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How organizational structures in science shape spin-off firms: the biochemistry departments of Berkeley, Stanford, and UCSF and the birth of the biotech industry

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This article examines how the organizational capabilities of academic spin-off firms in new industries are shaped by the organization of the research communities in universities from which these spin-off firms emerge. Contrasting the organization of research in the biochemistry departments of the University of California at Berkeley (Berkeley), Stanford University (Stanford), and the University of California at San Francisco (UCSF) and key biotech firms spun-off from these departments, this article attempts to explain the central role UCSF scientists played in comparison with their Berkeley and Stanford counterparts, in the formation and development of the biotech industry in the San Francisco region during the late 1970s and early 1980s. It is demonstrated how the research environment at UCSF during this period positioned UCSF scientists comparatively well to identify in the context of their research new technological opportunities in therapeutic product markets and pursue these opportunities in the industrial research environment of the biotech industry. Finally, drawing parallels between this study on the role of UCSF in the formation of the San Francisco biotech industry and other studies on the role of Stanford in the formation of the Silicon Valley high-tech electronics industry, this article attempts to infer some general insights into the institutional dynamics that give rise to new science-based industries.

1. Introduction

Universities are central to the industrial development of capitalist economies, having contributed to the growth of some of today's most important industries. For example, universities played a key role in the formation of the chemistry and pharmaceutical industries in Germany during the second half of the nineteenth century (Beer, 1959), the high-tech electronics industry in the United States during the Post Second World War period (Mowery and Rosenberg, 1998) and more recently the biotech industry (Kenney, 1986). Although universities have thus the proven potential of supporting the formation and development of new science-based industries, significant variation persists both across and within countries, in the extent to which universities are in fact achieving this potential.

In order to explain cross-national variations in the success with which universities support firms in new science-based industries, recent studies have tried to link these variations to different organizational structures of national university systems. Analyzing the comparative success of the American academic system since the Second World War in fostering the growth of new science-based industries, these studies have argued that the relatively competitive nature of the American academic system and its higher level of intellectual pluralism and flexibility have resulted in a scientific knowledge production that is more radically innovative (Whitley, 2003) and a type of scientist that is more entrepreneurial (Gittelman, 2001).

This article analyzes how this high level of pluralism of the American academic system plays out at the local level and how differences in the organization of science across universities shape the organizational capabilities academic spin-off firms develop. In order to illustrate this, this article presents a historical analysis of the different roles scientists from the biochemistry departments of the San Francisco region's most prominent research universities—Stanford University (Stanford), the University of California at Berkeley (Berkeley), and the University of California at San Francisco (UCSF)—played in the birth and early development of the biotech industry in this region during the late 1970s and early 1980s.

Most of the genetic engineering research, which formed the core around which the biotech industry would be organized, was concentrated inside the biochemistry departments of these three universities, and from all of these three departments, molecular biologists contributed to the development of new technologies, which would later be used in the context of therapeutic product development in the biotech industry. Scientists from these three universities, however, played very different roles in the development of the biotech industry.

In light of the literature on science transfer, which highlights the importance of formal tech transfer institutions for commercializing university science, the comparatively minor role scientists from Stanford and Berkeley played in the formation and early development of the biotech industry as compared to their counterparts at UCSF is surprising. While Stanford, during the 1970s already had in place a sophisticated technology transfer infrastructure and had made important contributions to the development of the Silicon Valley high-tech electronics industry (Kenney, 2000, Lee *et al.*, 2000, Saxenian, 1994), UCSF had neither a significant science transfer infrastructure nor a tradition of academic entrepreneurship among its faculty members.[1]

[1] In fact only in 1996, two decades after the birth of the biotech industry and six years later than Berkeley, was an independent technology licensing office established on the UCSF campus (see the Annual Report University of California Technology Licensing Office, Fiscal Year 1997). Both the Berkeley and UCSF campus offices for technology licensing were set up by Niels Reimers, who was the Director of the Stanford Office for Technology Licensing from 1968 until 1996 and during this period transformed this office into the model for technology licensing it now represents. An extensive history of the technology licensing offices of Stanford and the University of California can be found in a study by Mowery *et al.* (1999).

Yet, UCSF scientists played a central role in the formation and development of the key therapeutic biotech firms during the early days of the industry. Herbert Boyer, a Professor of UCSF's biochemistry and biophysics department founded the first therapeutic biotech firm, Genentech, and UCSF scientists were also involved in the formation of most other major biotech firms in the San Francisco region that dates back to the late 1970s and early 1980s.[2] Furthermore, an analysis of the roots of the ten largest biotech firms measured in terms of their market capitalization today in the San Francisco region shows the continuing central position of UCSF within the region's industry: six biotech firms out of the top ten are either directly or indirectly linked to UCSF—a direct link meaning that the firm was founded by a UCSF scientist, an indirect link meaning that the firm was spun-off from a firm founded by a UCSF scientist. Only three firms had a link to Berkeley and only one firm had a link to Stanford.[3]

Relying on a wide set of qualitative and quantitative historical sources, this article analyzes the comparative advantages of scientists from UCSF's biochemistry and biophysics department, relative to their counterparts at Berkeley and Stanford in identifying and exploiting the new technological opportunities of molecular biology,[4] which became apparent in pharmaceutical product markets from the mid-1970s. By contrasting the organization of the research communities in and around the biochemistry departments of Berkeley, Stanford, and UCSF, just before the formation of the biotech industry in 1976 this article highlights the significant overlaps that existed between on the one hand the organizational routines governing research inside UCSF's biochemistry and biophysics department and on the other hand the organizational routines that would be required to pursue commercial research opportunities in the industrial environment of biotech firms.

This article continues as follows. First, it is outlined how organizational structures of scientific institutions matter in shaping the ability of academic scientists to further develop their research in an industrial environment. After that, the followed research design is discussed. The empirical part of this article starts with an analysis of the extent to which scientists from the biochemistry departments of Berkeley,

[2]All three of the therapeutic biotech firms in the San Francisco region founded after the formation of the industry in 1976, which an analysis of the United States Congress Office of Technology Assessment in 1984 identifies as employing 20 or more PhDs, were spin-offs from UCSF's biochemistry and biophysics department (OTA, 1984).

[3]Analysis of the ten largest biotech firms in the San Francisco region measured in terms of their market capitalization on 12 July, 2004. Data obtained from Reuters. In measuring the number of firms linked to each university, three of the firms in the top ten were counted twice [Chiron (Nr 3), Tularik (Nr 6) and Onyx Pharmaceuticals (Nr 7)], being both linked to UCSF and Berkeley; three firms [Gilead Sciences (Nr 2), Affymetrix (Nr 4) and Impax Laboratories (Nr 8)] were not linked to a university.

[4]Even though the term *molecular biology* has sometimes been used more narrowly, especially up to the 1980s, this article uses the term *molecular biology* (and the derived term *molecular biologist*) as it is more broadly used nowadays to refer to research, pursued in the context of a wide range of different disciplinary communities in biology, that focuses on biological processes at the sub-cellular level.

Stanford, and UCSF were able to benefit of their experiences inside these departments in the industrial research environment of spin-off firms. Subsequently, the comparative advantages UCSF scientists enjoyed in spinning off biotech firms are illustrated in the context of the early development of three important San Francisco biotech spin-offs founded during the late 1970s and early 1980s, namely Chiron, DNAX and Genentech. Finally, this article attempts to formulate some general implications of this study for our understanding of how universities support the development of spin-off firms in new industries by drawing parallels between this case study on the role of UCSF in the formation of the biotech industry and existing case studies on the role of Stanford in the formation of the Silicon Valley high-tech electronics industry.

2. Universities and the organizational capabilities of spin-off firms

University research communities play a central role in supporting technological innovation in science-based industries such as the biotech industry, and firms in these industries are to a large extent dependent on ties to these communities for the development of their technological and organizational capabilities. As a result, firms in science-based industries make significant investments in cultivating relationships with academic research communities, for example encouraging firm scientists to publish in academic journals, to attend scientific conferences, and to develop collaborations with leading university laboratories (Cohen and Levinthal, 1989; Liebeskind *et al.*, 1996; Owen-Smith and Powell, 2004; Rosenberg, 1990).

A particularly crucial academic tie, shaping the early development of the technological and organizational capabilities of science-based firms is the tie, which links science-based firms to the "founding laboratories," from which these firms were spun-off. Analyzing the early development of biotech firms spun-off from university laboratories, recent studies have pointed out how "founding laboratories" constitute a key source on which science-based firms rely for their comparative advantages, highlighting not only the tacit knowledge regarding founding ideas (Zucker *et al.*, 1998), which founders bring into a firm but also the social capital (Murray, 2004) and the professional networks on which firms rely for recruitment efforts (Casper and Murray, 2004; Casper *et al.*, 2004; Jong, 2002). Although highlighting the importance of ties to founding laboratories for the development of the capabilities of firms, these studies do not address the large *variation* across scientific institutions in the extent to which these institutions are successful in providing support for the development of capabilities of spin-off firms.

The existing literature, which does attempt to address variations across scientific institutions in the success with which university science is commercialized, on the one hand consists of studies that focus on the practices of technology-licensing offices (Mowery *et al.*, 2004; Sampat *et al.*, 2003; Owen-Smith, 2003; Owen-Smith and Powell, 2003) and on the other hand consists of historical case studies, which generally focus on a broader set of support institutions shaping science transfer such as science parks, industrial affiliate programs, prior traditions of science–industry relationships, and various university policies aimed at encouraging faculty members to develop commercial ties (e.g., Saxenian, 1994; Kenney, 2001 on Stanford; Kenney and Goe, 2004 on Berkeley in comparison to Stanford; Etzkowitz, 2002 on MIT; Feldman and Desrochers, 2003 on Johns Hopkins University). Focusing primarily on the role of science transfer *support* institutions, these studies have largely left unexplored, the role organizational structures governing scientific research itself play in supporting entrepreneurial activities of scientists.

The almost exclusive focus on the role of tech transfer support institutions in the commercialization of science literature is likely the result of a "Mertonian" notion of science, which underlies this literature. This "Mertonian" notion of science is primarily concerned with the unifying rules and norms that hold together scientific communities at the macro level (i.e. Merton, 1979; Dasgupta and David, 1994). Building on a literature that studies the pursuit of science as being governed by a largely homogenous set of organizational arrangements, scholars interested in explaining variations in the level of academic entrepreneurship across scientific institutions have mainly focused on other institutional factors affecting the science transfer process than the institutional factors governing the pursuit of science itself.

Departing from this "Mertonian" notion of science, scholars in the history and sociology of science literature have however increasingly recognized that at the local level the pursuit of science is organized very differently across academic communities (e.g., Galison, 1996, Hacking, 1996, Knorr-Cetina, 1999 and Latour and Woolgar, 1979). As a result, these scholars have gradually shifted their research focus toward studying the interplay between the scientific knowledge production of local academic communities and the organizational routines, which guide research in these communities. Such organizational routines have been, for example, found to play an important role in laying out the research agendas of scientists in different academic communities and in stipulating the approaches that are considered to be sufficiently "scientifically rigorous" to pursue these agendas. As this article will demonstrate, analyzing the organizational routines that guide research in different local academic communities is not only important for understanding differences in the scientific knowledge production of these communities but also key to understanding differences in the support these communities provide for spin-off firms that emerge from these communities.

A long tradition in the neo-institutional literature on organizations points out that routines governing the activities of actors in firms are to a large extent shaped by the broader social environment, in which actors are embedded (Granovetter, 1985; DiMaggio and Powell, 1991). In line with this tradition, analyzing the formation and development of entrepreneurial firms, scholars have stressed the importance of prior organizational experiences of entrepreneurs in shaping the organizational routines of the spin-off firms these entrepreneurs found (e.g., Audia and Rider, forthcoming, Freeman, 1986, Klepper, 2001) and unveiled close relationships between the organizational routines of spin-off firms and those of parent organizations at various levels. Empirical studies, for example, demonstrate that there are often strong overlaps between the markets served and technologies used by spin-off and parent firms (Cooper, 1970; Klepper and Sleeper, 2002) and indicate that the success of entrepreneurs in dealing with key organizational challenges in a technological field is to an important extent determined by the organizational experiences acquired by entrepreneurs in dealing with similar challenges in parent organizations (Klepper, 2002).

In light of these findings, different levels of overlap between the organizational routines guiding scientific work in local academic communities and the organizational routines required to identify and exploit new technological opportunities in a specific industry are expected to account for variations across different academic communities in the support, which is provided for the development of the organizational capabilities of spin-off firms in this industry. This should hold particularly true for the development of the organizational capabilities of spin-off firms in new science-based industries such as the biotech industry of the late 1970s and early 1980s, in which the organizational routines required to deal with these industries' key technological and organizational challenges are still ill understood among actors in industry networks. In these new industries, it is therefore difficult for firms to rely on ties to industry networks to acquire these organizational capabilities and scientist–entrepreneurs primarily rely on their own academic experiences for building up the research organizations of their firms.

As highlighted by Zucker *et al.* (1998) in a study, which links the formation of spin-off firms in the biotech industry to the geographical proximity of so-called "star scientists," top scientists from leading universities play a crucial role in spin-off firms in science-based industries such as the biotech industry, in which technological innovation is closely intertwined with advances in academic research. Conducting research at the scientific knowledge frontier, these top scientists develop valuable tacitly held insights, on which firms founded by them are able to rely for comparative advantages.

In order to explain why top scientists from some leading universities are better positioned to identify and exploit the insights they develop in their academic research than top scientists from other leading universities, this study highlights that besides bringing in tacit insights from the scientific knowledge frontier into a firm, scientist–entrepreneurs are also required to bring into a firm the ability to successfully deal with the organizational challenges that are associated with developing these insights further in an industrial setting. It is argued that the industrial nature of the technological knowledge production inside firms imposes a whole set of additional organizational challenges on scientist–entrepreneurs with which top scientists coming from university research environments are not necessarily familiar dealing with. This article discusses how academic communities inside universities, in which scientists nevertheless have been guided in their research by organizational routines that overlap with routines required to deal with these key challenges, place top scientists from these communities in a comparatively advantageous position to build up spin-off firms. This article identifies two key industrial challenges that scientist–entrepreneurs face.

A first key industrial challenge for scientist–entrepreneurs is to identify research projects that answer questions with a high level of practical relevance. Whereas local academic research communities might be focused on producing knowledge regarding all kinds of natural phenomena with or without relevance to the development of some foreseeable practical application down the line, the pursuit of knowledge in industrial research organizations is constrained by its foreseeable practical applicability. Therefore, scientists belonging to those communities, of which the academic research focus overlaps with the technological research focus of an industry, are expected to be better positioned to spin off firms in this industry.

A second key industrial challenge for scientist–entrepreneurs is to integrate the activities of scientists with the various skills and expertise required in the context of the commercial research projects of the firm into a coherent and collaborative research community. Whereas in university labs, solving a single isolated research problem, which is not necessarily directly related to problems on which other scientists in the laboratory or department work, is generally seen as a valuable contribution, in an industrial research environment solving a single research problem is usually of not much value unless this problem fits in a larger scheme of problems of which the solution will enable a firm to develop a product of commercial value.

As a result, unlike for academic research organizations, the success of an industrial organization's research activities is determined by the attainment of collective research goals. Scientist–entrepreneurs must have the "integrative" ability to link together advances from the various academic fields of relevance to the product agenda of the firm and assemble a research community inside the firm, in which scientists with complementary skills collaborate on achieving the technological product goals of the firm.

The creation of collaborative and integrated research communities organized around new scientific fields, in which scientists develop the ability to incorporate advances from different disciplines in their work, has also often been cited as key to the rise of some of the world's most groundbreaking academic research organizations (de Chandervian, 2002; Hollingsworth and Hollingsworth, 2000). However, due to the organizational setup of academia, such research environments and integrative skills are usually difficult to cultivate inside universities.

One important barrier to this is the emphasis put on *individual* accomplishments in gaining recognition within the scientific community and making career advancements within the academic hierarchy. This does not lead to strong incentives for scientists to forge collaborative relationships in their research. Reflecting on the relatively individualistic nature of research in academia as compared with research in industry, Herbert Heyneker (2004), the first scientist employed by Genentech and a subsequent serial entrepreneur notes, for example, the following:

> In academe, the motivation is quite different. Graduate students are there to get a PhD thesis, so they focus on their little aspect. That's all there is to it. They don't have to integrate it into a bigger project. The postdocs are there to make a name for themselves because they want to become assistant

> professors, so they have to publish. Those are the most productive years. But again, the goal is very personal: “What contribution can I make to a certain understanding of whatever.” It can be very individualistic.
>
> In industry the goals are more clearly defined, but often you need different disciplines to reach them. So, indeed, out of Genentech came articles with twelve or fifteen names on them, and it was always viewed by academe as a funny way of doing science. I found the contrary it was a very different way of doing science, because this was a demonstration that you can accomplish a lot by working together with different disciplines.

As also highlighted in Heyneker’s quote, the disciplinary divides along which science is organized within universities constitute another major barrier to cultivating open and collaborative research communities within university organizations. Disciplinary research communities in academia with their own distinctive rules and norms regarding what constitutes good science are generally organized in isolation from each other with their own separate departments, teaching programs, journals, professional associations and conferences. These institutional barriers to cooperation significantly hinder the development of collaborative efforts among scientists with different disciplinary backgrounds, which make it easier to tackle many research problems, especially those in new fields that transcend existing disciplinary boundaries.

The lack of incentives to engage in collaborative cross-disciplinary research in academia also explains to an important extent why firms have proven so successful in tackling organizationally complex, but well-defined research puzzles, especially those that transcend existing disciplinary divides and require a concerted, integrated research effort involving a diverse group of scientists. The competition between academic research communities and Celera Genomics in the quest to sequence the human genome is one example of the comparative advantages firms have in organizing research (Shreeve, 2004); The scientific successes of biotech firms in the field of molecular biology during the 1980s,[5] in particular in the context of a number of key cloning races (e.g., Hall, 1987; Stern, 1995) are another example.

Thus, scientists, who are embedded in academic communities, which are organized around the study of empirical problems that are also relevant in an industrial context and of which the collaborative networks provide these scientists access to the knowledge and skills required to solve these problems, are expected to be in a comparatively

[5]Biotech firms played an important role in molecular biology research during the 1980s and the molecular biology departments of the leading therapeutic biotech firms during this era were often able to compete in terms of their scientific output with comparable top-ranked departments of-universities. For example, scientists from Genentech’s molecular biology department, in 1985, published 13 articles in *Science* and *Nature*, two of the most prestigious scientific journals, as compared with 14 published articles by scientists from UCSF’s biochemistry and biophysics department and 6 and 8 by, respectively scientists from Stanford’s and Berkeley’s biochemistry departments.

advantageous position to identify and exploit new technological opportunities that flow from their research in spin-off firms.

3. Research design

In order to examine whether the abovementioned arguments help explain the comparatively central role UCSF molecular biologists played in the formation and early development of the biotech industry, this study provides a historical account of the links between the organizational experience and expertise that were required to organize research inside therapeutic biotech firms and the research environments that were in place in and around the biochemistry departments of Berkeley, Stanford, and UCSF during the 1970s. These links will be, moreover, illustrated by discussing how the early organizational and technological development of three key San Francisco therapeutic biotech firms of the late 1970s and early 1980s, namely Chiron, DNAX, and Genentech, was shaped by the research environments from which these firms were spun-off. In constructing this historical account, this study relies on three kinds of sources: oral histories, archival documents, and scientific citation data.

The oral histories used in this study first of all consist of a set of extensive oral histories gathered by Sally Smith Hughes of Berkeley's Regional Oral History Office and by Nancy Rockafellar of UCSF's Oral History Program with industry pioneers and important scientists in the field of molecular biology among whom the most renowned scientists from the biochemistry departments of Berkeley, Stanford, and UCSF. A second set of complementary interviews with faculty members of these departments and industry scientists was conducted by the author himself.

Second, this study relies on documents collected from the Archives and Special Collections Sections of the Bancroft Library at Berkeley, the Green Library at Stanford and the Kalmanovitz Library at UCSF on the development of the biochemistry departments of Berkeley, Stanford, and UCSF and key biotech firms, which were spun-off from these departments.[6]

Third, in order to get a better quantitative grasp of the organizational dynamics shaping the knowledge production of these three departments, the analysis is supported by citation data, obtained from the ISI Web of Science Database. In particular, information regarding the interdepartmental ties underlying the scientific knowledge production of the three biochemistry departments in the San Francisco region and the one major San Francisco therapeutic biotech firm, Genentech, which lists departmental affiliations of its scientists on scientific publications, is valuable in understanding variations in overlaps in the knowledge networks of these departments and firms in the biotech industry.

[6]Documents from these libraries used in this study are mainly departmental records and personal papers of retired faculty members, which often also contain documentation on the involvement of these faculty members in firms.

The main unit of analysis, on which this study focuses, is the university department. Although less so nowadays, around 1970, institutional settings at the departmental level were among the most important settings at the local level determining the organizational parameters within which scientists of a certain discipline conducted their day to day research (e.g., Blau, 1973). In the biochemistry departments of Berkeley, Stanford, and UCSF, during the examined period, organizational decisions made at the departmental level, for example, included decisions about faculty recruitment, joint appointments, the overall research orientation of the department, the organization of graduate and postdoctoral programs, the admission of students, and the organization and allocation of resources among faculty members.

Due to the followed research design, this study is able to control for important external factors and focus on the question of how capabilities of spin-off firms are shaped by the academic environments from which these firms emerge. First of all, this study is largely able to control for the scientific quality of the knowledge output from the three examined departments (Table 1). Although the UCSF biochemistry and biophysics department clearly was a department on the rise in national rankings, it had still not achieved the same reputation and level of excellence in basic research as the departments of Berkeley and Stanford during the 1970s. Also measured in terms of the average and median number of citations to articles published by faculty members of the three biochemistry departments in the San Francisco region, UCSF around 1975 was still lagging behind Berkeley and Stanford in its scientific standing in the field of molecular biology.

Second, the more or less similar level of isolation from industry research networks of scientists inside the three biochemistry departments in the San Francisco region, prior to the formation of the biotech industry, enables this study to primarily focus on the impact of the organization of research in and around these departments as a variable explaining the different roles scientists from these departments played during the

Table 1 Indicators of scientific quality of knowledge output from biochemistry departments of Berkeley, Stanford, and UCSF

	1969/1982 National rankings	Average number of forward citations 1975	Median number of forward citations 1975
Berkeley	2/3	250.5	48.5
Stanford	2/1	153.5	51
UCSF	Not ranked/7	78.3	44.5

Berkeley, University of California at Berkeley Stanford, Stanford University.

Source: Citation data on publications of Berkeley, Stanford, and UCSF biochemistry departments compiled from ISI Web of Science–Science Citation Index/rankings obtained from Roose and Andersen (1970) and Jones *et al.* (1982).

early days of the biotech industry. Although before the birth of the biotech industry some of the leading professors from these departments had ties to firms as scientific consultants,[7] faculty members were generally not involved in spin-offs, industrial affiliate programs,[8] or commercially funded research[9] and top graduate students and postdocs from these departments leaving for industry positions were a rare exception.[10] Therefore, during the early days of the biotech industry, lacking significant industrial experience, scientists from the three analyzed departments were especially reliant on their academic experiences for "guidance" in the commercial research activities they would pursue.

Third and finally, scientists at Berkeley, Stanford, and UCSF, were all located in close proximity to Silicon Valley, one of the most entrepreneurial regions of the world and had roughly equal access to expertise and services required to set up entrepreneurial firms such as those offered by specialized legal firms and venture capital firms.

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[7]Scientists with consultancy contracts included renowned biochemists at all these three departments; for example, Arthur Kornberg of Stanford's biochemistry department was since 1968 affiliated with ALZA, a pharmaceutical firm as a member of the scientific advisory board (Kornberg, 1998); William Rutter of UCSF's biochemistry and biophysics department was a scientific consultant for Abbott Laboratories before the formation of the biotech industry (Rutter, 1998).

[8]The biochemistry department of Stanford started its industrial affiliate program in 1980, (see Kornberg papers, available for consultation in the Special Collections and University Archives section of the Stanford Bing Wing Library); UCSF started its industrial affiliate program in 1982 (see an uncatalogued binder on the UCSF biochemistry and biophysics department's Industrial Affiliates Program, available for consultation in the Archives and Special Collections of the UCSF Kalmanovitz Library); no records of an industrial affiliate program tied to the Berkeley biochemistry department were found.

[9]The 1975 Annual report of the Department of Biochemistry and Biophysics at UCSF (available for consultation in the Archives and Special Collections section of the UCSF Kalmanovitz Library), for example, does not mention any firms as research sponsors in the breakdown of funding sources of different faculty members; Also the "Available funds and projected income 1/1/75-12/31/75" of Stanford's biochemistry department (see Kornberg papers), which details the funding sources of faculty members does not list any firms as a funding source for research, except for a grant of USD 4457, paid to Ronald Davis by the Research Corporation.

[10]While currently approximately one third of graduate and postdoctoral students from the three discussed departments leave for industry positions, primarily in the biotechnology industry (Brutlag, 2004 and personal communication on 21 May, 2004 with Eileen Bell, Head of the Graduate Affairs Office of the Department of Molecular and Cell Biology at Berkeley, into which Berkeley's biochemistry department merged in 1989), before the formation of the biotech industry almost no graduate or postdoctoral students moved to industry positions after their studies. For example, an overview compiled in 1982, of the affiliations of former members of the laboratories of Stanford's Department of Biochemistry shows that only 17 of the 218 scientists who left one of the department's laboratories from 1971 onward were in an industry position in 1982 (see Kornberg papers). Moreover, the annual reports of 1975 and 1976 of the UCSF Department of Biochemistry and Biophysics (available for consultation in the Archives and Special Collections section of the UCSF Kalmanovitz Library) list no graduate students or postdoctoral fellows who had left UCSF during these years and moved to industry positions.

4. Biochemistry departments of Berkeley, Stanford, and UCSF at the beginning of the 1970s

This section discusses in detail the different organizational environments, which were in place in and around the biochemistry departments of Berkeley, Stanford, and UCSF just before the formation of the biotech industry and the extent to which these environments positioned scientists from these departments well to identify and pursue new technological opportunities, which became apparent in therapeutic product markets during the late 1970s and early 1980s.

4.1 The Department of Biochemistry at Berkeley

Despite being one of the first American universities to recognize the future importance of the field of molecular biology for medicine after the Second World War, Berkeley's attempts to create an integrated research community in and around its biochemistry department, which could contribute to solving medically relevant research problems was a failure in many respects. By the beginning of the 1970s, the research community of scientists interested in biology at the sub-cellular level, although excelling in a number of scientific sub-fields, lacked coherence and was characterized by a factious atmosphere.

Many of the divisions, which characterized the organization of molecular biology research at Berkeley at the beginning of the 1970s, can be traced back to the period just after the formation of the biochemistry department in 1948. The then University of California President Robert Sproul attracted the renowned biochemist and Nobel Prize winner Wendell Stanley from Rockefeller University to set up a biochemistry department. Stanley's main task upon his arrival at Berkeley was to organize Berkeley's scientists in the field of biochemistry from various departments inside one new freestanding department, dedicated to basic biological research at the sub-cellular level.[11]

Wendell Stanley, however, would encounter significant resistance and eventually the attempt to unify biochemistry research at Berkeley turned out to be a failure. Many of the university's top scientists engaged in biochemistry research were not enthusiastic at all about leaving their prominent positions in different departments and subordinating themselves to Stanley. This lack of enthusiasm was worsened by Wendell Stanley's disregard for biochemists interested in "practically oriented" research focused on medical and agricultural research topics and his unwillingness to share with these scientists the new facilities and resources that were tied to the new Virus Laboratory and biochemistry department, which Stanley headed. Eventually, the university administration withdrew its support for Stanley, and he had to resign as head of the department in 1953.[12]

[11]Documents related to Wendell Stanley's recruitment, mainly correspondence, are available from the Wendell Stanley papers (available for consultation in the Berkeley Bancroft Library).

[12]See Creager (1996) for an elaborate account of the in-fighting among biologists interested in studying biological processes at the sub-cellular level at Berkeley and the resignation of Wendell Stanley as head of Berkeley's biochemistry department.

Not only did Stanley's resignation leave the research community within Berkeley's biochemistry department without a clear programmatic direction, Stanley's resignation did also not end the factious atmosphere among biologists interested in studying biology at the sub-cellular level at Berkeley. Reorganizations during the 1960s further scattered various groups of molecular biologists across isolated departments on the Berkeley campus when in 1962, Stanley's Virus Lab split-off from the biochemistry department to become an independent Department of Virology, which in turn would form the core for a new Department of Molecular Biology, founded in 1963. Thus, by the beginning of the 1970s molecular biologists were scattered across the Berkeley campus focusing on distinctive, often highly specialized research agendas in isolation from each other.[13] Edward Penhoet (2001), who joined Berkeley's biochemistry department in 1971, for example, notes the following about the relationship between scientists from two of Berkeley's leading molecular biology departments, the biochemistry department and the Department of Molecular Biology:

> Nobody in that building including me, called themselves a molecular biologist. I don't call myself a molecular biologist today. On this campus, molecular biology and biochemistry were two distinct and very different things. This is a **cultural** thing [emphasis added]. Here we had this split, and it was a deep split. I mean, real animosity; people not talking to each other. If you were a molecular biologist, you were up the hill and you were part of molecular biology; and if you were a biochemist, you were part of this group in Barker Hall, and that's how we were divided.

Moreover, not only did the research community of molecular biologists lack coherence, there were also no institutional mechanisms linking the research activities of scientists inside these departments in a systematic way to the research activities of scientists in more clinically oriented departments. Most clinically oriented research had moved from Berkeley to San Francisco during the 1950s and 1960s including the Departments of Anatomy, Physiology and Physiological Chemistry, and scientists from the remaining departments such as the Departments of Immunology and Bacteriology were largely isolated from other departments at Berkeley.[14] Consequently, the

[13]See for a similar assessment of the dispersed nature of biology research at Berkeley and the lack of coordination among Berkeley's biologists, the following internal and external reports on the state of the biological sciences at Berkeley at the beginning of the 1980s, which set the stage for a major reorganization of biology departments in 1989; "Internal Biology Review Committee, 1981, Final Report, University of California, Berkeley" and "External Review Committee, 1981, The Biological Sciences, University of California, Berkeley" (both available for consultation from the binder "Reorganization in the Biological Sciences" in Berkeley's Bancroft Library).

[14]See for an overview of the different research and teaching activities which moved from Berkeley to the UCSF campus, the document "UCSF 1864–1989: 125 years of excellence" (available in the Archives and Special Collections section of the UCSF Kalmanovitz Library from a binder of documents prepared for the 125th year anniversary of UCSF).

biological sciences at Berkeley were organized in an environment where important scientific breakthroughs made by scientists from Berkeley's biochemistry department in the context of more simple organisms could not easily spill-over into the research activities of departments more focused on the study of higher organisms and therefore were not linked to medically relevant research problems.[15]

As a result, when research in the field of biochemistry opened up new technological opportunities in the field of biomedicine, biologists from Berkeley's biochemistry department lacked the practical orientation in their research and the links to other biological and clinical research communities which were required to identify and successfully pursue these new technological opportunities.

4.2 The Department of Biochemistry at Stanford University

Recognizing the potential contribution of basic research in the biological sciences to clinical applications in medical practice, Stanford University relocated its medical school from San Francisco to Stanford in 1959 in order to bring the clinical practitioners of the medical school closer to the basic biological research departments of Stanford (Wilson, undated). However, the new biochemistry department of Stanford's Medical School, which was to be the center of the School's basic biomedical research organization, developed into a department that during the 1970s was largely detached from practical concerns and from other (clinical) research communities within the medical school.

To head the biochemistry department of the new medical school, Stanford's University Provost Frederick Terman recruited the prominent biochemist Arthur Kornberg from Washington University. In order to attract Kornberg, who initially seemed hesitant to leave his department at Washington University, Terman offered Kornberg significant resources for his new department, the opportunity to bring with him to Stanford as many of his colleagues from Washington University as he wanted and the freedom to fill remaining faculty positions as he saw fit. The scientists who accompanied Kornberg from St.Louis would constitute the core of the new biochemistry department at Stanford up until the late 1980s.[16]

Kornberg was convinced of the fact that science in general and biochemistry research in particular is best moved forward by isolating oneself from practical concerns and by only focusing on empirical puzzles, which can be solved by using and perfecting one particular disciplinary research approach. As a result, Kornberg organized his department not only around the study of one subject, he also undertook significant efforts to ensure that faculty members in their research would not deviate from the rigorous disciplinary research approach, focusing on isolating individual enzymes in biochemical processes involving DNA, for which the department became world

[15] See footnote 9.

[16] See for a personal account of the recruitment process leading to Kornberg's arrival at Stanford, Kornberg (1998).

renowned.[17] Unlike the traditional biochemistry departments at the time in which each professor represented a different subfield and in which there was no shared research agenda among professors, Kornberg recruited around himself a small internally cohesive department with a clear shared programmatic research focus on DNA.

The research of Kornberg and his colleagues on biochemical reactions involving DNA in the experimental context of simpler organisms, in particular *E.coli* bacteria made Stanford's biochemistry department the number one rated biochemistry department in the United States by the end of the 1970s (Jones *et al.*, 1982) and resulted in many awards for its faculty members, including two Nobel Prizes, one for Arthur Kornberg himself for his research on DNA replication in 1959 and one for Paul Berg for his research on recombinant DNA in 1980.

In order to enhance the internal cohesion and coordination among the research activities of his biochemistry department, Kornberg went to great length to create a cooperative, open research environment. For example, following a tradition started in his department in St. Louis, all departmental resources were to be shared equally among faculty members, a very unusual tradition in the American science system which continues up to the present day.[18]

Because of the long shared history of the department's faculty, the shared research focus and the department's communal practices, Arthur Kornberg also dubbed the biochemistry department he created at Stanford his "extended family" (Kornberg, 1989, p. 177). For outsiders, however, the familial atmosphere, which characterized the biochemistry department had a flip side; due to the inward orientation of the research community of the biochemistry department, the department was often seen as exclusive and elitist by scientists from other departments on the Stanford campus. Although at the time of his arrival, Kornberg played a key role in the foundation of the Department of Genetics and the reorganization of existing departments in the biological sciences at Stanford, Kornberg and his successors opposed joint appointments, and there was little research interaction between laboratories of the biochemistry department and laboratories of the other departments at Stanford, in particular the

[17]See for an elaboration on the enzymatic approach favored by Kornberg, Kornberg's scientific autobiography *For the Love of Enzymes* (1989); See Paul Berg (2000) for a discussion of the strict adherence by Arthur Kornberg to the enzymatic approach as the main approach to use inside his department and the *E.coli* bacteria as the only experimental system worthwhile to study. Berg discusses tensions to which Kornberg's perseverance on this issue led within the department and the difficulties scientists interested in studying biological processes in higher organisms experienced; for example, Paul Berg himself, when he developed an interest in tumor viruses, encountered significant disapproval from Kornberg and left the department for a year in 1967.

[18]For more on the efforts Kornberg undertook to maintain a communal, familial research environment, in which resources are shared equally, see Kornberg (1989, pp. 177–186). This communal atmosphere sometimes led to tensions with "high-flyers"; for example, Kornberg (1998) recounts how the prominent biologist Lubert Stryer left the department after being told by Kornberg not to apply for new federal grants and after being denied laboratory space for his exclusive use.

laboratories of clinical practitioners inside the medical school.[19] About the department's relationship with the clinical departments of the medical school Kornberg (1998) for example noted

> Clinical medicine to this very day constantly has to make adjustments that I would find distasteful in science. You deal with an individual, uncontrolled; you apply something, and you don't know whether it has been useful or not. I'm very respectful of clinical medicine because I'm a patient; my family members have been patients, and I'm curious about and interested in clinical medicine. But would I take a group of people from the department of medicine and include them as full and active members of the biochemistry department? In some cases, yes, but in a blanket way, no. And so the Department of Biochemistry here has had the reputation of being very exclusive, elitist, and we have not had the kind of joint appointments that are common in other institutions.

As a result, there were only limited overlaps in the organizational expertise and experience, which were required to successfully identify and exploit new technological opportunities in the biotech industry and the scientific expertise and experience scientists developed in the research environment of Stanford's biochemistry department. Although the research environment inside Stanford's biochemistry department was highly open and collaborative, due to the organizational setup of Arthur Kornberg's department, this openness did not extend to scientists from other biological and clinical research departments. Though of great scientific importance to the field of biochemistry, Stanford's biochemistry department was not organized in a way that encouraged faculty members to link their day to day research activities to the clinically relevant research problems around which the biotech industry would emerge.

4.3 The Department of Biochemistry and Biophysics at UCSF

UCSF was the last university in the San Francisco region to recognize the importance of the field of molecular biology for the future of medicine. Due to the dominance of clinical practitioners within the medical school, UCSF was increasingly lagging behind other medical schools during the 1960s. In a ranking commissioned by Clark Kerr, the President of the University of California, UCSF had even fallen to the twentieth place

[19]See for example Paul Berg (2000), the successor of Kornberg as the departmental chairman on the policy of not granting joint appointments:

> But you also have to remember that Biochemistry was somewhat aloof. Biochemistry itself was quite snooty; it didn't interact with anybody. It had a policy: it would not offer joint appointments to anybody, whereas lots of other places would help in the recruitment of a person for one department by giving them a joint appointment.

among US medical schools.[20] The refusal of the UCSF chancellor at the time, John Saunders to develop a commitment toward basic research at UCSF's medical school resulted in a direct appeal to intervene, directed at the President of the University of California Clark Kerr in 1964 by a group of dissatisfied, predominantly junior UCSF faculty members. After an external report on UCSF confirmed the complaints that had been brought forward and acknowledged the importance of developing a basic research capability at UCSF's medical school, Clark Kerr replaced John Saunders, thereby opening the way to the beginning of the new era of molecular biology also at UCSF.[21]

A key challenge for the new university administration was to reorganize its biochemistry department into a department that would give UCSF credibility as a top medical school not only in clinical practice but also in basic research. However, because of the reputation of mediocrity that surrounded basic research at UCSF, it was difficult to attract prominent scientists willing to move to UCSF. Finally, after a recruitment effort which lasted several years, UCSF was able to recruit the prominent biochemist William Rutter from the University of Washington in Seattle. Among other enticements to attract Rutter to UCSF, UCSF offered Rutter significant resources in terms of space and open faculty positions, the autonomy to organize the newly named biochemistry and biophysics department according to his vision and an important say in the organization of other departments at the UCSF medical school.[22]

The research environment, which William Rutter cultivated in and around his department upon his arrival, was very distinctive from the research environment in which molecular biology research was conducted at Berkeley and Stanford. Above all, Rutter saw the opportunity which was provided to him by UCSF as an opportunity to build up a research organization dedicated to uncovering the molecular mechanisms in higher organisms, in particular humans.[23] This was an unconventional research agenda since

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[20]Based on a survey conducted in 1966 commissioned by Clark Kerr, President of the University of California (John Saunders papers, available for consultation in the Archives and Special Collections section of the UCSF Kalmanovitz Library).

[21]See Kerr (1996) and Kerr and Meyer (1996) for elaborate accounts of the decline of UCSF in the rankings of medical schools and the subsequent turmoil which led to the removal of John Saunders as UCSF's Chancellor.

[22]See for correspondence related to Rutter's prolonged negotiation regarding coming to UCSF, the William Rutter papers (available for consultation in the Archives and Special Collections section of the UCSF Kalmanovitz Library); see Rutter (1998) and Smith (1996) for personal accounts from both sides of the negotiations.

[23]See, for example, the introductory statement of the UCSF Biochemistry and Biophysics Department Annual Report for 1970 in which Rutter makes explicit his intention to focus the department's research activities on the systems of higher organisms. In the Department's Annual Report for 1972, Rutter singles out seven of UCSF's faculty members involved in clinically related programs. Five of these seven scientists would later found their own biotech firms (John Baxter, David Martin, William Rutter, David Zakim) or become affiliated with a biotech firm as a senior executive (Dov Michaeli). Both annual reports are available for consultation in the Archives and Special Collections section of the UCSF Kalmanovitz Library.

owing to the limitations of the techniques employed in the field of biochemistry at the time, biochemists tended to limit their research to the study of lower, simpler organisms.

In order to bring his ambitious research agenda within reach, Rutter used his autonomy at UCSF to build up a research community in and around his biochemistry department that was different from the "traditional" way of organizing a biochemistry department. As Arthur Kornberg at Stanford, William Rutter at UCSF recognized the importance of constructing an open atmosphere and stimulating interaction between different laboratories for fostering a productive research environment, in which scientists would be able to tackle complex research problems. However, Rutter's strong desire to move the research agenda of molecular biologists toward the study of higher organisms led him not to limit this open atmosphere to only his own department, even though the multidisciplinary approach, which such an agenda required, would lead to research outcomes that were not always as "pure" from a "biochemistry perspective." In order to extend biochemists' understanding of biological processes in simpler organisms to complex organisms, Rutter integrated the activities of the research community of biochemists at UCSF with the activities of researchers in other biological and clinical disciplines. In this respect, Rutter distinguished himself sharply from Kornberg who was much less willing to compromise the "purity" of research in his department in order to move the research agenda of his department toward the study of molecular biology research problems of relevance to clinical medicine.

Thus, after his arrival at UCSF in 1969 Rutter's primary goal was to create a unified interdisciplinary research community, in which scientists from different biological and clinical disciplinary backgrounds with their own perspectives and skills were encouraged to work together on complex human biology problems using molecular biology approaches.[24] In his own words, Rutter (1998) explains why eventually he accepted the invitation to build up UCSF's Department of Biochemistry and Biophysics:

> The reason why UCSF was attractive for this kind of development was that there were many open [faculty] positions. I felt that a collective approach was required to extend understanding of simple organisms to

[24]UCSF pioneered many of the organizational mechanisms, which would since the late 1980s be adopted by leading American research universities to better integrate various disciplinary communities in the biological sciences and mobilize their research activities around more clinically relevant research agendas. For example, Rutter was a strong proponent of the development interdepartmental research and teaching programs (see for example his proposal in the Departmental Annual Report for 1973 for a series of such programs) and actively used joint appointments to enhance the cohesion of the research efforts of clinical and basic researchers at UCSF. In his oral history, Rutter (1998) elaborates on the benefits and drawbacks he saw of such appointments. Later, during the mid-1980s, UCSF would also become a trendsetter in implementing the Program in the Biological Sciences, in which the different graduate programs in the biological sciences at UCSF were united, see for example, the 1985–1986 Annual Report of the UCSF biochemistry and biophysics department and the Bruce Alberts papers for discussions of this program (both available for consultation in the Archives and Special Collections section of the UCSF Kalmanovitz Library).

> complex organisms. One didn't know from which branch of science the solutions would come. The issues were multidimensional; there wasn't just one simple solution. There had to be chemical solutions, genetic solutions, structure solutions, biological solutions. If you didn't have all of these approaches working collectively, the risk would be higher. It would take a longer time. This feeling gradually crystallized in my mind. So after all the declining of the UCSF job offers, I finally decided to go to San Francisco and see what I could do.

Under Rutter's stewardship, the fortunes of the UCSF biochemistry and biophysics department changed radically. Upon his arrival, Rutter filled up the many open positions in his department and other departments in the medical school by recruiting scientists, who could bring new skills and innovative perspectives to the interdisciplinary networks that he organized at UCSF around a number of novel important research areas. As a result, by the 1980s UCSF had raised from obscurity in basic research circles and had become a respectable research institution in the field of molecular biology. Eventually, in 1993, UCSF's biochemistry and biophysics department would even overtake the Berkeley and Stanford departments and become the number one ranked research program in biochemistry and molecular biology in the United States (Goldberger *et al.*, 1995).

Thus, at UCSF by the mid-1970s, a unified interdisciplinary basic research community had emerged, in which the research efforts of molecular biologists from various disciplines were integrated and mobilized around the pursuit of a common research agenda with a focus on topics of relevance to clinical medicine. It was this community out of which with the foundation of Genentech in 1976, the biotech industry, was born.

5. Linking comparative advantages of academic entrepreneurs to scientific "parent organizations"

William Rutter and his colleagues at UCSF in many ways played an "agenda setting" role for the first wave of biotech firms in the San Francisco region and had built up the collaborative networks on which scientists could rely in their pursuit of this agenda both inside UCSF and inside their spin-off firms. Analyzing the early development of two of UCSF's first therapeutic biotech spin-offs, Genentech and Chiron and of the only significant therapeutically oriented biotech initiative coming out of Berkeley or Stanford during the late 1970s and early 1980s, the DNAX Research Institute of Molecular and Cellular Biology, this section highlights how the overlaps, which are outlined in Table 2, between conducting research at UCSF and conducting research inside therapeutic biotech spin-off firms, positioned UCSF scientists comparatively well to identify and exploit new technological opportunities in the biotech industry.

Table 2 Research environments surrounding core molecular biology departments Berkeley, Stanford, UCSF, and therapeutic biotech firms

	Berkeley	Stanford	UCSF	Industry
Research agenda	No unified research agenda	Uncover molecular mechanisms involving DNA, predominantly in simple organisms such as *E.Coli*	Biological processes in cells of higher organisms, especially humans	Development of human therapeutic products
Organizational structure of research community within department	Mature department; relatively isolated laboratories; little coordination individual laboratories	Familial and many collaborative ties among various laboratories	Many collaborative ties among various labs	Scientists tied together around a limited number of therapeutic projects
Organizational structure of research community across different departments	Little interaction across departments and strained relationships between two key departments	Biochemistry department as an "elite" department, isolated from laboratories of other departments	Interdepartmental collaborations encouraged and "fit" in interdepartmental networks key in recruitment of faculty	Many collaborative ties as therapeutic development requires input from a wide range of disciplines

The close links between the initial product focus of UCSF spin-off firms and research activities organized in and around UCSF's biochemistry and biophysics department illustrate well the abovementioned "agenda setting role" that the UCSF research community played for the first wave of therapeutic biotech firms.

The scientific founder of the first and most successful biotech firm during the early days of the industry, Genentech, founded in 1976, was Herbert Boyer, who had co-discovered the recombinant DNA technique, and the initial product focus of Genentech, the cloning of insulin, was closely related to Boyer's own recombinant DNA research at UCSF. In fact, important parts of the first projects of Genentech were carried out in the context of Boyer's work inside his own UCSF laboratory by postdocs who were an integral part of the research community at UCSF's biochemistry and biophysics department.[25] Also during its subsequent development, research at Genentech would often overlap with research carried out inside various laboratories at UCSF, which eventually led to fierce competition between some of the academic laboratories of UCSF and commercial laboratories of Genentech.[26]

Similar overlaps can be observed in the case of Chiron, which was founded in 1981 by William Rutter and two of his former students, Edward Penhoet and Pablo Valenzuela. Chiron was explicitly founded to continue on an industrial scale academic research projects, many of which were initiated inside William Rutter's laboratory at UCSF.[27] For example, Chiron's first important discovery, a genetically engineered hepatitis B vaccine, was based on a project directly transferred from Rutter's academic laboratory at UCSF.[28]

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[25]See for a description of the tensions to which this led among scientists inside UCSF's biochemistry and biophysics department, Boyer (2001), Betlach (2002), McKelvey (1996), and Rutter (1998).

[26]Most notably, in the important scientific race to clone human insulin, the biotech industry's breakthrough product, laboratories inside Genentech were in direct competition with the laboratories of Howard Goodman and William Rutter at UCSF. See for a popular account of the race to clone human insulin Stephen Hall's book, *Invisible Frontiers* (1987); see Stern (1995) for a discussion of how different organizational structures of academic laboratories and industrial laboratories involved in the race to clone human insulin affected the strategies followed by these laboratories and the outcome of this race; for a more general look at the interaction between researchers at Genentech and UCSF and the tensions that arose among scientists at UCSF after the formation of the biotech industry as a result of the significant commercial value which was increasingly being attributed to UCSF's clinically oriented research, see Maureen McKelvey's book *Evolutionary Innovations: The Business of Biotechnology* (1996).

[27]For an outline of Chiron's initial product goals see Chiron's summary statement in its initial business plan (available for consultation in the Bancroft Library of Berkeley as part of a collection of papers and documents gathered in the context of the 25th anniversary of the discovery of recombinant DNA in 1999).

[28]See Penhoet (2001) for a personal account of the formation of Chiron and the development of its first products including the Hepatitis B vaccine.

In contrast, almost no therapeutic biotech firms emerged from Berkeley's and Stanford's biochemistry departments, in which molecular biologists were largely conducting their research in isolation from practical concerns. Apart from Edward Penhoet, who joined his former supervisor William Rutter to build up Chiron, largely based on research Rutter had transferred from his UCSF laboratory (Penhoet, 2001), faculty members from Berkeley's biochemistry department would not be involved in the formation of significant therapeutic biotech spin-off firms during the early days of the industry.[29]

From Stanford's biochemistry department only one therapeutically oriented spin-off firm would emerge during the early days of the biotech industry, namely the DNAX Research Institute of Molecular and Cellular Biology (DNAX). Being arguably the most renowned molecular biologist in the San Francisco region at the time, after the initial successes of Genentech, Arthur Kornberg was approached by many Silicon Valley venture capitalists, urging him to start up a biotech firm. Eventually, Kornberg convinced fellow Stanford scientists Paul Berg and Charles Yanofsky to join him and the Silicon Valley entrepreneur Alex Zaffaroni to found the biotech firm DNAX in 1980.[30]

In contrast to founders of therapeutic biotech firms spun-off from UCSF, however, the founders of DNAX were not from a department in which day to day research activities were as much linked to clinical concerns and they were not directly involved in research of direct clinical relevance that could be continued as a product development project for their firm. Instead, the DNAX founders had to find a set of product targets outside their own departments and relied to a significant extent on "outsiders" in selecting the initial research focus of the firm. In the end, the first research project

[29]Even if not founded as a therapeutic biotech firm and not spun-off from Berkeley's biochemistry department, Cetus was a spin-off firm from Berkeley which should be mentioned for the completeness of this overview of the most important biotech firms in the San Francisco region during the early days of the industry. Cetus was founded in 1971, primarily as a bioindustrial firm, which commercialized machines originally developed by Donald Glaser, Professor of Physics and Molecular Biology at Berkeley that could rapidly screen and isolate mutants that were more efficient in producing complex compounds such as antibiotics and vitamins. During its early days, Cetus predominantly did contract research for large chemical, pharmaceutical, and oil companies seeking to augment their bio-industrial expertise and was not engaged in genetic engineering or monoclonal antibodies research, which would become the two main research areas that formed the basis of the drug discovery projects of the biotech industry. However, after the first successes of Genentech, Cetus radically altered its business strategy and recruited David Gelfand from UCSF's biochemistry and biophysics department to set up a molecular biology department at Cetus, which led to the transformation of Cetus into a biotechnology firm. See Rabinow (1996) for more about Cetus' foundation, its later venture into the world of molecular biology, and eventual acquisition by Chiron.

[30]See Berg (2000) and Kornberg (1998, 1995) for accounts of various attempts by venture capitalists to woe Arthur Kornberg into starting up a biotech firm and Kornberg's decision to start up DNAX together with Paul Berg, Charles Yanofsky, and Alex Zaffaroni.

of DNAX was a research project on antibodies proposed by Edgar Haber, Chief of the Cardiology Division at Massachusetts General Hospital.[31]

However, unforeseen scientific obstacles prevented DNAX scientists to move Edgar Haber's antibodies project forward once DNAX was founded and the antibodies project never really got off the ground.[32] In need for cash, DNAX was acquired by Schering Plough two years after its formation. Valuing DNAX's scientists and scientific advisory board members (which included three Nobel Prize winners) rather than the research projects of DNAX as the main assets of the firm upon its acquisition,[33] Schering Plough abandoned DNAX's antibodies research and directed the research activities of DNAX's scientists to projects, which in its eyes were more feasible.[34]

Also contributing to the lack of an industrial research focus of the activities of DNAX scientists was the "scientific culture" from Stanford's biochemistry department, which the firm's founders took with them into the firm. Interested in developing a "fundamental understanding of biological processes" rather than in developing products, DNAX's founders cultivated a research organization, which in the words of Kornberg was "remote from the imperatives of product development and marketing" (Kornberg, 1995, p. 259). Reflecting on the research environment he managed to create with his co-founders at DNAX, Kornberg, moreover, noted "the operation at DNAX has really been–I wouldn't say 'pure'–but there hasn't been any adulteration by the need to do something that will produce a profitable entity within any fixed length of time" (Kornberg, 1998). As a result, although DNAX, like Chiron and

[31]See for an extensive elaboration on DNAX's initial science plan, Kornberg (1995, pp. 50-54).

[32]Since none of the founders was directly tied to or had a vested interest in the antibodies research project which was chosen as the initial product focus of DNAX, the antibodies project never became the central focus of the research activities of DNAX in a similar way as the initial product projects of Chiron and Genentech. Looking back on the early days of DNAX, the founders say that they had expected that once a good group of scientists was in place, these scientists out of themselves would gravitate toward an alternative, better technological focus. Paul Berg (2000), for example, notes about the antibodies project,

> Nobody felt totally wedded to the antibody project. That was always viewed as being just to get us in the door, just to get the company started.

and Kornberg (1998) reflecting on the prospects of the antibodies project at the time of the formation of DNAX notes the following:

> I recall that when we went on the trip to Japan to solicit money for the support of DNAX, I said, "Alex, I'll bet that within a couple of years when DNAX is underway, we'll be doing something entirely different than working on antibodies."

[33]See approval request for acquisition of DNAX, addressed at Schering-Plough board, which identifies DNAX's scientific advisory board and scientists as DNAX's main assets in the eyes of Schering-Plough's management (as quoted by Kornberg, 1995, pp. 124–126).

[34]See Kornberg (1995, pp. 131–132) for a discussion of the reorientation of research at DNAX after its acquisition.

Genentech, did eventually grow into a world leading research organization in the scientific fields in which its scientists were active and has become an important center of scientific expertise for Schering-Plough, DNAX has never let practical concerns guide the direction of its research as strongly as Chiron and Genentech.[35]

In addition, the integrated research community, which linked together scientists from a wide range of disciplinary backgrounds around a therapeutically relevant research agenda, positioned UCSF scientists well to pursue the therapeutic product development projects biotech firms focused on during the early days of the industry. As has been pointed out, research focused on understanding the biological processes inside complex organisms required the integration of expertise from a wide range of academic disciplines. As a result, research inside the first therapeutic biotech firms was highly interdisciplinary. For example, an analysis of publications by Genentech scientists in 1985, compiled from the ISI Web of Science database, shows that 34% of the publications by Genentech scientists were the fruit of interdepartmental collaborations within Genentech.

Figure 1 clearly highlights the comparatively high level of integration of the research activities of the various basic and clinical research communities around UCSF's biochemistry and biophysics department. As indicated, these differences in the level of integration of the various research communities on the three university campuses in the San Francisco region around a common scientific agenda remained fairly constant during the whole early period of the biotech industry. Moreover, note that in 1985, 37% of publications by scientists affiliated with the UCSF biochemistry and biophysics department were the fruit of interdepartmental collaborations, only slightly more than the 34% of publications by Genentech scientists that were the fruit of interdepartmental collaborations (compared to 9% at Berkeley and 4% at Stanford).

The advantages of the integrative skills and interdisciplinary networks scientists were able to develop at UCSF became apparent during the early development of the first wave of therapeutic biotech firms in the San Francisco region. The ability of Genentech to rely on Boyer's broad scientific network at UCSF for its recruitment proved to be crucial for Genentech's success. McKelvey (1996) and Hall (1987), for example, discuss how for its important human insulin project, Genentech managed to

[35]While Chiron and Genentech in many ways have developed into pharmaceutical firms discovering, developing, and marketing their own therapeutic products, DNAX has largely remained a research institute and as of 1998, there was only one therapeutic product on the market directly coming from DNAX's laboratories (Kornberg, 1998). See also Kornberg's remarks (1998) on DNAX's scientific research focus on both industrially relevant and irrelevant projects and DNAX's resulting comparative disadvantages in successfully completing commercially interesting research projects before other biotech firms that were more narrowly focused on industrially relevant projects:

> Yes. The atmosphere at DNAX was to make basic discoveries in immunology. They were not as focused on getting quickly to an interleukin discovery. Other ventures, like Immunex, had no objective to pursue an understanding of basic questions in immunology, but rather were gung ho and competent to clone. So they could throw twenty people at a project like that in which DNAX might have two or three. Very serious.

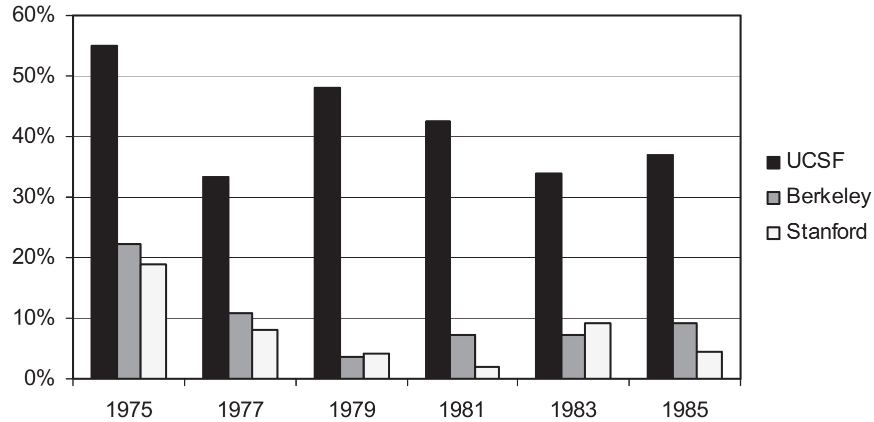

Figure 1 Percentage of publications by faculty members of Berkeley, Stanford, and UCSF biochemistry departments involving scientists tied to at least one other department within the university. Source: International Scientific Institute.

recruit some of UCSF's best postdocs, not only from Boyer's own laboratory but also from various other UCSF laboratories, and described how many of these postdocs continued to work on the same projects at Genentech as they had worked on at UCSF.

Moreover, when William Rutter started his biotech firm, Chiron, departmental documents show that he did not solely rely on his own laboratory but was also able to attract fourteen scientists to his company from at least six different laboratories from UCSF's biochemistry and biophysics department, during Chiron's founding year alone, making Chiron the largest destination for departing UCSF graduates and postdocs, surpassing Berkeley and MIT in 1981.[36]

In contrast, lacking similar overlaps between the networks of expertise which were required to pursue the initial product focus of DNAX and the collaborative networks inside Stanford's biochemistry department, scientists inside DNAX had to overcome comparatively large challenges in order to bridge the various disciplinary boundaries dividing the groups of scientists which were recruited into DNAX.[37] Scientists who were recruited into DNAX generally neither had experience in working with scientists of the other disciplines with whom they were to collaborate at DNAX nor were involved in research overlapping with DNAX's initial research projects. Moreover, the

[36]See UCSF Department of Biochemistry and Biophysics Annual Report 1981–1982 (available for consultation in the Archives and Special Collections section of the UCSF Kalmanovitz Library), which lists subsequent occupational affiliations of departing graduate and postdoctoral students from various laboratories of the department.

[37]See Kornberg (1998) for a discussion of the tensions between biochemists and immunologists at DNAX during its early days.

relative isolation of Paul Berg and Arthur Kornberg inside their department from scientists of other disciplinary communities at Stanford led to significant challenges in recruiting scientists from outside the field of biochemistry, in particular from the field of immunology which was central to DNAX's initial product focus. As a result, during DNAX's early days, biochemical approaches were overrepresented within the research community at DNAX.[38] In order to attract the immunological expertise, required to successfully pursue the technological research goals of DNAX, DNAX's founders did not rely on their own scientific networks but largely relied on networks of immunologists who were attracted to the scientific advisory board of DNAX, which was constructed to broaden the scope of the scientific expertise available to DNAX.[39]

6. Some concluding remarks

An issue worth addressing in this final section is what the more general implications of this study are for our understanding of the role universities play in the technological and industrial development of capitalist societies. Although it is difficult to formulate generalizations on the basis of one case study, linking the findings of this article to other historical accounts of the emergence of new science-based industries might help to deepen our knowledge of the dynamics through which new science-based industries emerge from open science communities. In particular, extensive historical studies on the ascent of Stanford as a leading research university (Gillmor, 2004; Lowen, 1997) and on the development of the surrounding Silicon Valley high-tech electronics industry (Kenney, 2001; Lee *et al.*, 2000; Saxenian, 1994) provide an opportunity to extend the insights of this study.

Contrasting the histories of Stanford and UCSF during the periods, in which these universities gave rise to the formation of new industrial clusters, in particular a parallel stands out between the role William Rutter played at UCSF and the role Frederick Terman played at Stanford in creating a research environment supportive of entrepreneurship. Like William Rutter, Frederick Terman, who by some has been labeled the "Father of Silicon Valley" (Saxenian, 1995), was a highly successful institution builder and the rise of Stanford, both as a first-rate research university and as an important institution fuelling innovation in the Silicon Valley high-tech electronics industry after the Second World War has been directly linked to Terman's tenure at Stanford, first within Stanford's School of Engineering and later as the University's Provost.

[38]See for more about the overrepresentation of biochemical approaches, relative to immunological approaches at DNAX during its early days, and subsequent attempts to adjust this "imbalance," Kornberg (1995, p. 50).

[39]According to Goeddel (2003), the UCSF spin-off Genentech, for example, did not have such a scientific advisory board during the early days of its development.

Sensing the major technological opportunities that were made possible by wartime advances in engineering and physics research, during his tenure as the Dean of Stanford's School of Engineering, Frederick Terman set out to create integrated communities of scholars, focused on a limited number of research fields that proved to be central to the emerging high-tech electronics industry. Very much like William Rutter, who created a pioneering research organization at UCSF, in which research activities of molecular biologists from various biological and clinical research disciplines were integrated and mobilized around a research agenda of therapeutic relevance, Terman, like no one else before him, was able to integrate research activities of scientists from the School of Engineering and from basic research departments, primarily from the university's physics department, around the study of research fields of relevance to solving a number of important technological problems in the high-tech electronics industry.

The research environment Terman cultivated in and around Stanford's School of Engineering helped Stanford researchers to develop valuable expertise and networks required to identify and exploit new research opportunities in the technological fields that were driving innovation in the high-tech electronics industry. Stanford spin-offs were often able to rely on the expertise and networks their founders brought with them from Stanford for the development of key organizational capabilities, starting with the formation of Hewlett Packard by two of Terman's students, Bill Hewlett and Dave Packard, in 1939, who relied on their ties to Stanford's School of Engineering for the technological development of their first products, for recruiting their first key employees, for attracting their financing, and for finding their first customers.[40]

Interestingly, after being promoted to the position of University Provost in 1955, Terman, as a university administrator also played a major role in turning the Stanford Medical School into a leading center for basic research in the field of molecular biology. By moving the medical school from San Francisco to Stanford, the university administration attempted to integrate better the clinical activities of the medical school with the basic research organization of the university in order to position Stanford scientists better to pursue new basic research opportunities in the field of biomedicine that had emerged as a result of the rise of molecular biology. However, as discussed, Arthur Kornberg, who was attracted to head the most important of the new basic research departments, which were created in the medical school, had a vision about how to move science forward that excluded the close integration of his department's research with research pursued outside his department, in particular with research pursued in the clinical departments of the medical school. As a result, in contrast to their counterparts from Stanford's engineering departments, scientists from Stanford's

[40]Based on accounts of the early days of Hewlett Packard by Packard (1996) and Saxenian (1994, 1995).

biochemistry department were organized largely in isolation from practical concerns when the industrial opportunities of their research became apparent.

Thus, at the level of individual universities, both the emergence of the San Francisco biotech—and high-tech electronics—industries highlight the important role that integrated interdisciplinary basic research communities in scientific fields of direct practical relevance play in supporting the growth of science-driven industries. As the discussed case studies indicate, the expertise and networks, which scientists in such communities acquire, provide these scientists with significant comparative advantages in developing the organizational capabilities of spin-off firms.

Finally, at a more macro-level, the findings of this case study confirm the importance of space for organizational experimentation and pluralism, which has often been cited as key for supporting technological innovation within socioeconomic systems (e.g., Nelson, 1990; Whitley, 2003; Rosenberg, 1992). Both in the Stanford and UCSF cases, the broader social environment, which encouraged and rewarded the entrepreneurial efforts headed by Frederick Terman and William Rutter was a key precondition for the creation of the research communities that supported the formation of new industries. As in the case of the emergence of the biotechnology—and high-tech electronics—industries in the San Francisco region, the emergence of future science-driven industries will likely to an important extent rely both on the success of future scientific entrepreneurs such as Terman and Rutter to identify scientific opportunities in new research fields of industrial relevance and on their ability to mobilize different research communities within their universities around the pursuit of these opportunities. Fostering technological progress, driven by science-based firms in new high-tech industries thus requires strong support for basic research as well as support for entrepreneurial efforts aimed at redefining the organizational and disciplinary structures within which this research is pursued.

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