

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

by

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- 1. Research puzzle; explaining the central role of UCSF in the birth of the biotech industry in the SF region**
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Research puzzle

Historical context of birth and growth of San Francisco biotech cluster

- Up to 1976 biological sciences played a marginal role in the drug discovery process within pharmaceutical industry; biological sciences were considered to be too underdeveloped to shed light of practical value at the molecular level on human biology in general and on the drug discovery process in particular
- Assumptions about limited role biological sciences had to play in pharmaceutical industry were proven wrong by Herbert Boyer who founded Genentech in 1976 with the venture capitalist Robert Swanson who used insights from different biological disciplines to discover new drugs
- Development of SF biotech firms has remained closely intertwined with academic research inside universities as product innovation in biotech industry is driven by basic research in biomedical sciences
- San Francisco houses up to the present day the largest and most successful cluster of biotech firms in the world

Three SF research universities interesting case studies to help better understand how universities support innovation in high-tech industries

Berkeley, Stanford and UCSF biochemistry departments, in which key technologies were developed for biotech industry, of roughly equal academic standing

	Berkeley	Stanford	UCSF
Nr. of publications	54	53	84
Average nr. of citations	250.5	153.5	78.3
Median nr. of citations	48.5	51	44.5

Source: ISI Science Citation Index data on three biochemistry departments for 1975

Also, close proximity to Silicon Valley provided scientists roughly equal access to specialized services for entrepreneurial firms (e.g. venture capital, legal services)

Although at first sight scientists of three SF biochemistry departments equally well positioned to benefit of commercial opportunities of biotechnology during 1970s, the key role UCSF scientists played in the biotech industry stands out:

- First biotech firm, Genentech, spun-off from UCSF in 1976; also other still independent therapeutic biotech firms from the early period of the San Francisco biotech industry are UCSF spin-offs
- Up to present day 6 out of top 10 biotech firms in market cap directly or indirectly linked to UCSF; three linked to Berkeley; one linked to Stanford

Focus on organization of research rather than on technology transfer to explain central role UCSF scientists played in early growth biotech industry

Existing literature emphasizing role of tech transfer infrastructures in supporting firm formation around universities would have predicted Stanford and not UCSF to have been driving force behind formation of biotech industry

- **Stanford developed foundations for Silicon Valley cluster from 1950s; had build up entrepreneurial culture, tech transfer expertise and infrastructure (OTL, science parks, industrial affiliate programs, etc.) by the mid-1970s; UCSF had no technology licensing organization on its campus up to 1996 and no experience with handling industry relationship at time of formation of biotech industry**

Literature on corporate spin-off firms suggests that success of start-up firms largely determined by prior experiences of entrepreneurs in dealing with key organizational challenges

- **Klepper (2001, 2002) and others show that organizational capabilities of firms (i.e. which technologies does a firms develop? How successful is a firm in dealing with particular organizational challenges) are largely shaped by founders' experiences at 'parent firms'.**

Which are key challenges academic entrepreneurs are confronted with when they spin-off a firm and build up a commercial research organization?

Key challenges for academic entrepreneurs in organizing commercial research

Scientist entrepreneurs likely familiar with many challenges related to organizing research inside science-based spin-offs (i.e. building departments in different disciplines, tying research to academic communities); however, also challenges with which scientist entrepreneurs are not necessarily familiar with;

	University	Science-based firm
End product	Scientific publication	A useful innovation
Type of research problem	Single 'interesting' research problem, which fits in a disciplinary research agenda	A practically relevant problem; Complex product driven research projects consisting of a set of interrelated research problems
Disciplinary basis of research	Mono-disciplinary; disciplinary affiliation determines type of research problem scientists investigate and how they solve it	Multidisciplinary; complex nature of therapeutic research project requires interdisciplinary project teams in which different approaches are represented
Level of coordination among scientists	Scientists can work largely independent	Problems on path towards innovation interdependent and unpredictable; high level of coordination required among scientists/across departments

Quotation Herbert Heyneker (2004), first Genentech scientist on differences between conducting science in firms and universities

“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.”

So how did prior experiences position UCSF biochemists rather than Berkeley or Stanford biochemists so well to deal with new challenges of organizing therapeutic product development research during the 1970s?

Organization biochemistry departments Berkeley, Stanford and UCSF during 1970s

UC Berkeley biochemistry department

- UC Berkeley most forward looking university in Bay Area; Was first to create a freestanding biochemistry department in 1948, recognizing opportunities for understanding better human health at the sub-cellular level
- University attracted star scientist Wendell Stanley from Rockefeller Univ. just after World War II to unify biochemistry research at Berkeley
- However, Wendell Stanley was a divisive figure, proved unsuccessful in uniting biochemists from various departments in one new department at Berkeley
- Eventually, Stanley resigned due to in-fighting among biologists at Berkeley and biochemistry department was split into two separate departments, the Department of Molecular Biology and the Department of Biochemistry, which operated in isolation from each other and other more clinically oriented and integrative biology departments
- Attempts to bring together biologists interested in biology at the sub-cellular level proved counterproductive; strong divisions among various biological departments lasted until the early 1990s.

Edward Penhoet, Biochemistry Professor during the 1970s on department's relationship to Molecular Biology Department

“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.”

Though some individual labs world renowned in particular subfields, during the 1970s knowledge and skills to solve more complex 'human biology' problems dispersed across various departments, in between which there was animosity and little interaction

Stanford University Biochemistry Department

- Stanford Biochemistry Department founded in 1959; Fred Terman, recruited Arthur Kornberg from the Washington University School of Medicine, St Louis to lead the new department in the medical school, which was moved from SF to Palo Alto to bring clinical practice of medical school closer to basic research departments
- Arthur Kornberg brought his whole lab to Stanford from St Louis, and turned the Stanford biochemistry department into a world renowned department
- Familial atmosphere characteristic for the department; all resources were shared and faculty was conducting research on an equal footing
- Kornberg organized department around a common research subject 'DNA' and a common research approach to uncover molecular pathways, the traditional 'enzymatic approach'
- Kornberg very concerned about keeping research in department purely biochemical and separate from other departments, in particular applied clinical departments of the medical school; Biochemistry Department was an elite department with two Nobel laureates but very closed towards faculty of other departments at Stanford

Quotation Arthur Kornberg (1998) on biochemistry department's ties to clinical departments within Stanford's medical school

“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.”

During 1970s Stanford biochemistry department world renowned; However, due to department's isolation from other medical school departments, research was remote from clinical concerns and different approaches required to solve complex human biology problems were dispersed across departments

UCSF Biochemistry and Biophysics Department

- Rapid decline in rankings of UCSF Medical school during 1960s because of UCSF's failure to recognize importance of basic research; in the end, UC administration intervened
- UCSF managed to attract star scientist, Bill Rutter from the U. of Washington, Seattle to lead the UCSF Biochemistry and Biophysics Department in 1969
- In order to attract Bill Rutter, UCSF offered 20 FTEs and a significant say in the organization of the different departments within the medical school
- Bill Rutter accepted because UCSF offer presented an opportunity "to make an onslaught on human biology"; previously limitations to biochemistry approach limited biochemists to the study of more simple organisms such as the E.Coli bacteria
- Main strategy to achieve this goal was to bring together scientists using different disciplinary approaches who were willing to work together across disciplinary boundaries to solve complex "human biology" problems.
- Bill Rutter's arrival constituted the beginning of a new era at UCSF

Quotation William Rutter (1998) on accepting offer to join UCSF

“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 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.”

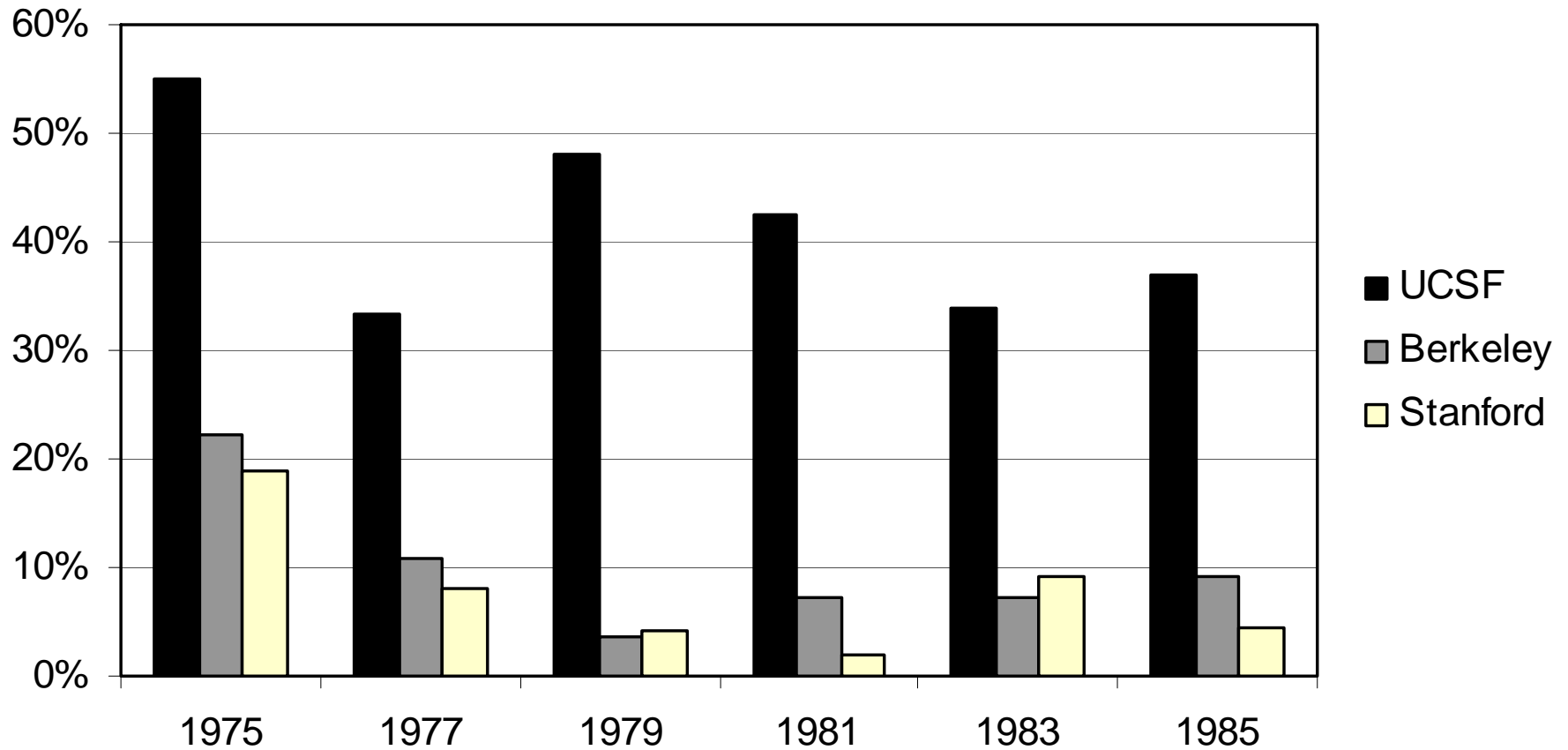
During the 1970s, research at UCSF dramatically improved. Around the biochemistry department, an interdepartmental network of faculty was recruited with a common research interest in complex human biology problems; it was this department from which in 1976 the biotech industry emerged

**Linking comparative advantages of academic entrepreneurs to
scientific “parent organizations”**

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; Isolated laboratories; little coordination individual labs	Familial and many collaborative ties among various labs	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 labs of other departments	Interdepartmental collaborations encouraged and "fit" in interdepartmental networks key in faculty recruitment	Many collaborative ties as therapeutic development requires input from a wide range of disciplines

Percentage of publications by faculty in biochemistry departments in major scientific journals which involved interdepartmental collaborations



Scientists at UCSF were embedded in comparatively interdisciplinary research networks, on which they could rely when spinning off firms

Illustrating the impact of the founding environment on the development of three SF biotech firms of the late 1970s and early 1980s

	Genentech (UCSF)	Chiron (Berkeley/UCSF)	DNAX (Stanford)
Early product focus	Closely tied to research projects carried out in UCSF founder's laboratory	Mainly research projects transferred from UCSF founder's laboratory	Initial research project transferred from Massachusetts General Hospital
Recruitment	Reliance on extensive UCSF networks	Reliance on extensive UCSF networks	Limited networks; reliance on SAB for recruitment of scientists from outside founders' discipline
Scientific culture	Product oriented	Product oriented	Research oriented
Current status	Currently operates as an integrated pharmaceutical company	Currently operates as an integrated pharmaceutical company	Currently operates as a research institute

Organizational environment at UCSF positioned scientists in a comparatively advantageous position in building up commercial research organizations

Reflections and final remarks

Implications for our understanding of how universities support the formation and development of new science-based industries

At the micro-level, the findings of this study highlight the importance of interdisciplinary research; value of creating communities within universities of scholars with different disciplinary backgrounds in exploring new research fields of practical relevance.

At the macro-level, the findings of this study highlight the importance of creating space for organizational experimentation within academic research systems and pluralism