universities must create a faculty culture that is seen as rewarding commercialization. Given pressures surrounding the generation of research funding, teaching, and publishing, it is often difficult to convince faculty to devote time to commercialization.

There is evidence that universities in the Los Angeles area have been tardy in developing systems to commercialize science. Caltech, for example, did not establish a formal technology licensing office until 1995. While a small number of well-known Caltech professors, such as John Baldeschweiler, have developed spin-out biotechnology companies, prior to the mid to late 1990s Caltech did not actively attempt to commercialize discoveries made on its campus. UCLA is another case in point. Despite having large departments in chemistry and biology as well as a world-class medical school, the school has traditionally been a laggard in developing and commercializing intellectual property. More specialized biomedical research institutes in the region, such as the Children's Hospital Los Angeles (CHLA), have also been slow to develop credible capabilities in technology transfer. CHLA only established a formal TLO in the mid 2000s.

In recent years, however, Los Angeles universities have dramatically improved their TLO capabilities. Caltech, for example, has dramatically changed direction, launching a highly effective TLO operation post 1995 that has explicitly focused on start-ups. Caltech claims to have launched over 80 spin-outs across all technological fields, including several recent biotechnology spin-outs. There has also been a noted uptick in TLO activity at UCLA and UCI. Dedicated biomedical research institutes and hospitals in the region, such as CHLA and the City

of Hope, have established professional technology licensing operations. As part of this project, TLO officers were interviewed at several universities and biomedical research institutes within San Diego and the Los Angeles area. From these interviews, it became clear that Los Angeles area universities and medical research institutes have in recent years made a strong push to develop professional TLOs and a broader culture within the university that rewarded commercialization. Very little variation existed in the current practices across Los Angeles and San Diego universities, and most offices were staffed by teams of licensing officers with experience in commercializing biomedical research and, in several cases, previous industry experience within the pharmaceutical industry.

Over the past few years universities in the Los Angeles area have caught up with their peers in Northern California and San Diego, in terms of creating effective TLO operations. While the ability to commercialize technology has no doubt increased, an open question remains as to whether an effective marketplace exists to capture it. As discussed earlier, an active marketplace contains interconnected networks of experienced founders and managers, scientists, and venture capitalists and other investors. A well-functioning marketplace for ideas can dramatically reduce the barriers perceived by university professors and TLO officials in commercializing scientific companies into spin-outs. A strong marketplace for ideas acts as a magnet, creating a conduit whereby faculty within universities learn of opportunities to commercialize their research. Within successful clusters teams of experienced managers and venture capitalists actively work with TLO directors to identify and incubate promising technology. In areas lacking a well-functioning marketplace to capture and incubate promising discoveries, professors and TLOs face a more daunting task in organizing and financing new firms.

One piece of evidence supporting "pull" explanation is the frequent occurrence of start-up companies originating from Los Angeles area universities choosing to set up shop outside the Los Angeles area or, after briefly establishing themselves in Los Angeles, deciding to move elsewhere. At least four companies within San Diego have their scientific origins within Los Angeles area universities. Moreover, many of the recent spin-offs from Caltech have gone elsewhere.[6]

Co-inventor networks

Additional support for the pull explanation focusing on the marketplace for ideas can be found through comparing broader networks of inventors across California. Social ties linking scientists, engineers, and managers across organization can help diffuse knowledge across a region's firms and, through doing so, raise the innovative capacity of companies that are well positioned within local technological communities. The existence of decentralized networks linking inventors is especially important in fast moving industries, such as biotechnology. A study of competition within the Alzheimer's Disease segment of medical research, for example,

[6] A list of recent Caltech start-ups is available through the Caltech Office of Technology Transfer web-site. At least 11 companies listed on this site have established headquarters outside of the Los Angeles region. The list of companies can be found at: http://www.ott.caltech.edu/?p=CaltechStartups&n=1,0,0,1,0

found over 20 distinct technological approaches being pursued by competing teams of biotechnology firms, basic research labs, and large pharmaceutical companies (Penan 1996). Most of these approaches will presumably fail. Within highly competitive new technology, informal ties across firms may provide market or technological intelligence, allowing companies to make superior decisions as to which technologies to adopt or, at times discontinue. Firms may be able to react to technological developments faster than competitors.

Networks linking scientists and companies with researchers at nearby universities are especially important. Due to their emphasis on basic research, most fundamental advances within the biosciences originate within university labs. Companies that have ties to these labs may benefit from early knowledge of important advances and may develop an advantage in licensing new technology and in hiring graduate students or postdoctoral fellows from leading labs (Murray 2004). Moreover, university labs and companies often develop a division of labor within fast moving technology fields. Universities often develop the basic scientific framework for new medicines, diagnostics, or other biomedical advances and sometimes perform pre-clinical research. Companies then obtain the financing and necessary experience in pharmaceutical development to conduct downstream commercialization, including expensive clinical trials.

This section examines the broader existence and organization of networks of inventors across the three California regional biotechnology clusters, and also investigates the extent to which universities within each region are embedded within co-inventor networks. Patents are again used as the primary data tool in this study. Data is drawn from 19,299 biotechnology related patents with California addresses filed between 1970 and 2000. Patent applications list names and the city of residence of all inventors, as well as the organization originally filed for the patent, called the assignee. The address information of inventors was used to sort patents into one of the three California biotechnology regions, and all patents were classified by organizational type based on the assignee. Organizational types included universities, biotechnology firms, pharmaceutical firms, medical device companies, general industry, or, in some cases where an organization is not the assignee, individual inventor.

Co-inventor networks were created in two ways. First, in patents with multiple inventors, all inventors on such patents have network ties to one another. Ties linking individuals across patents are created as inventors filed subsequent patents with different co-inventors. Thus, if patent A listed Cindy and Doug as inventors, and patent B listed Doug and Melissa as inventors, a network linking Cindy and Melissa would be formed through their common link to Doug. Following methods used in previous studies of co-inventor networks, inventors were assumed to be active within regional networks until five years after their most recent patent; after this time inventors were removed from the network. (Fleming et. al 2007)

Before examining the co-inventor network results, it is worthwhile to first compare the number and composition of patents by organizational type across the three regions. Figures 6 and 7 display the number of new biotechnology patents filed by inventors and the total number of inventors in the three regions between 1980 and 2000. This data shows a general rise in biotechnology patenting over this period, linked to the general rise and maturing of biotechnology as industry. The San Francisco region, however, has far more scientists active in

commercial biotechnology, with over 4500 active inventors by 2000 and a total of 9913 patents. This compares to 5200 total patents in the San Diego region and 4182 in Los Angeles. Interestingly, however, Los Angeles and San Diego, by the late 1990s had a similar number of scientists actively patenting (about 1750 in San Diego and 1500 in Los Angeles), whom had filed about 450 patents per year.

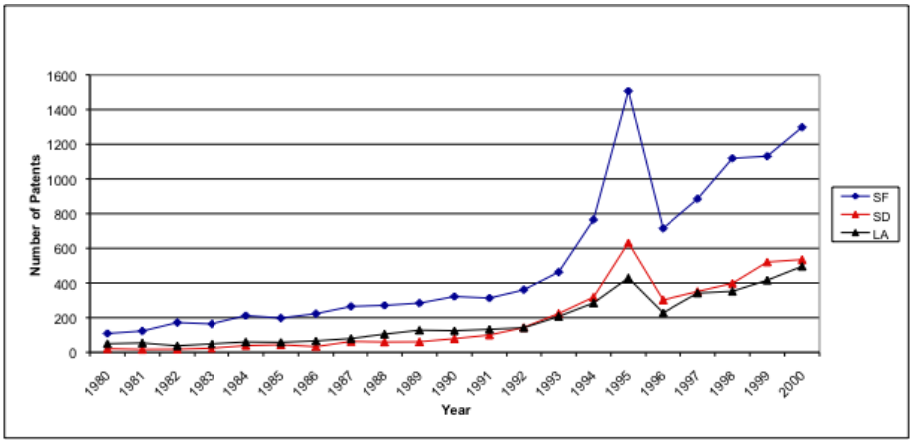

Figure 6: Total number of biotechnology patents by California region, 1980-2000

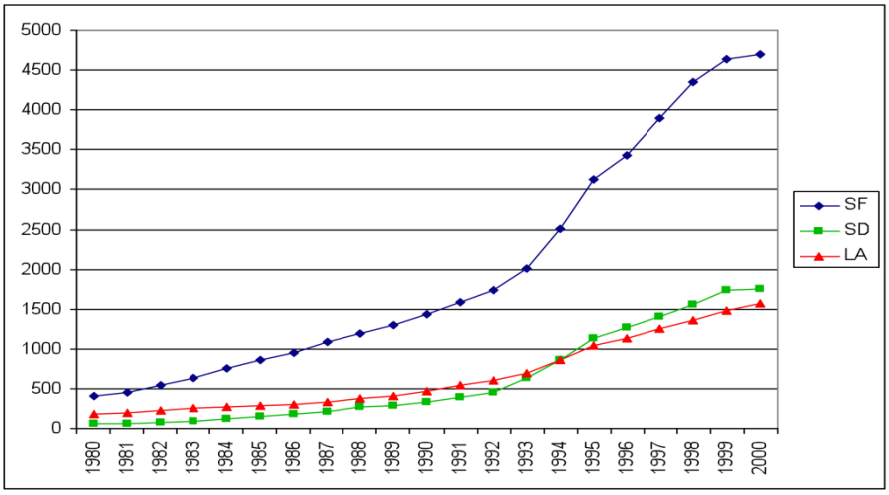

Figure 7: Number of active inventors per year by region, 1980-2000.

Figures 8 and 9 present data on the composition of patents across the three regions based on the organizational type of the assignee. Figure 8 displays cumulative patent counts for each type of assignee, while figure 9 provides a percentage breakdown of the distribution of patents held by each type of assignee for the three regions. A key finding from these graphs in that the San Francisco Bay Area, as a region, has far more patents assigned to biotechnology companies, at 5217, than either San Diego, at 2062 or Los Angeles, at 1181. If patenting is

correlated with innovativeness, then San Francisco has a dramatically more innovative biotechnology industry than San Diego, despite the two regions having a similar number of companies. San Francisco inventors working within biotechnology companies have filed almost five times as many patents as Los Angeles inventors, and San Diego biotechnology companies hold twice as many. It should also be noted that of the Los Angeles biotechnology patents assigned to inventors living in the Los Angeles region, slightly more than half are owned by Amgen (212 patents) and Allergan (455 patents), and about 10% of the patents were assigned to San Diego biotechnology companies with inventors living in southern Orange County. The number of biotechnology companies that have actively filed patents is much smaller in Los Angeles than either San Diego or San Francisco.

An unanticipated finding contained in figures 8 and 8 is the number of patents assigned directly to inventors. These are patents in which an individual has independently filed the patent application and is the assignee. Patents individually held by inventors sometimes represent cases where a scientist develops an invention privately as an entrepreneur before establishing a company. They also frequently develop when a scientist discloses an invention to an employer, but the employer chooses not to file a patent on the invention and transfers intellectual property back to the inventor, who then independently files an application. Within Los Angeles about 17% of biotechnology patents (706 total) are assigned to inventors, compared to 8% in San Diego and 6% in the San Francisco region. This finding speaks to the vibrancy of entrepreneurship in the Los Angeles region, as hundreds of inventors are willing file costly patent applications for new biotechnology inventions. However, it may also illustrate a conservatism by organizations in the region – a significantly higher number of scientists in the Los Angeles region are not able to find organizations willing to commercialize their inventions. The much lower percentage of patents assigned to the inventor in San Diego and San Francisco attest to the more active marketplace for commercializing science in these regions.

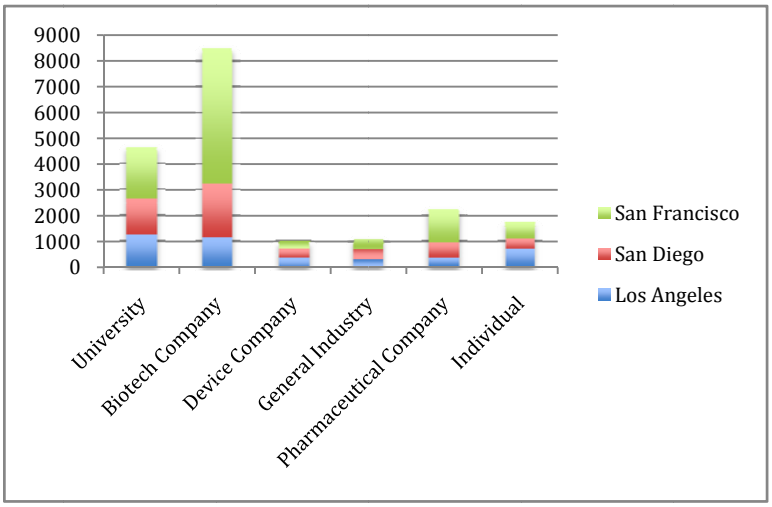

Figure 8: Cumulative count of California biotechnology patents by assignee type

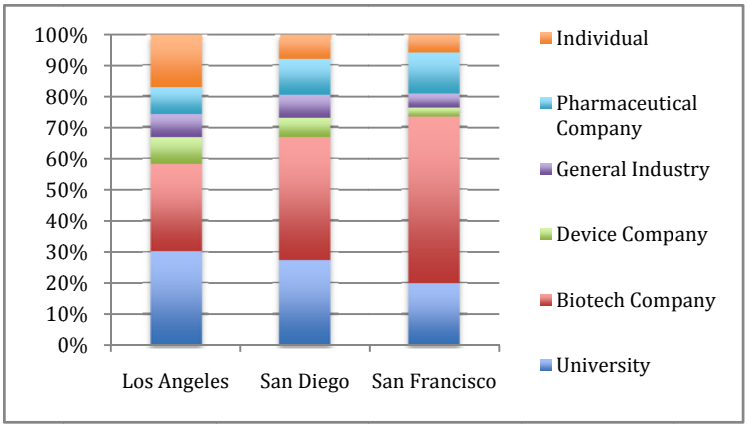

Figure 9: Percentage distribution of California biotechnology patents by assignee type

Substantial communities of biotechnology inventors exist in each of California's main biotechnology clusters, but are these inventors organized into meaningful networks? A key factor to examine is connectivity within the network, examined in part through comparing the size of the grouping of individuals within a network in which ties link all individuals, commonly called the "main component" of a network. Figure 10 compares the size of the main component of each region's co-inventor network to the total size of the inventor population. This figure shows that over 2700 inventors were in the main component of the San Francisco co-inventor network by the year 2000. San Diego had a smaller inventor network, but one with over 550 inventors and a general trend towards increased connectivity. Only 56 people were connected to one another in Los Angeles. In other words, the size of the main network component in Los Angeles is 10% that of San Diego and 2% the size of the San Francisco network.

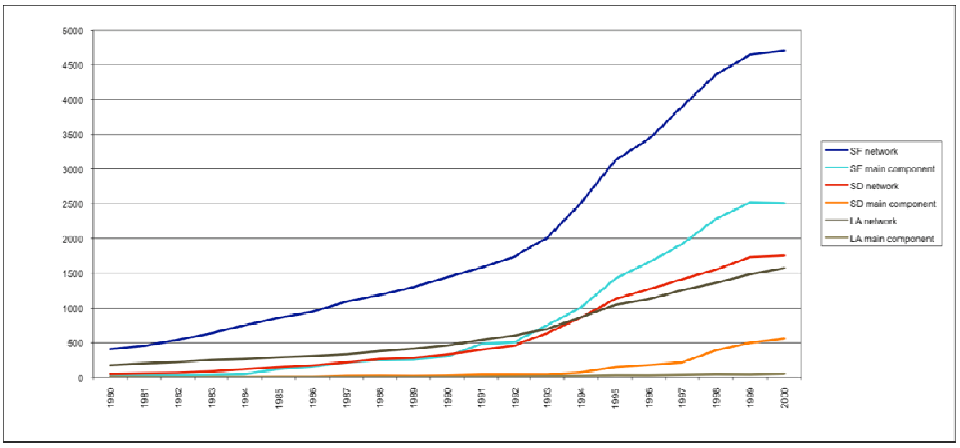

Figure 10: Total network size and main component size for California biotechnology clusters, 1980-200

Figure 11 displays the percentage of scientists that are in the main component on a yearly basis. This figure demonstrates that Los Angeles has never been able to develop an active inventor network. San Francisco has the most developed network, with more than 55% of

scientists connected to one another. Network connectivity increased rapidly in San Diego over the late 1990s, to over 30% by 2000. A similar rise in network connectively never occurred in Los Angeles. Roughly 2% of scientists are connected to one another in Los Angeles throughout the 1980s and 1990s.

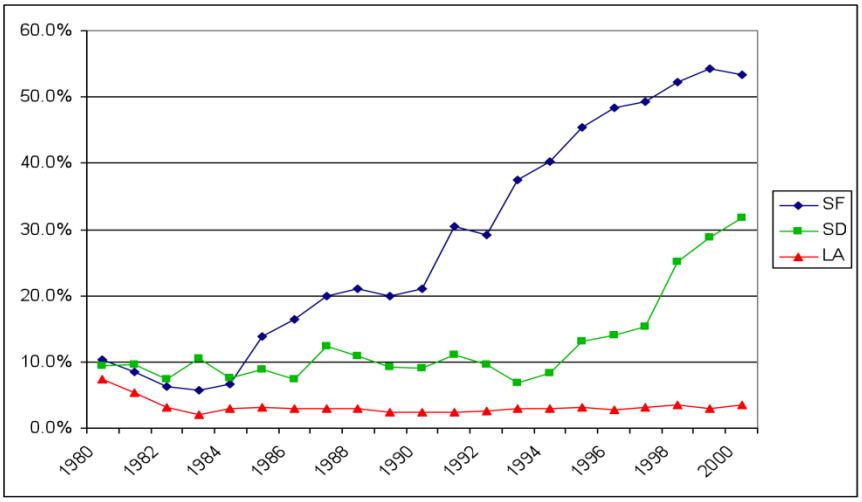

Figure 11: Percent of inventors within the main network component, CA biotech regions

Network visualizations provide a starker contrast in the development of co-inventor networks across these regions, and can also help explore the role of universities in each cluster. Figures 12 through 14 display the main component of each region's inventor network as of 2000. Within these figures the dots or "nodes" represent individual inventors, while lines connecting them represent ties created by co-patenting. The color of the dots represent the organizational type of the patent assignee, with red signifying a tie to a university and blue a tie to a biotechnology firm. While over 1500 scientists are listed on Los Angeles biotechnology patents, the region hasn't developed a sizeable network linking these scientists. Compare the embryonic Los Angeles network shown in figure 12 to vast San Francisco biotechnology network, displayed in figure 13. Given San Diego's success in biotechnology, it is surprising that networks linking scientists are smaller than in San Francisco and formed relatively late, in the mid 1990s. However, as of 2000 a coherent and dense network exists.

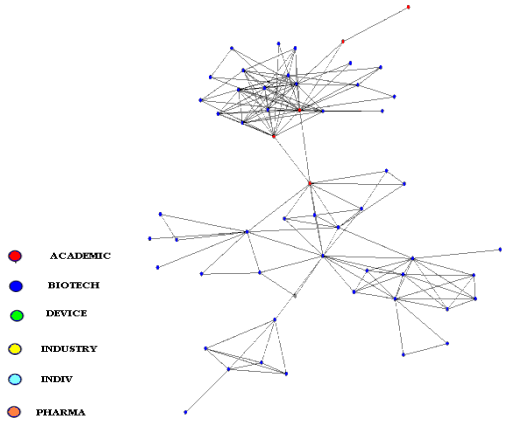

Figure 12: Los Angeles co-inventor network, 2000

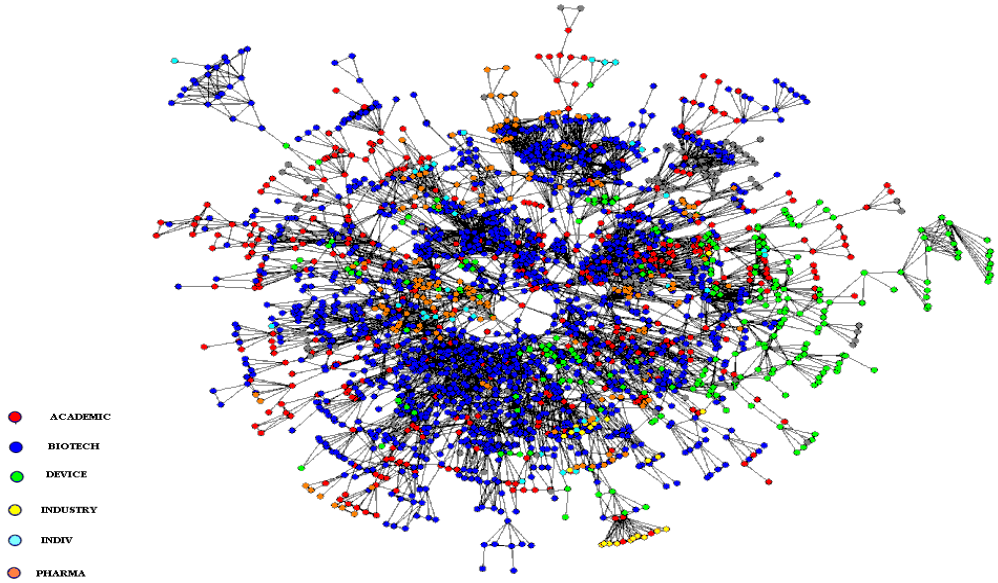

Figure 13: San Francisco co-inventor network, 2000

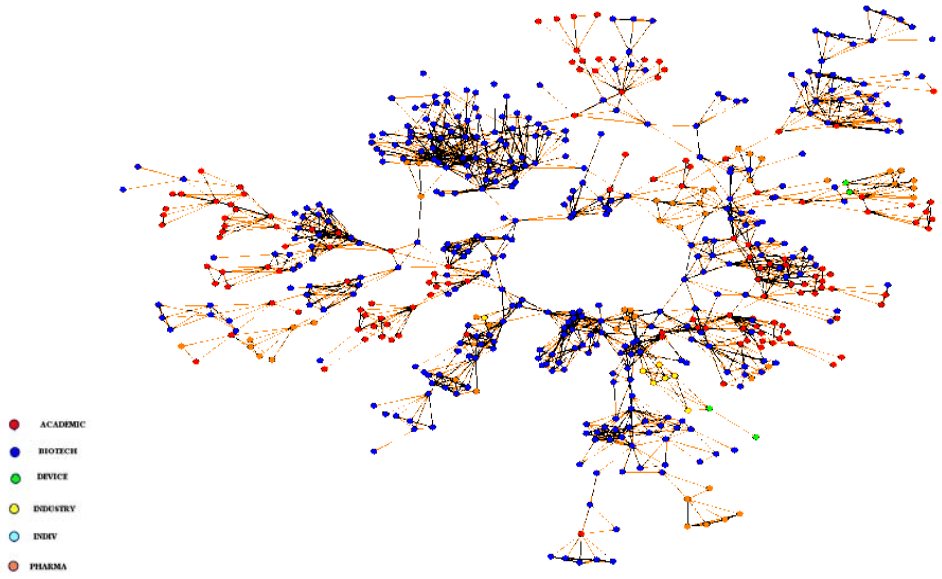

Figure 14: San Diego Co-inventor network, 2000.

In addition to having developed large and dense co-inventor networks, San Diego and San Francisco have successfully integrated scientists from both academic and industrial backgrounds into the core network. Within figures 13 and 14 this can be seen through the intermixing of individuals representing academia and commercial organizations (red and blue colored nodes). Ties linking academia to universities are particularly pronounced in San Francisco, noted by the frequent interspersing of university scientists within patches of biotechnology patents. A large number of academic, biotechnology, and pharmaceutical company based inventors can also be found in the San Diego network. However, notice in figure 14 that there is less evidence of direct collaboration; academic scientists in particular tend to cluster together more in San Diego, meaning that academics tend to patent most frequently with other academics rather than collaborate industry scientists. The Los Angeles network is too tiny to notice any trend in this direction, though most members of the main component do represent biotechnology companies.

Another way to demonstrate the differing role of universities within co-inventor networks is to examine how often scientists are involved in patenting activities at both universities and companies over their career. Research on industry-university research has identified such "linked" scientists are especially important (Lam 2007). Such scientists are responsible for creating network ties linking academic researchers and firms. Moreover, their research might be particularly valuable to companies, in that these scientists have been able to direct basic research within universities towards a commercial orientation. Figure 15 displays the number of scientists that are listed as inventors on at least one patent with an academic assignee and one patent with a commercial assignee. San Francisco has over 250 linked inventors. This helps to explain the greater independency of academic and commercial patents that was noted in the San Francisco network visualization. San Diego has over 100 linked

inventors, and Los Angeles has over 75. The data on San Diego and Los Angeles are again comparable, showing that universities within Los Angeles have increasingly permitted scientists to patent their research and then obtain jobs within industry. San Diego, however, has been more successful in integrating its linked inventors into a coherent network of inventors.

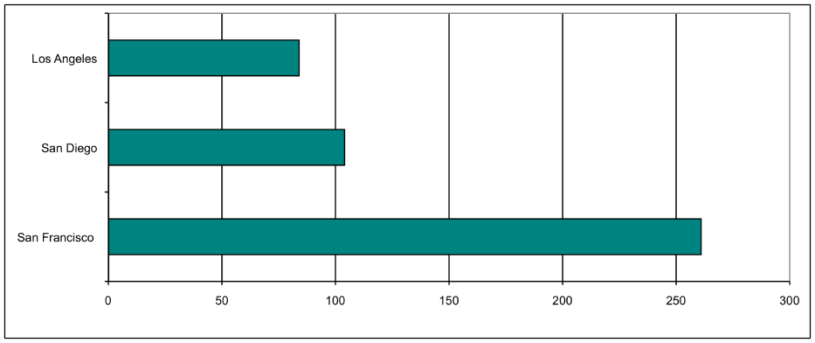

Figure 15: Number of inventors with both an academic and commercial patent by region, 1980-2000.

Summary

Two broad conclusions emerge from this analysis. First, universities in the Los Angeles region have been slow to actively commercialize scientific discoveries. This limits the supply of potential biotechnology projects flowing into the local marketplace for ideas. Second, inventor networks within the Los Angeles area are, in terms of network linkages, virtually non-existent and only weakly link university scientists to the commercial inventor community. This limits the flow of technological knowledge within the local inventor community, possibly lowering the innovative capacity of the region's firms. In order to succeed in biotechnology, universities in the region need to more actively participate in commercialization processes – an area in which improvement has been noted in recent years. However, unless a more coherent network linking life scientists in the region develops, the ability of local companies to effectively invent in fast moving biotechnology fields will be limited.

Social networks linking entrepreneurs, managers, and financiers

A second set of core networks within well-performing marketplaces for ideas connect entrepreneurs, experienced managers, and investors. This section focuses on the size and organization of these networks. While information on venture capital across California biotechnology is provided, this section focuses attention on networks linking senior managers and company founders. Because of the high-risk of failure, social networks linking managers and entrepreneurs have been shown to be an especially important underpinning of successful high-technology clusters. This section focuses first on exploring labor market dynamics within technology clusters, then again uses network analysis tools to compare the organization of

social networks linking managers and entrepreneurs in the Los Angeles region as compared to San Francisco and San Diego.

Labor market dynamics within technology clusters

The success of technology start-ups is in part determined by their ability to entice skilled managers and employees to leave lucrative and often 'safe' jobs in established companies or universities to join a new venture. Individuals joining a technology start-up face a distinctly high-risk, high-reward scenario. Skilled employees and managers are typically given grants of company stock or stock-options as an incentive to join work intensive start-ups (Kenney and Florida 1988). Should the company succeed and "go public" through a stock offering or be acquired at a favorable valuation early employees can earn vast payouts (Lerner and Gompers 2001).

However, the potential benefits of working within a start-up are countered by a high likelihood that employment tenures within start-ups will be short due to dismissals or outright failure. Most start-ups fail to reach a lucrative exit, be it an initial public offering or acquisition by a larger firm at a favorable valuation. Within California over 40% of biotechnology companies have failed or been acquired by competitors. Venture capitalists often decide to halt investments in new technology companies that fail to meet key milestones. Dismissals of top management are often a common response by VC-led boards to firms that have failed to meet development milestones. Managers and employees within start-ups also find themselves at risk of dismissal due to strategic decisions to change the competency structure of the firm. Moreover, as a condition to invest, many venture capitalists insist that early technical founders of companies often need to be replaced by professional managers as a company develops.

Within a well-functioning marketplace for ideas social networks linking experienced managers reduce the career risk of working within an entrepreneurial start-up. The existence of regional social networks can provide companies with an edge in recruiting highly skilled employees. From the point of view of individuals, there is a strong rationale for choosing to work only within start-up companies embedded within a regional cluster in which social ties promoting mobility are strong. Doing so can dramatically lower the career risk for founding teams and R&D staffs by creating numerous alternate employment options should a given venture fail, undergo managerial shakeups at the behest of investors, or need to change its competency structure due to technological volatility (Bahrami and Evans 1999). This helps explain why successful and presumably risk adverse scientists and managers would give up prestigious careers in established companies or university labs to work within lucrative but highly risky start-ups: within successful clusters the embeddednes of individuals within social networks makes it safe to do so.

The social network explanation also helps explain why many regions do not successful develop a well-functioning marketplace for ideas. Most clusters, even if they reach sufficient size, do not develop the social networks or norms of high labor market flexibility needed to create the 'regional advantage' associated with successful clusters such as Silicon Valley. Lacking a safety net provided by career affiliation networks, leaving a safe job to work within a

failure prone start-up is truly a risky proposition, one that risk-averse individuals will likely resist. 1980s.

Social networks of senior managers and founders

A central focus of this research project was to investigate whether social networks linking senior managers and company founders exist within Los Angeles, as compared to San Diego and San Francisco. Social networks form through a variety of activities, such as conferences, collaborative work linking companies, or involvement in shared social activities such as club or church membership. One of the most important sources of social ties, however, are relationships formed through joint employment at the same company. This project examined the emergence of *career affiliation networks* formed between senior managers and founders of California biotechnology firms on the basis of ties between individuals that are formed through joint employment at the same organization.[7]

An advantage of focusing on career affiliation networks is that they can be systematically mapped and studied. A variety of sources was used to capture this information, including career histories for senior managers contained in Securities and Exchange Commission filings for the 137 California biotechnology companies that were publicly listed on stock exchanges, company web-sites (including archived web-sites), and information from press releases and other information found through Internet searches.[8] Data was obtained from 1976, the year Genentech was founded in San Francisco, until 2005. Social networks linking 2285 senior managers employed in 448 California biotechnology firms are analyzed. Over half these individuals, 1229 were employed in San Francisco, with 867 employed in San Diego and a much smaller number, 199, employed in Los Angeles. These results mirror the earlier data on the number of companies, demonstrating that San Francisco and San Diego have developed significant labor market pools for senior biotechnology managers, while Los Angeles has not.

Network visualizations allow a direct comparison of the organization of social networks across the three regions. Figures 16 and N17 display network visualization of networking linking senior managers and founders working in the San Francisco and San Diego biotechnology clusters in the year 2005. Within these figures the nodes (dots) represent senior managers and founders. Within the San Francisco and San Diego networks individuals with employment ties to two important anchor firms, Genentech (in SF) and Hybritech (in SD), are colored red. Lines connecting these nodes represent social ties, formed through joint employment at a company. As a result, all senior managers within a company that were employed during the same year will have ties to one another. Ties linking senior managers at different companies within a region are formed through job-hopping from one company to another. Following a method used in

[7] Within the biotechnology industry senior management usually includes a company's chief executive, chief scientific officer, chief finance officer, and a number of vice presidents and senior personnel involved in research and development, business development, and, within some companies, human resources and legal affairs. Senior managers must define a firm's strategy and mobilize the necessary resources to implement it. Recruiting talented senior management is strongly linked to the success of biotechnology companies (Higgins and Gulati 2003). In this respect, an emphasis on top management again links directly to the emphasis on career mobility.

[8] For a full description of the methodology used to create the database, see Casper 2007a

similar studies, an assumption was made that social ties fade away or decay five years after a person leaves a company, unless they are renewed by subsequent joint employment at the same firm. (Fleming et. al. 2007) As a result, dense networks linking senior managers across companies will only form through extensive job mobility.

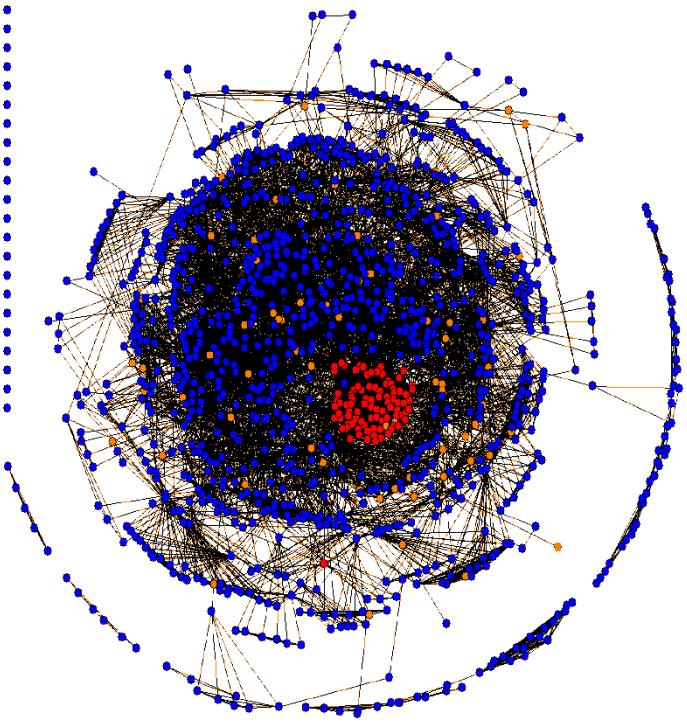

Figure 16: San Francisco career affiliation networks of biotechnology senior managers and founders, 2005

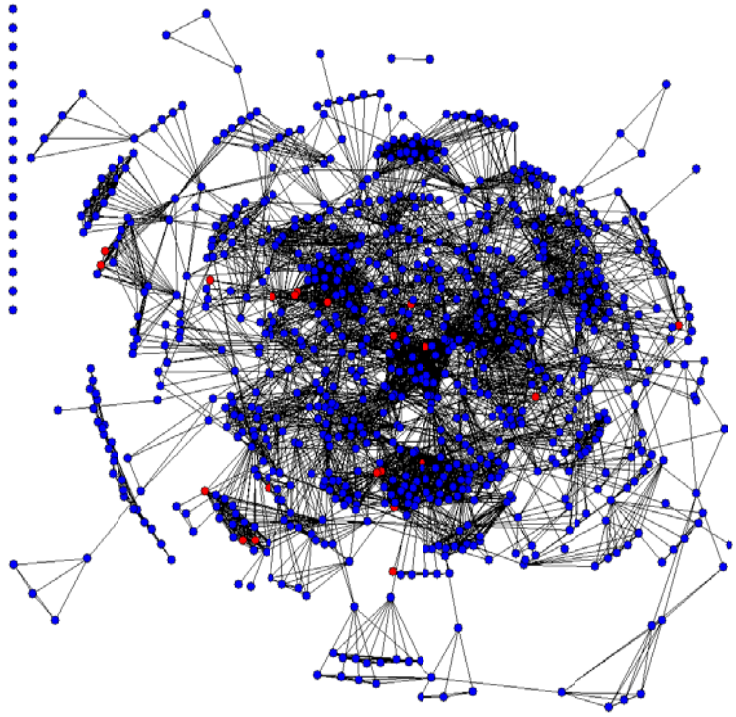

Figure 17: San Diego career affiliation networks of biotechnology senior managers and founders, 2005.

The results displayed in figures 16 and 17 are striking. The San Francisco and San Diego clusters have developed extremely dense local career affiliation networks. Within both regions over 90% of the senior managers and founders within the network are connected to each other within an interconnected network, or the main component. Within San Francisco over 1000 individuals belong to the core career affiliation network, while over 800 are members of the San Diego network. These successful biotechnology clusters have developed a large pool of talented managers and entrepreneurs willing to work within high-risk biotechnology companies. They have also developed a social structure linking individuals through a dense web of ties formed through joint career experiences. This social fabric is a key component of a well-functioning marketplace for ideas.

Figure 18 displays the organization of career affiliation networks within the Los Angeles region for 2004.[9] Los Angeles has failed to generate significant social ties linking companies. Amgen and Allergan, the two large biotechnology companies in the region, are both well-represented with large teams of senior managers. However, the data for 2004 shows no recent history of senior managers leaving either firm to work within another Los Angeles biotechnology firms. This data shows suggests that very few individuals employed within Los Angeles biotechnology firms have changed jobs to another biotechnology firm in the region.

[9] 2004 was chosen as this is a particularly representative year; some improvement is shown for 2005 and will be discussed in the future scenarios section of the report.

Figure 18: Los Angeles area career affiliation networks of biotechnology senior managers and founders, 2004.

Moreover, when people did leave Los Angeles biotechnology firms, they usually moved to jobs outside of the region, or left biotechnology for jobs in other industries, when doing so. Between 1981 (the year Amgen was formed) and 2005 there were 170 instances of individuals leaving jobs at Los Angeles biotechnology firms. In only 21 cases (12% of moves) did people relocate to other LA biotech firms. Eighty eight percent of the time, when a senior manager left a job within a Los Angeles area firm, it was to leave the local biotechnology community, often to relocate to San Diego or San Francisco. This compares, for example, to 343 lateral career moves within San Francisco biotechnology. While San Francisco and San Diego may have developed patterns of high career mobility across their firms needed to generate a web of social ties needed to help diffuse innovations and lower the risk of working within a high-risk industry, Los Angeles has not.

A similar finding surrounds networks of founders. As a supplemental database, career histories for all founders of each region's biotechnology companies were collected. This database includes 534 founders, but includes several dozen academic founders of companies that did not leave their university job to work full-time as a biotechnology managers, and are thus not included in the social network analysis. The San Francisco region has the largest pool of founders, with 269, followed by 179 in San Diego and 106 in Los Angeles. By 2005 almost all founders active in San Francisco and San Diego were active members of large regional social networks. Membership in regional networks of senior managers is important, as it provides access to a pool of talented individuals that founders of new companies have access to when seeking talent to develop new companies. Looking over the database, dozens of instances were spotted in which managers recruited individuals with which they had previous career affiliations to new firms. In San Francisco, for example, 23 biotechnology companies had at least one

founder whom had previously been a senior manager at Genentech. Another striking instance of founder networks being deployed surrounds a clique of managers of Hybritech, an early San Diego company that will be discussed in the 'scenarios' section below. Within Los Angeles potential founders of companies have historically not had the social network ties enjoyed by many founders of San Francisco and San Diego companies, due to the lack of cohesive networks in the region.

Research on new venture formation has highlighted the importance of cultivating founders active in the formation of multiple companies, so called serial entrepreneurs. Repeat founders have often learned from experiences at earlier ventures and, moreover, have typically developed social ties within a region that can be used to secure finance and human capital for subsequent firms. Table 1 contains data on serial entrepreneurship in the three California regions. While serial entrepreneurs exist in each region, San Francisco appears to have a unique advantage in this area. Close to half of entrepreneurs active in starting biotechnology firms in San Francisco (46%) have started more than one company, and a sizable pool of individuals (54) have started three or more firms. The propensity of serial entrepreneurship is less in both areas of Southern California, at 25 and 20 percent for San Diego and Los Angeles, respectively, though San Diego has twice as many serial entrepreneurs due to its larger founder community.

Number of Companies Founded	LA	SD	SF
1	80% (85)	75% (134)	54% (146)
2	12% (13)	19% (34)	26% (69)
3	4% (4)	4.5% (8)	12% (32)
4	2% (2)	1% (2)	4% (11)
5 or more	2% (2)	.5% (1)	4% (11)
Repeat Founders	20% (21)	25% (45)	46% (123)
Total # Founders	106	179	269

Table 1: Incidence of serial entrepreneurship among biotechnology founders in Los Angeles, San Diego, and San Francisco

Communities of investors

Successful marketplaces for ideas contain a vibrant community of investors. While common investors within life science companies include individuals, angel investor groups, and, at times, corporations, venture capitalists (VCs) are a particularly important class of investor within the biotechnology industry. Venture capitalists are unique in that they typically package financial resources with in-depth industry expertise and social contacts that can be used to help

companies define strategies and attract key personnel (see Zider 1998). Venture capitalists, usually acting as part of syndicates, are also typically willing to fund companies over several stages of their growth, provided that companies can meet business development milestones. Venture capital financing processes typically conclude with a company "exit," commonly a initial public offering on a stock market or a trade sale of the firm to another company, which allows VCs and other investors to recoup their investments, in some cases at a multiple of the initial investments.

How have Los Angeles biotechnology companies fared, in comparison to San Francisco and San Diego, in attracting VC funding? Between 1976 and 2005 venture capitalists invested $8.33 billion in San Francisco biotechnology companies. Another $2.9 billion was raised in initial public offerings on stock markets. During the 1978 to 2005 period venture capitalists invested $5.4 billion in San Diego biotechnology companies; these companies also raised $1.9 billion in stock market offerings. Los Angeles biotechnology companies were able to raise $551 million during this period, about 10% of the amount raised by San Diego companies, and 6% of that raised in San Francisco. An additional $54 million was raised in initial public offerings.

What explains these dramatic differences? Clearly this is a complex issue. We have already seen that the supply of scientific ideas flowing out of universities into the commercial sphere, as documented by university patenting, was substantially lower in Los Angeles compared to the other regions of California. Moreover, technical communities of scientists have been far less organized in Los Angeles, as seen through the co-inventor network data. Finally, the community of experienced senior managers and entrepreneur-founders was much smaller in Los Angeles than in either San Diego or San Francisco. The relative inactivity of VCs within the LA bioscience sector could very well be a consequence of a broader lack of opportunity to organize and fund companies in the region.

That being said, venture capitalists, through the process of incubating companies, are often prime catalysts of in creating networks of founders and managers. It is possible that if there was a more active local VC community in Los Angeles, other components of the marketplace for ideas could be strengthened. One way to measure this is to examine the geographic composition of venture capital syndicates over the history of a regional cluster. Venture capital syndicates are typically geographically diverse, containing VCs from across the country, and frequently, the world. However, venture capital syndicates commonly employ a lead investor, which is often a VC that is most active in the early incubation of companies. Because most scientific founders of companies within universities do not have business experience, they frequently turn to VCs to help incubate spin-off companies. Incubation work by VCs often includes negotiating licensing agreements with universities to gain access to technology, working with university scientists to develop initial business plans, and performing early stage business development work for the company, such as recruiting managers and scientists and locating facilities for the new company. Due to this high level of involvement, a VC is much more likely to be willing to incubate an early stage biotechnology company if that company is local.

Using a well-known database of venture capital investments called VentureXpert, data was gathered on the geographic composition of biotechnology related VC syndicates

surrounding Los Angeles and San Diego companies, and for San Francisco companies up until 1992. The VentureXpert database unfortunately does not have data on all companies. Companies financed primarily by angel investors, individuals, or other companies are frequently not contained in this database. As a result, over half the Los Angeles companies were not included in the database, and a smaller minority of San Francisco and San Diego firms are also missing. Nevertheless, the results of the analysis, presented in table 2, are indicative. San Francisco biotechnology firms have had strong participation of local VCs throughout the 1976-1994 period. Los Angeles biotechnology firms have had to rely primarily on VCs from outside the region. In fact, during the 1980-2005 period only two local VC companies had invested in Los Angeles biotech start-ups. The San Diego industry was initially structurally similar to that in Los Angeles, dependent on out of area VCs. However, the region has witnessed the growth of a local VC industry as its local biotechnology industry blossomed during the 1990s

	Los Angeles		San Diego		San Francisco	
	Percent	Total Companies	Percent	Total Companies	Percent	Total Companies
1976-1979	n/a	n/a	0	2	100	5
1980-1984	0	3	22	9	82	11
1985-1989	17%	12	33	18	84	19
1990-1994	0	2	32	19	80	15
1995-1999	0	5	60	35		
2000-2005	100	1	67	33		

Table 2: Percent of companies and number of companies with a local venture capital investor. Source: VentureXpert data.

San Francisco's ability to quickly establish a local VC presence in biotechnology is explained by the existence, by the mid 1970s, of a vibrant local venture capital industry specialized primarily around the Silicon Valley electronics industry. Following the widely publicized and successful investment in Genentech by Kleiner Perkins in 1976, over 20 additional San Francisco VCs jumped into the biotechnology industry, primarily backing additional San Francisco regional biotech start-ups (see Casper 2008). In this respect, the San Francisco had a tremendous starting advantage compared to other regions in the United States active in biotechnology in the late 1970s and early 2000s – the region was home to a community of VCs that were experienced in incubating firms.

The San Diego case is most interesting as a comparison to Los Angeles. A closer analysis of San Diego's VC companies (see Casper 2007a and 2008) reveals that many of the local VC companies, such as Convergent Capital and Biovest, both influential seed capital firms VCs emerged during the late 1980s, were founded by local entrepreneurs that had previously been senior managers or scientists in Hybritech, an important early San Diego biotechnology company. Hybritech was initially incubated by the San Francisco VC Kleiner Perkins. After the sale of Hybritech, Kleiner Perkins actively partnered with Convergent Capital and Biovest in launching several other San Diego companies, and through doing so helped launch the local San Diego VC industry.

Los Angeles, by comparison, has lacked a similar series of biotech success stories that could cultivate a local VC industry. The only local company that could clearly cultivate local VCs is Amgen, and over most of its history, as discussed earlier, Amgen executives have proven remarkably loyal to the company. Only recently, in the post 2005 period, has there been some evidence of Amgen executives becoming active in company incubation (discussed in more detail below). Over the 1980-2005 period only two Los Angeles area VCs, the MedCorp Development Fund and Convergent Ventures, had invested within the 55 biotechnology companies located as part of this project. All other companies had non-local VCs as lead investors, often from the San Francisco or New York areas, as lead VCs. Most of these companies limited their involvement in Los Angeles to one investment (though it is possible they invested in other local industries, including medical devices), potentially limiting the volume of VC investments into Los Angeles biotechnology. Interestingly, at least two other Los Angeles based VC firms had biotechnology investments, but in other parts of the state. Brentwood Associates had several investments in San Francisco and San Diego biotechnology companies. Ventana, originally based in Orange County, was an early investor in several San Diego biotechnology companies during the early 1980s, and eventually relocated to San Diego.

While cause and effect are difficult to disentangle when exploring the lack of VC investment in Los Angeles, over the 1980-2005 period the lack of sustained VC activity has been an important missing ingredient in helping to create a successful marketplace for ideas. During the 2006-2009 period there has been a strong uptick in local VC activity, spurred in part by the increased activity of Caltech as a hub for spin-off activity and the growth of the medical device industry in Orange County. An important area for on-going research, addressed below, is whether these hubs of activity can invigorate a more vibrant investor marketplace for LA biotech.

Summary

A key element of a well-functioning marketplace for ideas that has been insufficiently developed in Los Angeles are social ties linking area entrepreneurs, managers and, we will see below, scientists and inventors. The pool of available talent working directly in biotechnology in Los Angeles is smaller than in San Diego or Los Angeles. However, this is a consequence of the region not developing a social structure conducive to the development of an effective labor market needed to entice talented individuals to work within high-risk biotechnology firms. A key issue facing Los Angeles is developing catalysts to form more effective labor markets. San Diego's experience is a key reference point that Los Angeles might learn from. This case is explored in more detail below.

Creating a viable marketplace for ideas in Los Angeles: scenarios for network emergence

The poor performance of the Los Angeles biotechnology cluster is, as we saw in this report's introduction, the normal state of affairs across the country. Most regional biotechnology clusters have failed to obtain the large, sustainable agglomeration of high-risk

human therapeutics firms that characterize San Diego and San Francisco. It is likely, though not substantiated by empirical research, that most of the poor performing clusters in the United States and elsewhere have failed to develop a viable marketplace for ideas, and particularly the social network ties linking entrepreneurs, managers, scientists, and financiers.

Can Los Angeles succeed in biotechnology? This section investigates three plausible – but nonetheless difficult – scenarios by which a marketplace for ideas could emerge in the Los Angeles region. First, however, it is important to examine whether conditions surrounding potential entrepreneurs today in Los Angeles has improved in recent years. Here there are in fact favorable local developments, but also problematic trends within the broader biotechnology industry.

The good news is that, compared with the early 1980s, the Los Angeles region now has a much richer local constellation of supporting industries within the life science sectors that may heighten the competitiveness of biotechnology start-ups (see Porter 1990). While Los Angeles has fared poorly in the extremely competitive and volatile world of drug discovery related biotechnology, in a range of other life science oriented industries the Los Angeles region has performed well. Most of these companies are in lower risk industry segments, compared especially to the high-risk human therapeutics research undertaken by most biotechnology firms. At least 316 device companies have been established in the region, with Orange County being a particularly strong center of excellence. In the field of medical diagnostics, 49 companies are located in the region, including both large instrument manufacturers such as Beckman Coulture and small dedicated research firms. Ninety five companies are active In the pharmaceutical industry, broadly defined. About half these companies were involved in the generics drug industry or in contract research activities for the pharmaceutical and biotechnology industries. The pool of biotechnology companies has also grown since the 2005 cut-off used for the present study. About 50 biotechnology companies exist as of 2009.

The existence of a large supporting life science industry in the LA region helps biotechnology companies in a number of ways. First, a large labor market now exists in the region, particularly for research scientists, technicians, and engineers with life science experience. The existence of large generic manufacturers, such as Watson Pharmaceuticals in Corona or Teva in Irvine, creates a pool of personnel trained in pharmaceutical development and regulatory processes that local biotechnology firms may be able to tap into when launching drugs into clinical trials. Second, a vibrant broader life science industry in the region helps create a physical infrastructure that local biotechnology companies can tap into. A limiting factor for the development of biotechnology firms in the region that was mentioned frequently during interviews is the lack of pre-existing laboratory space available for lease by local companies. The growth of companies active in other research active fields, such as bioengineering, diagnostics, and contract research, helps establish a more liquid marketplace for commercial laboratories. Finally, there is a vibrant start-up scene in these related industries, particularly in medical devices. As discussed in more detail shortly below, the creation of an active marketplace for ideas in this sub-sector, though distinct in many ways from biotechnology, might encourage the growth of the biotechnology industry.

While the growth of supporting life science industries within the Los Angeles region is a favorable development, industry dynamics within the biotechnology industry itself may create barriers to the emergence of a stronger cluster. Within the short-term, the 2008-2009 recession has severely weakened financial markets supporting high-technology start-ups, both venture capital and especially follow-on initial public offerings. More broadly, experts have pointed towards a long term trend away form the venture funding of small biotechnology companies. Gary Pisano (2006) has published a widely debated book on the biotechnology industry, arguing that the fundamental "business model" underpinning the industry is unsustainable. Pisano points to a range of problems facing the industry, including the historic lack of profitability of the biotechnology industry and a shift of drug research funding away from small biotechnology firms and towards basic research laboratories and public private partnerships funded by advocacy groups. On the other hand, advocates of biotechnology have pointed out that most of more innovative, "first in class" drugs to have been approved by the FDA in recent years were first discovered by biotechnology firms (see e.g. Ernst and Young 2009). While start-up biotechnology firms continue to find funding, competition over this funding may be increasing. This could give an advantage to well-established regional clusters, such as San Diego, Boston, or San Francisco, in which well-functioning marketplaces for ideas create an advantage for local companies in organizing high quality teams of entrepreneurs, scientists, and managers.

Developing a "network backbone": the San Diego experience

The rarity of well-performing technology clusters suggests that the construction of a viable marketplace for ideas is difficult to achieve. A good place to explore possible scenarios by which a viable marketplace for ideas could develop is the development of San Diego biotechnology.[10] The region went from having virtually no presence in commercial biotechnology at the start of the 1980s to developing one of the world's most vibrant biotechnology clusters by the late 1990s. While San Diego has recently developed a cluster of wireless telecom companies to complement its biotechnology presence (see Simard 2004), the region did not have a presence in high technology industry during the late 1970s, and was primarily known for its large naval base. Biotechnology was the first high-technology industry to develop in the region, with the implication that early companies could not draw on previously established local venture capitalists, labor market pools, or other resources. Using network analysis tools, it is possible to study the social organization of the region's marketplace for ideas and identify the factors that lead to the development of the large, dense, and well-connected communities of scientists, managers, and founders that populate the region today.

What are the mechanisms by which regions move from a starting position in which neither the agglomeration of companies or social networks a successful marketplace for ideas exist to one in which they do? Idea marketplaces, and particularly the social networks

[10] This section draws from Casper (2007a) and (2008). Research on managerial networks in San Diego was originally supported by a NSF Undergraduate Summer Research Experience grant awarded in 2004 and 2005. However, funding from the Haynes Foundation grant was used to update the research on managers and develop the research on universities and scientist inventor ties reported in this project.

underpinning them, share characteristics analogous to a collective or public good: their benefits accrue to most if not all individuals and companies within a regional economy. However, unlike traditional public goods maintained by governments or other dominant actors (roadways, the air), social network infrastructures supporting technology clusters may be difficult to orchestrate or maintain in a systematic fashion. They are emergent property, a product of the collective behavior of individuals and firms within a regional economy. As such, it is unlikely that individuals or firms can single-handedly develop the necessary mesh of social ties needed to sustain a highly innovative cluster. A relatively large number of individuals must develop and mobilize social relationships in order to develop a density of ties sufficient to generate an overarching social structure capable of providing benefits to firms and individuals.

A key theoretical metaphor is that, to gain momentum, a "backbone" of social ties must exist in a region (Powell et al. 2004). The nucleus of a network backbone is often a group of individuals with high status within a local community, often a group of entrepreneurs and scientists linked to one more highly successful ventures within a region. Companies that can link into this core network may have an advantage in recruiting managers and scientists or raising funding, as they can use ties to high status individuals as social capital. Moreover, a credible network backbone may form the basis of a credible referral network other individuals could tap into to obtain jobs and, as the network expanded, reduce the career risk of working within one of the region's technology companies.

Within San Diego a network backbone did develop, and can be attributed almost entirely to the career strategies of a set senior managers with ties to Hybritech, the prominent early biotech company mentioned above in relation to the development of venture capital firms in San Diego. While a small number of biotechnology companies existed in San Diego by the early 1980s, only Hybritech, founded in 1978, was launched by a world class team of venture capitalists, scientific founders, and general managers. The company commercialized technology developed at UCSD by Ivor Royston and Howard Birndorf. Hybritech received immediate credibility due to its ability to attract funding from Kleiner Perkins. The VC firm had recently hired Brooks Byers as venture capitalists specializing in biotechnology. Byers assumed responsibility for the initial organization and business direction of Hybritech and became the firm's interim CEO. Byers went on to recruit an experienced management team, lead by Howard Greene, one of several up and coming young general managers who left the medical device firm Baxter to accept leadership positions within the first generation of US biotechnology start-ups (Higgins 2005). During the early 1980s, Hybritech developed a range of diagnostic tests drawing on monoclonal antibody technology. Because these tests did not require a significant regulatory approval process, they could be marketed within months of their invention.

Hybritech thus became one of the few biotechnology firms to achieve profitability early in its existence, and successfully completed an IPO in 1981. While an important early biotechnology firm, Hybritech has become much more famous for its role in "seeding" biotechnology in San Diego. After its IPO the two scientific founders of Hybritech, became interested in founding additional companies. While staying involved with Hybritech, in 1983 Royston and Birndorf helped launch Gen-Probe, another molecular diagnostics company drawing on technology developed at UCSD and Hybritech. The lead venture capital investor in

Gen-Probe was again Kleiner Perkins. In 1985 a second spin-out called IDEC was launched by Royston and Birndorf. The company applied Hybritech monoclonal antibody technology to conduct drug discovery research. IDEC was again initially funded primarily through Kleiner Perkins, with Birndorf becoming CEO. IDEC eventually became arguably San Diego's most successful biotechnology company, developing an important cancer therapy, Rituxan.

In 1986 Hybritech was acquired by the large pharmaceutical firm Lilly for $300 million plus about $100 million Lilly shares (Crabtree 2003). This acquisition had the immediate effect of transforming Hybritech's top management team, all of whom owned shares in the company, into extremely wealthy individuals. As part of the acquisition, the top management team was encouraged to remain, but Hybritech became a subsidiary of a large Indiana based pharmaceutical company with a relatively conservative managerial ethos. Hybritech had developed a free-flowing, informal corporate culture typical of technology start-ups. This created immediate clashes with the Lilly managers. Tina Nova, one of the senior scientists at Hybritech, reflects that "It was like 'Animal House' meets 'The Waltons.'" (Fikes, 1999). Lilly was unable to integrate Hybritech's management and scientific team into its corporate culture, and in the years immediately following the acquisition most of the former Hybritech senior managers left the firm.

The cadre of former Hybritech managers are now widely credited within San Diego for "seeding" the San Diego biotechnology industry. This group of managers could serve as a reliable and trusted referral network to one another. They became the nucleus of the network backbone within San Diego's biotechnology cluster. These managers had the financial resources, managerial experience, and a reputation for developing one of the biotechnology industry's early and rare success stories. Their credibility and status as successful biotech entrepreneurs was also important in recruiting highly skilled individuals to join San Diego start-ups to which the Hybritech managers were linked. Managers from Hybritech went on to found or take senior management position in at least twelve companies formed between 1986 and 1990. A study conducted in 2002 found over 40 biotechnology companies in San Diego employing a senior manager or board advisor linked to Hybritech (UCSD Connect, 2002).

In addition to founding numerous companies, a credible social network backbone was forged around the former Hybritech managers. Network visualizations, shown in figures 18-20, can help document this process. Within these figures the dots or nodes represent senior managers, and the edges between them represent ties. To simplify the network figures, individuals with no ties to other people within the network (so-called isolates) were removed from the analysis. Managers with career affiliations to Hybritech are colored black, while all other individuals are shaded gray. The visualization from 1984 shows that while a few biotechnology firms existed within San Diego, there were no career affiliation network ties linking any firm except Gen-Probe, the Hybritech spin-out. By 1987, the development of new firms founded primarily by ex-Hybritech managers was well-underway. While fragile, a coherent network backbone linking many of the region's firms now exists. By 1995 a robust network has formed linking a large number of companies. Combined with the venture capital and inventor networks that were also forming during the 1990s, a viable marketplace for ideas had formed in San Diego.

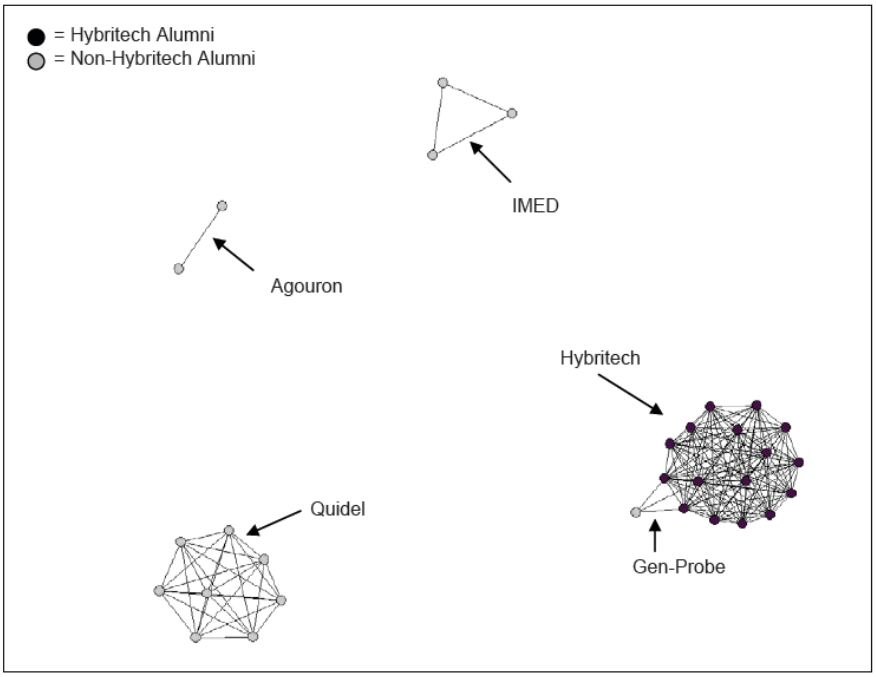

Figure 18: San Diego career affiliation network for biotechnology managers, 1984. Source: Casper 2007.

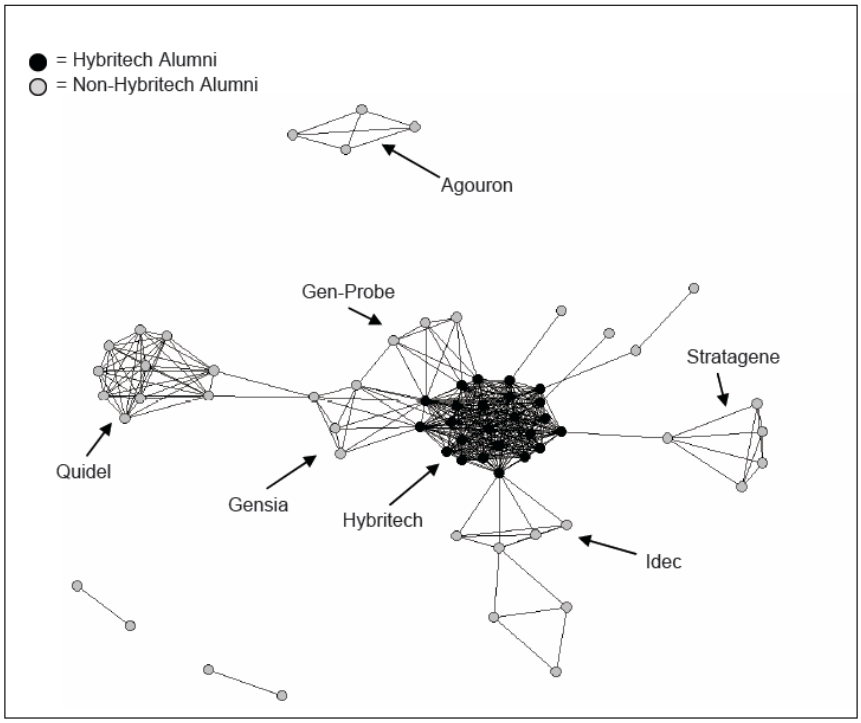

Figure 19: San Diego career affiliation network for biotechnology managers, 1987. Source: Casper 2007.

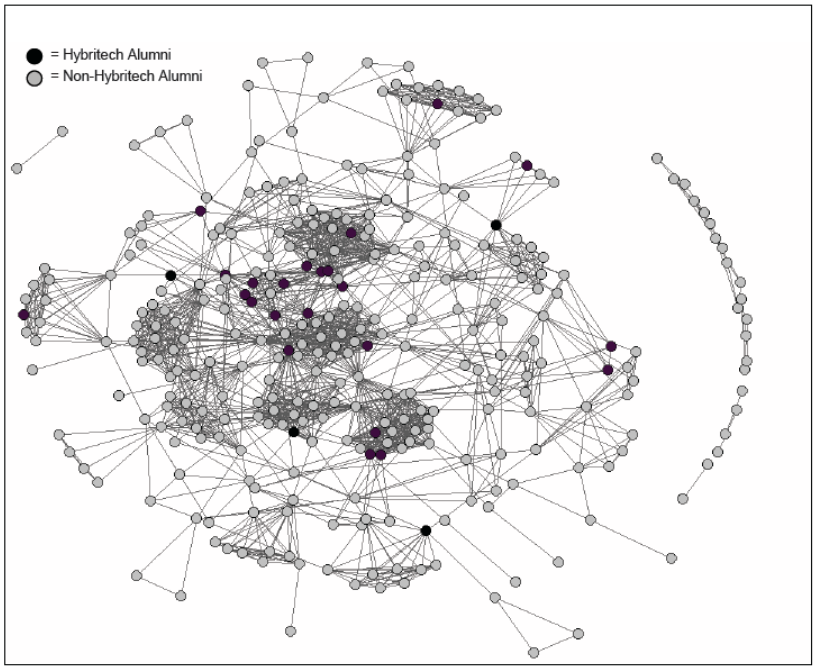

Figure 20: San Diego career affiliation network for biotechnology managers, 1995. Source: Casper 2007.

Scenarios of social network formation within Los Angeles biotechnology

The history of San Diego biotechnology suggests one scenario by which a vibrant marketplace or ideas may emerge. However, the key mechanism in San Diego was the failed acquisition of a central company. This scenario of marketplace emergence seems unlikely to repeat itself in Los Angeles, at least in the near future. The only candidate firm for a similar "acquisition gone bad" scenario in Los Angeles in Amgen. However, Amgen is currently the most profitable biotechnology company in the world. While Amgen may well be positioned to play a positive role in the development of a biotechnology cluster in the Los Angeles region, it is unlikely to occur via the "failed acquisition" route.

That being said, there are at least three scenarios by which credible social networks needed for a viable marketplace for ideas may emerge in Los Angeles. Each scenario is linked to a different mechanism that could possibly help create a viable network backbone for Los Angeles biotechnology. The mechanisms pertain to a) anchor firms, b) universities and c) "spill-overs" from other high-technology sectors within a region. Each scenario is now explored, drawing in examples from other successful clusters when relevant.

<u>a) The role of anchor firms</u>

Large, successful companies are a source of experienced managers and entrepreneurs that can be recruited to work in new regional start-ups. Senior executives within a regional anchor firm, such as Genentech in San Francisco, Biogen (now Biogen-Idec) in Boston, or Amgen

in Los Angeles, may have the financial wealth (gleaned through ownership of stock options within the anchor firm), managerial experience, and status within local industry circles needed to credibly entice scientists, managers, and investors to back new start-up firms. Studies of Silicon Valley have documented very high mobility into and out of successful companies (see Almeida and Kogut 1999; Saxenian 1994). Drawing on the widely known history of the founding of Fairfield Semiconductors by the "traitorous eight" engineers from Shockley Semiconductors in 1957 (see Lécuyer 2006), Silicon Valley is rife with instances of senior employees leaving their firm to found rival companies. Networks of highly mobile scientists and managers, especially when linked through common career experiences at a regional anchor company, may form a viable network backbone that a successful marketplace for ideas can coalesce around.

The emergence of San Francisco biotechnology is a good case in point. Senior managers and scientists within Genentech have helped forge a network backbone within San Francisco biotechnology. While the founder database assembled for this project located 23 Genentech senior managers that went on to start other Bay Area biotechnology companies, a partial list of Genentech "progeny" compiled by Cynthia Robbins Roth contained 52 Genentech employees associated with 37 biotech companies established between 1980 and 2000; most but not all of these companies are located in the San Francisco region (Abate 2001). Most of the managers and scientists that left Genentech to work with start-ups can be presumed to have social ties with one another through their Genentech days, helping to create a credible network backbone within the San Francisco biotechnology marketplace. Referring back to figure 16, the extremely high density of links between Genentech managers (colored red) and managers working with other companies exemplifies Genentech's role as a regional anchor firm.

Amgen is the world's most profitable biotechnology company. We have already seen, however, that the firm has not historically played a strong role within the Los Angeles biotechnology community. During the 1981-2005 period only five senior managers have left Amgen to start other companies, and only one of these firms are in the Los Angeles region. Labor market mobility out of the Amgen is low; the company prides itself as having one of the lowest employee turnovers within the industry, at less than 5% (Binder 2008). Moreover, the company is headquartered in Thousand Oaks in Ventura County, a relatively far commute from the core metropolitan Los Angeles and Orange County hubs of biotechnology activity. The question, then, is *could* Amgen begin to play more an anchor role within Los Angeles biotechnology?

In part, the answer to this question depends on the relative success of Amgen going forward, coupled with internal human resource policy at Amgen. Genentech, compared to Amgen, had a much more tumultuous history, created by less stable revenues during the 1980s and a disruptive acquisition of the firm in 1990 by Roche (see Robbins-Roth 199). By comparison, Amgen was a much more stable company over much of its history, particularly from the late 1980s onwards, in which hundreds of million of dollars from its first blockbuster drug, Epogen, were ploughed back into internal research and development. Moreover, widespread dispersal of stock options within the company, coupled with the steady rise in the company's stock price, made many employees rich. Unlike many Genentech employees,

however, its scientists were, overall, much more content with developing long-term careers at Amgen.

Genentech's embeddeness within America's most entrepreneurial region, Silicon Valley, is another factor helping to explain the high mobility into, and out of, Genentech. The extremely active marketplace for ideas within San Francisco's biotechnology sector, and in particular the existence of several dozen VCs active in organizing biotechnology start-ups, created a very powerful "pull" effect on successful Genentech employees. All evidence surveyed in this report points to the lack of a similar pull towards entrepreneurialism in Los Angeles. As a result, the career risk of leaving a safe job in Amgen to work within a Los Angeles area start-up is dramatically higher than for a Genentech employee contemplating a move into San Francisco biotech.

During the 2007-2009 period Amgen has been financially hurt by an unexpected FDA safety warnings on Aranesp and Epogen, two of the company's blockbuster drugs in 2007, followed by the 2008 recession. Amgen responded to these setbacks by reducing its workforce by about 12%, or 2200 people, 675 of which were in Thousand Oaks (Bruce 2007). While these employees could move into Los Angeles regional biotechnology companies, it is unlikely that these individuals had the experience, wealth, or status to create the backbone of a social network needed to invigorate Los Angeles area biotechnology. They were, after all, asked to leave Amgen, and are likely to be employees of more junior status.

A more promising development has been the retirement of several senior executives at Amgen, including long-term CEO Gordon Binder in 1999. Several retired Amgen senior executives have become active in Los Angeles biotechnology. A prominent example is Kythera, a Calabasis based company founded in 2005 that focuses on aesthetic medicines, a market pioneered in the region by Allergan with Botox. Kythera's CEO is Keith Leonard, a former senior executive at Amgen. Dennis Fenton, long-term Amgen senor executive in charge of operations, is a board member.

In 2002 Binder started a Los Angeles based venture capital company, CoastviewCapital, with the goal of raising over $100 million funding (Laurence 2002). Initially the company aimed to invest in Los Angeles area biotechnology companies. The resulting investment portfolio of this company, however, is indicative of the weakness of Los Angeles as a biotechnology marketplace. According to data from VentureXpert, sixty percent of the firm's investments during the 2003-2009 period were in San Diego, with additional investments in Massachusetts and Connecticut. CoastViewCapital has so far not invested in a Los Angeles area biotechnology company.

b) Universities as an anchor

A second scenario for cluster emergence centers on the potential role of universities as a nexus around which entrepreneurial activities can take shape. As we have seen above, most biotechnology companies are founded to commercialize discoveries made at universities. Universities can differ widely, however, in the density and type of transactions developed with local companies. Many, possibly most, universities view their role as centered primarily around

technology licensing and technology transfer. TLOs broker licensing agreements between universities and companies, while faculty involved in spin-outs take on relatively passive advisory roles within companies. Within this type of system spin-offs emerge through a capture process, as venture capitalists pull out promising technologies and do most of the early incubation work needed to develop a new company. With the possible exception of Caltech's recent push towards developing spin-outs, most technology transfer processes within Los Angeles area universities resemble this ideal type, and, as we have seen, have produced very few spin-out biotechnology firms.

Research by Jason Owen Smith, Walter Powell, and colleagues (Owen-Smith and Powell 2004; Porter et al. 2005) has suggested that universities can be much more active in processes of cluster creation. Much of this research focused on the strong involvement of public institutions in the emergence of the Boston biotechnology cluster. MIT in particular has emerged as a key player in the Boston marketplace for ideas. MIT has taken a similar role as Stanford in the Bay Area in terms of spinning out dozens of companies. However, Powell's analysis shows that MIT faculty have assumed central positions within co-inventor networks, networks of founders, and networks of scientific advisors to companies. While faculty from Stanford and UCSF are important members of co-inventor and founders networks in San Francisco, they do not monopolize central positions within these networks to the extent seen in Boston. To give an extreme example, Professor Robert Langer, a well-known member of the bioengineering faculty at MIT who has been particularly active in spinning of companies, was shown not just to be the most central member of the combined Boston biotechnology network, but his level of centrality, or connectedness within this network was 17 standard deviations higher than the mean member of the network (Porter et. al. 2005). Langer achieved this position by being a highly active member of multiple networks, ranging from the founder network, to the inventor network (measured through patenting), to the advisory board network.

MIT, and to a lesser extent, Harvard, have numerous faculty that are actively involved in the commercialization process. Rather than working in a relatively passive manner with TLO offices, faculty have personal ties with venture capitalists and other members of the local biotechnology community, and use these ties to push forward the commercialization of technologies developed within their labs. MIT is also well-known for having a large and well-functioning TLO office that sees itself as a partner within such commercialization processes. Finally, the Cambridge area has two leading business schools, the Harvard Business School and the MIT Sloan School of Management, that have also emerged as key players within local technology industries. The Sloan School has a strong focus on the management of technology commercialization processes. It developed one of the country's first entrepreneurship centers, which pioneered the use of business plan competitions as a tool to encourage the formation of teams of scientists and managers interested in commercializing technologies.

Turning to Los Angeles, could local universities develop a similar anchor role within the regional biotechnology industry? Starting first with positive developments, local universities are taking a much more active role in commercializing technology. This will increase the supply of promising technologies that could be packaged into start-up companies. UCLA and especially UCI have become more active, as have biomedical research centers attached to local hospitals,

such as CHLA and the City of Hope. While clearly more active in licensing, however, there is little evidence that any of these universities or institutes has reached the level of activity seen in Boston, and especially at MIT.

The local university that appears best positioned to follow the MIT trajectory is Caltech. Could technologies emerging from Caltech transform Pasadena into a local technology hub in a similar manner as MIT helped transform Kendall Square in Cambridge? As mentioned earlier, since launching a technology transfer office in 1995 Caltech has focused on spinning out companies. At least 80 companies have emerged across all industries, though many are not located in the Pasadena or greater Los Angeles area. Caltech has also worked to transfer what was once an insular academic culture focused primarily on basic research into a more open system in which faculty have been encouraged to commercialize their research. This has created incentives to become more active in the incubation of companies. The Caltech faculty member most famous for actively working on commercializing basic research is probably Carver Meade, a pioneer within the semiconductor and computer industry (see Gilder 2005). However, Caltech faculty that were early pioneers in spinning off biotechnology related companies, such as John Baldeschweiler, are increasingly recognized for their ability to combine basic and applied research and are being followed by a newer cohort of Caltech faculty more actively engaged in commercialization. Professor Mark Davis, a bioengineering faculty member interested in drug delivery, has in recent years founded Pasadena based biotechnology companies Insert Therapeutics and Colando Pharmaceuticals, in which he was active in the early company incubation processes.

While Caltech has taken important strides in terms of embedding itself with an emerging local high-tech economy in and around Pasadena, there are still important differences between it and MIT that may limit the university's long-term impact on regional development. Caltech is a much smaller university than MIT, roughly 1/4th the size. Caltech has over 300 faculty, 900 undergraduate students, and about 1000 graduate students. This compares to about 1100 faculty, 4500 undergraduate students, and 6100 graduate students at MIT. MIT has a much larger critical mass for research than Caltech, which can potentially have a bigger impact on the development of its regional high-tech cluster. Caltech also does not have a business school. Business schools often emerge as hubs of activity for local entrepreneurs, and also usually provide opportunities for interested in business to obtain management training.

Of course, the Cambridge area benefits enormously from having Harvard just down the road from MIT, not to mention several world class teaching hospitals associated with the Harvard Medical School. Combined, the Cambridge area has an enormous research infrastructure compared to Pasadena. While the Los Angeles region does have research oriented medical schools and several other universities, none are in close proximity to Caltech. The closest teaching hospital is the City of Hope, about a 20 minute car ride away, and there is evidence Caltech faculty and local spin-out companies from Caltech are collaborating with them on clinical research. Insert Therapeutics, for example, has organized trials at the City of Hope for one of its cancer treatments.

In sum, the emergence of Caltech, or possibly another regional university such as UC Irvine, as an anchor university that can drive the development of a local market for ideas is not far fetched. Its success depends most of all on universities developing cultures and recruiting faculty supportive of commercialization. While the Boston/Cambridge comparison is useful and there are similarities between Caltech and MIT, it is also important to note the differences. The Pasadena region may indeed somebody become the Kendall Square of Los Angeles area biotech, but to do so a critical mass of bioscience companies must develop within the area. So far this has not occurred.

c) Spill-overs from other local high-technology industries: medical devices in Orange County

Spill-overs from the development of another high-technology industry are a third potential catalyst for the emergence of a viable marketplace for ideas in the Los Angeles. Orange County has developed a highly successful medical device industry. The region is home to 97 medical device companies, many of which have links to local teaching hospitals and the strong engineering school at UC Irvine. The region is now home to many prominent medical device companies, including Edwards Scientific, one of the primary innovators in the lucrative field of heart valves. The medical device industry shares elements of the industrial structure within biotechnology, especially an emphasis on start-up companies funded by venture capital as a primarily commercialization vehicle. Could the success of other high-tech fields, such as medical devices, provide a catalyst to the region's traditionally moribund biotechnology industry?

There are at least two ways in which the success of another local high-technology industry, such as Orange County medical devices, could promote the development of a more vibrant marketplace for ideas for biotechnology. Most directly, more actors involved in the funding and governance of high-technology firms would enter the region. We saw earlier the paucity of venture capital investment within the Los Angeles biotechnology industry. Much more money has flown into the regional medical device industry. According to data from PriceWaterHouseCoopers, $363 was invested in medical device companies in 2008, primarily into Orange County based companies. This compares to $63 million in VC investments in biotechnology, itself a major uptick compared to historical averages in the region, but 1/6th the amount invested into devices. Data from VentureXpert shows that between 2004 and 2008 over 150 venture funds invested into Orange County medical device companies. While it was not possible to obtain the geographic home of these VC companies, it is safe to presume that many have set up shop in Orange County.

While some VC companies limit their investments to one sector, most attempt to diversify across industries. The early development of biotechnology within San Francisco is illustrative. Kleiner Perkins, the first VC to invest in biotech, had previously focused primarily on the electronics industry. Within the Bay Area a sizeable VC industry had developed by the late 1970s, with most firms again specializing in electronics. Kleiner Perkin's success with Genentech

created an important demonstration effect within the Bay Area. Between 1976 and 1985 twenty Bay Area venture capitalists would become active in funding 26 San Francisco based biotechnology firms. The existence of a large venture capital industry in San Francisco helps directly why the region was first to develop a significant number of biotechnology firms. San Francisco had more venture capital companies, and thus could support more start-ups.

One product of the success of the Orange County medical device sector is an expansion of the pool of local VCs available to lead the incubation of biotechnology companies in the Los Angeles. The creation of a larger VC industry in the Los Angeles region, even if focused primarily around the medical device industry, strengthens the local community of investors potentially able to lead the incubation of local biotechnology firms.

The existence of a vibrant high-tech sector in a related industry might help also reduce the career risks facing scientists and managers potentially interested in biotech careers. Earlier, we saw the lack of social networks linking managers and founders of Los Angeles area biotechnology companies. Lacking dense social networks that managers can link into, the career risk of moving from a "safe" job to a high-risk biotechnology company is very high. Norms and expectations on career management, particularly the acceptability of frequent job mobility (which helps build the social networks underpinning successful ideas marketplaces), may become widely held within the Orange County high-technology community due to the dominance and success of local medical device firms. Research on the early history of the San Francisco biotechnology industry has documented how VCs imported norms of company organization, including the acceptability of frequent career moves, from the electronics industry to biotech (see Kenney 1986). A similar phenomena could develop in the Los Angeles region, helping to jump-start the willingness of local managers and scientists to take a more entrepreneurial attitude towards working in high risk biotechnology start-ups.

Due to the strength of the region's device industry, the spill-over mechanisms might be the most viable scenario leading to the eventual emergence of a more successful biotechnology industry in and around Los Angeles. It is important to emphasize, however, that the medical science industry is distinct from biotechnology. Most medical device firms draw on bioengineering as a core scientific discipline. The industry also has distinct regulatory environment. While companies with novel devices do need to conduct trials, many companies avoid costly trials through demonstrating equivalency with existing procedures, and thus can get to market without undergoing the 4-6 years of costly trials facing most human therapeutics firms. Moreover, there is a vibrant acquisition market for successful device companies, as larger device companies, such as Medtronics, frequently buy small device companies with novel technologies and then perform further downstream commercialization and marketing work. In sum, the simpler regulatory path and vibrant acquisition market reduce the financial risks facing investors of medical device companies and provide abundant "exits" in addition to the IPO route. Thus, while sharing a broad emphasis on bioscience innovation, it unlikely that the biotechnology and medical device industries will ever amalgamate into a common industry. The

success of the device industry might have a synergistic effect on the growth of a stronger marketplace for ideas within LA biotech, but it will not subsume it.

Concluding discussion: Is there a role for public policy?

Is there a role for public policy in the future shaping of Los Angeles's biotechnology marketplace? Governments around the world, at both the national and local level, have been pouring hundreds of millions of dollars into biotechnology. This money is spent on a variety of initiatives: capacity building, funding of commercially oriented research projects, direct funding of companies, tax breaks, and a wide variety of consulting, business prospecting, and networking events. While there is no doubt a role for governments in the economic development of biotechnology clusters, there is also little evidence that governments can orchestrate the development of large sustainable biotechnology clusters containing hundreds of venture backed companies, as has emerged in Boston, San Francisco, and San Diego. In Germany, Japan, South Korea, and Taiwan governments have spent billions trying to create biotechnology industries, with very little evidence of success (Casper forthcoming).[11]

State governments within the United States are also spending massively on biotechnology. Prominent examples of capacity building in the biosciences include Florida's expenditure of over $1 billion to entice California based research institutes to move to Florida, including a $500 million to establish a new Scripps Research Institute campus in West Palm Beach Florida, and a $335 subsidy given to the Burnham Institute, another San Diego based bioscience institute, to establish a new laboratory in Orlando. Colorado has spent over $4 billion to convert the Fitzsimons Air Force base near Denver into a major center of bioscience research, including a 60,000 square foot bioscience business incubator (Potera, 2007). North Carolina has also spent over $1 billion on bioscience industry related policies over the last decade. (North Carolina Biotechnology Center 2008).

The difficulty with capacity building projects is that while the development of scientific infrastructure is a necessary condition to develop a successful biotechnology cluster, it by itself is not sufficient. Large-scale capacity building projects ignore the importance of also achieving a vibrant marketplace for ideas - the social fabric of successful high-technology clusters.

Is there a role for capacity building policies in Los Angeles? Despite its limitations, the most effective policy instrument towards biotechnology is capacity building. Building scientific infrastructure in the life sciences is a first step towards achieving success in biotechnology, while also helping meeting education and basic research goals. The Los Angeles region is fortunate to have strong endowments in basic biomedical research. Policy-makers in the region should, of course, continue to invest in expanding and renewing this infrastructure. The recently announced decision to build a new medical school at UC Riverside, for example, is an important

[11] Singapore is the only case of large-scale government intervention in support of biotechnology that could possibly achieve the goal of developing a sustainable biotechnology cluster. However, even in Singapore a vibrant community of start-up companies is emerging slowly, creating doubt as to whether a marketplace for ideas capable of sustaining this cluster would be viable absent extensive government support. See Finegold et. al. 2004.

new project. But giant bioscience infrastructure projects, as seen in Colorado or Florida, are not needed in the Los Angeles region.

One infrastructure related area mentioned repeatedly during interviews with Los Angeles area entrepreneurs is a perceived lack of readily available laboratory space available for commercial lease by start-up ventures. Within many regions such space is developed within technology parks and, for early stage companies, incubators. While incubators do exist, such as the Pasadena Bioscience Collaborative, local governments in the region could stimulate the emergence of more local biotechnology companies through helping to increase the supply of laboratory space, especially within incubators and science parks that bundle other services needed by bioscience companies.

A controversial area of public policy towards biotechnology is the direct funding of companies. Biotechnology companies are given financial help in a variety of ways, ranging from tax breaks, building subsidies, research grants, and direct venture capital investment. Direct venture capital investment within biotechnology companies is on the rise in Europe and Asia, though there is little evidence that governments can successfully play the role of venture capitalist (see Casper forthcoming). Grant funding is also common across the world, including Canada and, through the Small Business Innovation Research (SBIR) program in the United States.

While the effectiveness of government venture funding is open to debate, it is likely that funding for companies in the form of research grants might be an effective tool (Wessner 2009). Research grants allow firms to focus on the development of risky scientific capacity, helping to offset one of the most pervasive risks facing venture capitalists. Moreover, research grants often stimulate stronger inventor links between academic and industry scientists. We saw in figure 15 that the San Francisco region has developed a pronounced advantage in developing such ties. On-going research spurred by this project shows that the value of patents within the main component of the San Francisco inventor network, as measured by forward citations, is markedly higher than patents not linked to this network (Casper 2009). Almost all of the inventors in San Francisco with that have patents with both universities and firms are members of this network; on-going research is investigating whether their patents are particularly valuable.

Given the strained finances of the California state government and many local governments in the Los Angeles region, it seems unlikely that public funding will be steered towards local biotech companies. Government policy within Los Angeles could usefully encourage more collaboration between academic scientists and companies. The federally funded Small Business Technology Transfer program (STTR), part of the broader SBIR initiative, is organized with the goal of encouraging academic labs to participate in commercialization efforts. While small in scope (typically $100,000 for a stage one grant, and up to $500,000 for a stage two grant), STTR grants fund proof of principle type research that are aimed towards commercialization. Moreover, as grants, they do not dilute the ownership structure of early stage companies (as occurs with angel funding). One goal of networking type policies within Los Angeles, as currently sponsored by organizations such as LARTA, Entretech, and Octane, could be to organize seminars to educate teams of scientists associated with embryonic start-up

companies of the opportunities available through this program. More aggressive policies could provide resources aimed at helping teams of inventors write competitive applications.

Governments do of course try to promote the development of social networks – this is a classic goal of cluster policy. Networking events aimed at developing social networks have been frequently held within the Los Angeles region, usually in connection with roundtables, investor forums, and other events organized by associations such as Entretech, SoCal Bio, LARTA, and Octane. Network oriented policies may help lower the transaction cost of participating within the local ideal marketplace.

However, the ties created by many government policies aimed at cluster generation, such as networking forums and government sponsored prospecting trips, are thin. Acquaintanceship ties created through networking events are unlikely to generate a vibrant marketplace for ideas. The history of the emergence of biotechnology in San Diego is again illustrative. In the case of Hybritech, a cadre of managers formed strong ties with one another, shaped through prolonged collaboration and risk taking within an entrepreneurial setting. After the collapse of Hybritech, these individuals readily drew upon their joint network to launch follow on ventures. The former Hybritech managers and scientists also had high social status within the region, which could be used to convince other talented scientists and managers, presumably with weaker ties to the Hybritech alums founding new firms, to join the new firms.

Most networking oriented policies towards biotechnology fail to spark the growth of clusters because they cannot orchestrate the creation of the social fabric underlying successful clusters – neither strong ties nor high social status can be bestowed upon individuals by governments. Within biotechnology, both are formed as the product of collaborations and experience, primarily within an industry setting. Government policy alone cannot orchestrate the social networks underlying the development of a vibrant marketplace for ideas. This is not to say that community building events within the Los Angeles region are not useful – many help diffuse expert industry knowledge. Moreover, the acquaintanceship ties they tend to foster may, over time, develop into stronger ties needed to promote cluster growth. They are unlikely, however, to lead to the generation of a vibrant marketplace for ideas.

To conclude, while creating a more successful biotechnology cluster in the Los Angeles region is an extremely challenging task, there is evidence that more effective social networks may be forming. While the region is still far behind San Diego and San Francisco in biotechnology, a more active marketplace for ideas may be forming in the Los Angeles region. Figure 21 shows the career affiliation network for Los Angeles senior managers as of 2005. As discussed earlier (figure 18), the 2004 network contained no ties linking Amgen, Allergan, or other firms in the region. For the first time in 2005 the major companies within Los Angeles biotech are connected to one another through career mobility of local managers. In many ways this network resembles San Diego during the mid 1980s. Ties held by single individuals hold the network together. In San Diego career mobility rapidly escalated during the late 1980s, creating a more robust network. Only time will tell if a similar phenomenon occurs in Los Angeles.

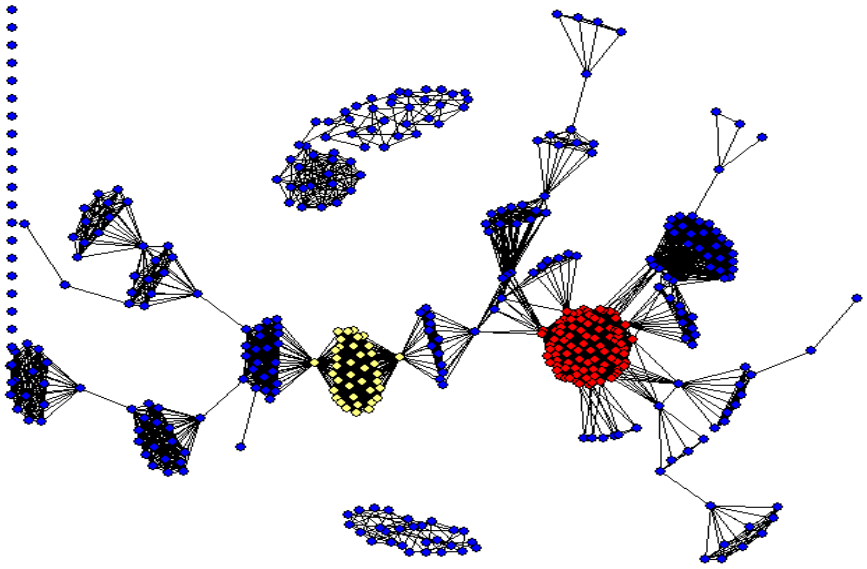

Figure 21: Los Angeles career affiliation network of senior managers, 2005. Managers from Amgen are colored red. Managers from Allergan are colored yellow.

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