Making Money from Microbes

Finance and the California Biotechnology Industry

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Abstract

The California biotechnology industry is widely acknowledged as the harbinger of the emerging biotechnology industry, both within the United States and internationally. This paper examines the financial status of the industry, revealing both its similarities to the whole U.S. biotechnology industry and its distinctiveness. We investigate the dynamics of the industry's financing pattern. Despite the substantial achievements of the California biotechnology industry, the majority of firms are not yet making profits and many are now being squeezed financially, with the financial market for biotechnology having become significantly more stringent recently. These factors are causing the industry to restructure in a number of ways, including changes in product lines, organizational patterns, marketing strategies and financing methods. The factor most at risk in the development of the California biotechnology industry is not its survival or importance, but California's own stake in it. It is the pattern of control and ownership which is likely to undergo the most significant changes.

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Table of Contents

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1. Introduction

"Biotechnology" is a new word associated with a set of techniques based upon the application of modern biological science. When biotechnology is defined in its broadest sense, as practical or industrial processes that involve biological systems, it is as old as cheese making, brewing, composting or pickling. Scientific advances within the last two decades, however, have led to the development of some new biotechnologies which present potentially radical changes in the scope for artificial manipulation of biological systems. It is this particular set of modern biotechnologies which has generated the recent flurry of commercial experiments more popularly known as "biotechnology".[22]

Modern biotechnology draws upon at least three distinct fields of scientific and technical endeavor: recombinant DNA technology (often known as "genetic engineering"), cell culture technology (or, in vitro cell manipulation technology), and

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[22] Some useful introductions to the science, technology and industrial context of this field include: "Biotechnology", Special Survey published in *The Economist* (April 30, 1988); S. Olsen, *Biotechnology: An Industry Comes of Age* (Washington, D.C.: National Academy Press, 1986); M. A. Levin, et al., *Applied Genetic Engineering: Future Trends and Problems* (Park Ridge, N.J.: Noyes Publications, 1983); J. L. Glick, "The Industrial Impact of the Biological Revolution", *Technology in Society*, 4 (1982), 283-293; S. Prentis, *Biotechnology: A New Industrial Revolution* (New York: George Brazillier,1984); J. Elkington, *The Gene Factory: Inside the Genetic and Biotechnology Business Revolution* (New York: Carrol and Graff Publishers, 1985).

monoclonal antibody technology.[23] Some commentators also include protein engineering, microbial fermentation of enzymes, and "bioinformatics" (the convergence of biotechnology and information technology).[24]

While much debate exists over what exactly constitutes "biotechnology", in this paper we will use the term to refer to the narrower spectrum of technologies which have been derived from modern biological science within the last 20 years or so and which are based loosely upon the fields of endeavor just listed.

2. Biotechnology in the Marketplace

The modern biotechnology industry has only recently emerged and exhibits much volatility as a new industrial form, but it is nevertheless substantial. California is widely acknowledged as the world leader in research, industrial and medical biotechnology.[25] Large investments have been injected into California's biotechnology firms in the expectation of huge global market opportunities. The market size of the biotechnology industry has been measured in various ways. The potential size of the market for all new biotechnology products by the turn of the century has been estimated at over $1.5 trillion per year.[26] The United States biotechnology industry is estimated (1988) to have accumulated over $8 billion in

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[23] W. F. Woodman, M.C. Shelley II and B.J. Reichel, *Biotechnology and the Research Enterprise: A Guide to the Literature* (Ames: Iowa State University Press, 1989).

[24] P. Daly, *The Biotechnology Business: A Strategic Analysis* (London: Frances Pinter, 1985).

[25] E. J. Blakely, *The Economic Development Potentials of California's Biotech Industry*, Working Paper No. 498, Institute of Urban and Regional Development, University of California, Berkeley, April 1989; California Legislature, Assembly Committee on Economic Development and New Technologies, *The Future of Biotechnology Industries in California*, Summary of Hearings, Toland Hall, University of California, San Francisco, June 28, 1984. Cf., ABAG, *Biotechnology in the San Francisco Bay Area* (Oakland, CA: Association of Bay Area Governments, September 1988).

[26] One trillion dollars equals $1,000,000,000. MITI estimate (see p. 60 of "Education and Information: The Japanese Experience", by Y. Mori, in *Industrial Biotechnology in Europe: Issues for Public Policy*, ed. D. Davies [London: Frances Pinter, 1986], p. 58-64).

assets, with about $3 billion of this accounted for by California firms.[27] The total annual revenue of biotechnology firms (1988) is estimated to be about $3 billion in California and almost $9 billion for the nation.[28]

While the industry is substantial, the vast majority of firms are still in the early stages of product development and along with their counterparts in other states most California firms are still not making a profit. The biotechnology industry has attracted great interest from the financial community and constitutes a significant business asset for California; yet it's novelty and it's failure to generate net income as yet makes it a financially problematic industry.[29] Biotechnology firms are increasingly facing difficulties in raising finances to support the expansion plans required to achieve long term profits.[30]

3. Financing the California Biotechnology Industry

The aim of this paper is to examine the financial status of California's biotechnology industry. We investigate the dynamics of the industry's financing pattern and the role various financial strategies have on the emerging shape of the industry. The data reported are based on information obtained in a telephone survey of the C.E.O.s of California's biotechnology firms conducted by the Biotechnology Industry Research Group (BIRG), of the University of California at Berkeley, combined with other reports from leading financial and consulting firms.

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[27] BIRG estimate based upon data from the Arthur Young High Technology Group. See BIRG file: Biotechnology Assets Estimates (6/10/89).

[28] BIRG estimates based upon data from BIRG, the Association of Bay Area Governments (ABAG) and the Arthur Young High Technology Group. See BIRG file: Biotechnology Revenue Estimates (6/10/89).

[29] J. J. Curran, "Will Biotech's Boom Go Bust?", *Fortune* (July 6, 1987), 75-76; S. Yanchinski, "Boom and Bust in the Bio Business", *New Scientist* (January 22,1987), 44-47; D. Shapley, "Silver Cloud with a Leaden Lining", *Nature*, 302 (March 10, 1983), 101; W. P. Patterson, "Where are the Biotech Products?", *Industry Week* (February 7, 1983), 48-55.

[30] D. Dickson, "Clouds on Biotechnology Horizon: Companies Run Short of Sales and Capital", *Nature*, 296 (March 4, 1982), 3.

Unless otherwise indicated data reported in this paper come from the BIRG survey.[31]

The biotechnology industry is a special industry with special financial requirements. These characteristics shape both the industry's needs for funds and the attitudes of the investment community towards biotechnology firms.

Biotechnology and bioscience are relatively new research fields accompanied by rapid developments in theory and technique. Many of the most exciting biotechnology developments require enormous cross disciplinary research efforts which lack the predictability and simplicity of various more established research fields.[32]

There is generally a very long time period required for the commercializing of biotechnology products. As a result investors are forced to adopt a long term perspective on their investments. The whole process of developing a product, testing it and taking it through regulatory reviews can a decade or more. The industry is research intensive. The commercialization chain is complicated and made uncertain by the perplexing web of regulatory processes faced by firms.[33]

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[31] The survey instrument was administered for BIRG by the Survey Research Center of the University of California at Berkeley, and involved a 20 minute telephone interview of C.E.O.s by trained professional interviewers. The population of firms was identified from *Bioscan*, the California Industrial Biotechnology Association directories, and other sources. One hundred and forty-five firms were listed in California, but BIRG was able to confirm only 114 as being in operation at the time the survey was conducted. Seventy two firms participated in the survey (response rate of 63%). Respondents were asked questions about the size of their firm, all of their locations, the strengths and weaknesses of California as a location for their firm, human resource requirements, and related matters. All respondents were assured anonymity.

[32] For a perspective on the complexity of the biotechnology industry, and the special skills required by managers to deal with this, see: M. Kenney, *Biotechnology: The University-Industrial Complex* (New Haven: Yale University Press, 1986); J. L. Fox, "Genetic Engineering Industry Has Growing Pains", *Chemical and Engineering News* (April 6, 1981), 17-22; J. Fiksel, ed., *Biotechnology Risk Assessment* (New York: Pergamon Press, 1986).

[33] C. Norman, "Another Biotechnology Company Bites the Dust", *Science*, 217 (September 10, 1982), 1016-1017; "Bio Backlash", *New Scientist* (April 17, 1986), 14; "Biotechnology's Hype and Hubris", *The Economist* (April 19, 1986), 96-97.

Biotechnology research is concentrated in the private sector to a greater degree than in most basic scientific arenas.[34] Financing research is essential to the biotechnology industry because selling their ideas is often a major source of revenue for firms, and property rights over scientific knowledge are frequently their main product. Patents are therefore of critical importance. Patents as products produce problems because of the direct complications involved in obtaining patent approvals, but further problems arise from disputes between companies over the validity of patents and the protection of intellectual property after the gaining of patent rights.[35]

Uncertainty is also created for firms because of competition in the market. A biotechnology firm may make substantial investments in developing a new biotechnology product with its associated production method, only to discover that a cheaper and superior alternative may be released by another company prior to production. This creates a continuing climate of uncertainty which is reflected in financial markets. Nonetheless, biotechnology in almost any form remains the darling of the Wall Street analysts, who continue to make buoyant pronouncements regarding the financial potentials of the industry.

4. The Importance of Finance to California Biotechnology Firms

The financial experiences of the California biotechnology industry represent some distinctive experiments in the financing of new ventures, and therefore contain

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[34] Special attention has been paid by Frederick Buttel and colleagues to the ways in which biotechnology is changing the public/private balance in science (see: F. H. Buttel, "Biotechnology and Agricultural Research Policy: Emergent Issues", in *New Directions for Agriculture and Agricultural Research*, ed. K. A. Dahlberg (Totowa, N. J.: Rowman and Allanheld, 1986), 312- 347; F. H. Buttel, J. Tadlock Cowan, M. Kenny, and J. Kloppenberg Jr., "Biotechnology in Agriculture: The Political Economy of Agribusiness Reorganization and Industry-University Relationships", *Research in Rural Sociology and Development*, 1 [1984], 315-348).

[35] D. Webber, "Patent Battles Spurt in USA", *Chemistry and Industry* (June 1, 1987), 377-378; D. Korn, "Note: Patent and Trade Secret Protections in University-Industry Research Relationships in Biotechnology", *Harvard Journal on Legislation*, 24 (1987), 191- 238.

some interesting lessons which may be of relevance to other industries and regions. The financial pattern of the biotechnology industry is not static. It has undergone changes which are linked with a number of other changes in the industry and its context, particularly an evolution in the organizational structure of the industry. We will discuss this in more detail in later sections.

The biotechnology industry is driven by technology and research factors rather than market factors to a greater degree than for most industries. This feature of the California industry seems more pronounced than for the American biotechnology industry as a whole. Nevertheless, financial factors have shaped the California industry's development and appear to be growing in influence over time. Some industry observers argue, furthermore, that the types of financing available are the key influence of the nature of ventures in the biotechnology industry.[36]

The importance of finance is reflected by the degree to which firms express concern over factors which affect the cost of operation. For example, 72% of California firms consider the cost of industrial space to be an important determinant of the location of their main research and development facility, and 58% of firms consider wage rates to be an important determinant of location. 80% of firms consider cost of industrial space in decisions on the location of manufacturing facilities, and 71% of all California firms consider the high cost of industrial space in the state to make California disadvantageous for manufacturing activities. Firms are worried about the financial cost of their activities. While finance clearly is important to the industry, its importance ought to be measured against the importance of other factors affecting the behavior of biotechnology firms.

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[36] E.g., G. S. Burrill, "Biotech Business Strategy: The Key is Financing", *Bio/Technology*, 4 (October 1986), 857-860.

The cost of industrial space and wage rates are both important determinants of biotechnology firms location decisions, but they are not critical. The most important factor taken into account by firms in deciding where to locate their main R & D facilities is the availability of qualified workers (89% of firms consider this to be the case), closely followed by proximity to research universities (80%). The cost of industrial space (72%) and wage rates (58%) rank third and fourth respectively.

Less than 6% of California firms consider proximity to venture capital or financial institutions to be a very important determinant of location decisions, and only 17% consider it to be somewhat important. This may represent the possibility that finance is readily available to California biotechnology firms irrespective of location, but it may also reflect the fact that companies tend to be more concerned about human and informational factors in location decisions than finance. Finance is obviously more mobile than human capital.

Deeper insights into the structure of the biotechnology industry may be gained by reconsidering these data on the importance of cost-related factors in biotechnology decision-making according to the market orientation, size and geographical location of firms. We will investigate each of these other dimensions of the above data in later sections.

5. The Argument: Financial Status of the Industry

The California biotechnology industry exhibits distinctive financial characteristics compared with the industry elsewhere in the United States. Many of the trends apparent at the national level are also apparent in California, sometimes pre-eminently so, but there are also important differences. The California industry is large and quite diverse, with a wide variety of sizes, market orientations and organizational forms apparent among its firms. The state's biotechnology industry

exhibits the extremes of large, well established and highly competitive market leaders, as well as the problems of small, relatively immature and unstable firms; and there is considerable geographical variance among the firms. We will argue below that that California biotechnology firms tend, on average, to be more substantial financially, but more costly to operate; they are also characterized by a financial structure which heavily emphasizes research and development, revealing an investment pattern aimed at at long term returns rather than short term profits. California biotechnology firms have incurred heavier losses than the firms from other states, but they nevertheless appear to offer, on average, very good long term prospects for investors.

The vast majority of California biotechnology firms are involved in the early stages of product development and only the minority are making a profit. Operating finance tends to come from capital raised rather than sales revenues. The same pattern holds true for the industry nationwide. There are some well known exceptions to the rule, such as Genentech, which has been making significant profits, or Cetus, which is heavily capitalized and appears likely to become profitable in the near future, but these are the exceptions.[37] While it may have been relatively easy to raise large amounts of cash for biotechnology ventures one decade ago, reports of industry shakeouts, waning investment and dipping cash reserves for firms are now commonplace.[38]

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[37] A. Klausner, "Corporate Strategies: And Then There Were Two", *Bio/Technology*, 3 (July 1985), 605-612; G. Bylinsky, "The Man Who Could Make Biotechnology Profitable - At Last", *Fortune* (January 5, 1987), 101; W. Boly, "The Gene Merchants", *California* (September 1982), 76-79, 170-179; D. Gilbert, Montgomery Securities, cited in *Biotechnology Newswatch* (April 17, 1989), 7.

[38] M. Crawford, "Biotech Market Changing Rapidly", *Science*, 231 (January 3, 1986), 12-14.

Table 1
Composite Revenue and Expenses
California and U.S. Biotechnology Firms

	California 1986		U.S. 1985		U.S. 1986		U.S. 1987	
	$000	%	$000	%	$000	%	$000	%
Revenue								
Product sales	$10,861	59%	$5,773	60%	$9,508	72%	$10,123	72%
Contract & collaborative research	$5,529	30%	$2,651	27%	$2,500	19%	$2,571	18%
Royalties & license fees	$670	4%	$122	1%	$265	2%	$187	1%
Interest	$1,084	6%	$698	7%	$627	5%	$778	6%
Other	$355	2%	$441	5%	$347	3%	$474	3%
Total revenue	**$18,499**	100%	**$9,685**	100%	**$13,247**	100%	**$14,133**	100%
Costs and expenses								
Cost of product sales	$4,165	15%	$3,199	30%	$5,047	30%	$5,071	33%
Marketing, general & admin.	$5,742	20%	$3,092	29%	$4,502	26%	$4,814	31%
Research and development	$7,078	25%	$3,839	36%	$3,542	21%	$4,399	29%
Interest	$182	1%	$280	3%	$234	1%	$354	2%
Purchase of R&D part'ship etc.	$11,307	39%			$3,502	21%	$265	2%
Other	$153	1%	$328	3%	$247	1%	$521	3%
Total costs and expenses	**$28,627**	100%	**$10,738**	100%	**$17,074**	100%	**$15,424**	100%
Income before taxes	**($10,128)**	**(55%)**	**($1,053)**	**(11%)**	**($3,827)**	**(29%)**	**($1,291)**	**(9%)**
Tax & extraordinary transfers	$727	4%	$153	2%	$272	2%	$386	3%
Net income	**($10,855)**	**(59%)**	**($1,206)**	**(12%)**	**($4,099)**	**(31%)**	**($1,677)**	**(12%)**

Source: Arthur Young, 1986, 1987, 1988; collated by BIRG.

Table 1 provides a composite statement of revenue and expenses for a sample of biotechnology industry firms from California and the United States as a whole.[39] It shows that during 1986, the year for which both California and U.S. figures are available, California firms incurred a mean loss of 59% of total revenue, while the equivalent loss for the U.S. industry as a whole was 29% of total revenue.

[39] The exact sources for Table 1 and 2 are: G. Steven Burrill with the Arthur Young High Technology Group: *Biotech 86: At the Crossroad*(San Francisco: Arthur Young, 1986), for 1985 data; *Biotech 88: Into the Marketplace* (San Francisco: Arthur Young, 1987), for 1986 data; and, *Biotech 89: Commercialization* (New York: Mary Ann Liebert, Inc. Publishers, 1988), for 1987 data. The 1986 figures for California were taken from a special extract from Arthur Young's "Biotech 88" data base provided for BIRG by the Arthur Young High Technology Group.

It is important not to place too much weight on "bottom line" figures, however, when evaluating the biotechnology industry. It is an immature and highly research-intensive industry, and it would be inappropriate to expect sizable profits at this stage. This appears to be recognized by many business analysts now. In fact, stock market values of biotechnology firms appear to be based more on marketing promotions, images and media razzamattaz than on actual product performance.[40] The fluctuations in net income for the national industry from 1985 to 1987 (Table 1), show that little significance ought to be given to the balance of revenue and expenses in any year. Long term trends provide more important evidence; but the youth of the industry makes the examination of such trends difficult and, in any case, comprehensive time-series data are not available.

The long time frame normally required for the commercialization of biotechnology products creates special challenges in the area of financing.

The losses incurred by the industry may equally well be interpreted as a sign that the industry has confidence in its future, than as a sign that it is a commercial failure. For example, Table 1 shows that the mean expenditure by California firms during 1986 on the purchase of R & D partnerships ($11,307,000) was actually greater than their mean net loss ($10,855,000). California firms appear to have been making substantial investments in R & D facilities in the hope of long-term pay-offs. Had such investments not been made the California industry would have recorded a profit during 1986; this would presumably have been unwise from the perspective of long term profitability. The national industry, in contrast, would not have made a composite profit during 1986 were such investments not made; but it is important to recognize that the mean expenditure on R & D partnerships during 1986 was almost as large (85%) as the mean loss incurred.

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[40] R. A. Bock, "Biotech Business Strategy: The Importance of Hype", *Bio/Technology*, 4 (October 1986), 865-866.

A difference in the character of the California and U.S. national biotechnology industries is suggested by the differing importance of this kind of long-term investment. Purchase of R & D partnerships constituted the equivalent of 61% of total revenue for California firms, but only 26% for the industry aggregated at the national level. This figure reduces to less than 2% by 1987 at the national level.

Table 2 provides a composite balance sheet for the same sample of firms represented in Table 1. It reveals that despite the California biotechnology industry being relatively young, the mean level of assets in the industry's firms is quite substantial, and significantly larger than for the national industry.

Chart 1 is based upon the data in Table 2 and reveals some interesting differences between the U.S. and California biotechnology industries over a range of financial parameters.

Table 2
Composite Balance Sheet
California and U.S. Biotechnology Firms

	California 1986		**U.S. 1985**		**U.S. 1986**		**U.S. 1987**	
	$000	% assets	$000	% assets	$000	% assets	$000	% assets
Total current assets	*26,526*	*65%*	*10,289*	*68%*	*17,524*	*70%*	*18,917*	*65%*
Non-current assets								
Tangible assets	9,469	23%	3,232	21%	5,089	20%	6,194	21%
Intellectual property, goodwill and other intangibles	2,839	7%	435	3%	1,313	5%	1,185	4%
Investments in part'ships etc.	456	1%	124	1%	307	1%	123	0%
Other non-current assets	1,208	3%	1,080	7%	854	3%	2,614	9%
Total non-current assets	*13,972*	*35%*	*4,871*	*32%*	*7,563*	*30%*	*10,116*	*35%*
Total assets	**40,498**	100%	**15,160**	100%	**25,087**	100%	**29,033**	100%
Total current liabilities	*4,123*	*10%*	*3,067*	*20%*	*3,020*	*12%*	*4,192*	*14%*
Non-current liabilities								
Long term debt	2,216	5%	1,496	10%	2,365	9%	4,534	16%
Deferred revenue	174	0%	34	0%	100	0%	121	0%
Other non-current liabilities	1,512	4%	373	2%	1,087	4%	1,275	4%
Total non-current liabilities	*3,902*	*10%*	*1,903*	*13%*	*3,552*	*14%*	*5,930*	*20%*
Total liabilities	**8,025**	**20%**	**4,970**	**33%**	**6,572**	**26%**	**10,122**	**35%**
Shareholders' equity	**32,473**	**80%**	**10,189**	**67%**	**18,515**	**74%**	**18,911**	**65%**
Debt/equity ratio	**25%**		**49%**		**35%**		**54%**	

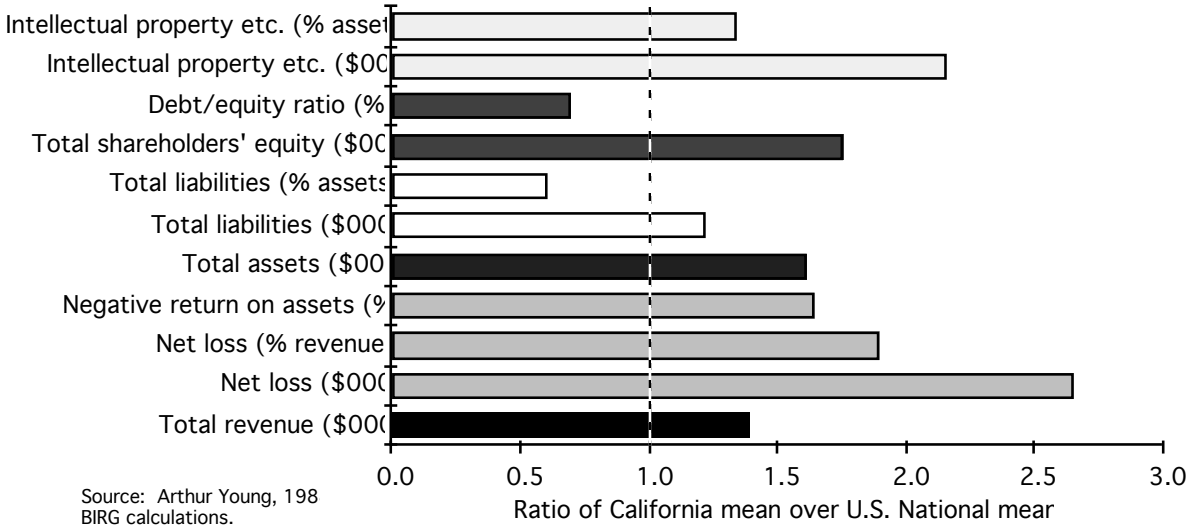
Source: Arthur Young, 1986, 1987, 1988; collated by BIRG.

California biotechnology firms, while on average earning 1.4 times the revenues of firms nationwide, and exhibiting 1.6 times the asset base of firms nationwide, recorded a net loss about 2.6 times larger (in real dollars per firm) and 1.9 times larger (as a percentage of revenue). The negative return on assets (i.e., loss as a percentage of assets) for California firms was about 1.6 times larger than the figure for firms nationally. These figures portray California firms as being more substantial financially as well as more costly to operate.

The total liabilities accumulated by California firms are larger on average than those accumulated by firms in other states (1.22 times larger than the national

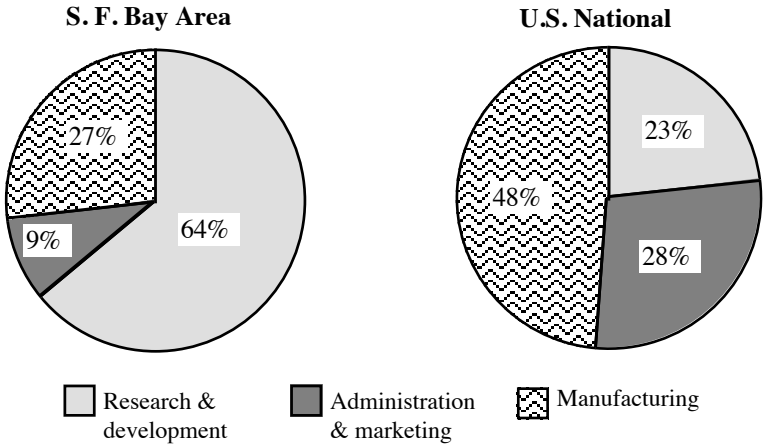
mean), yet California firms appear in a healthier position if liabilities are measured as a proportion of total assets (liabilities as a percentage of assets are about 1.65 times as large for the national industry as for the California industry). California firms also exhibit relatively high levels of shareholders equity (1.75 times the national average, in real dollars), which reflects a lower relative burden of long-term debt. Further, California firms have a relatively low debt/equity ratio (0.25 in 1986, which is only seven tenths the size of the mean debt/equity ratio for the national industry).

Chart 1
Relative performance of California and U.S. National biotec industries for a range of financial parameters, 198



Source: Arthur Young, 198
BIRG calculations.

Chart 2
Composition of biotechnology industry workforce



Sources: ABAG, 1988; Arthur Young, 1987.

In summary, California firms appear to have a relatively strong long-term financial footing, but exhibit relatively weak short term profitability. This may be interpreted, as suggested earlier, as a reflection of the stronger emphasis upon research in California firms. California firms in 1986 gained 30% of their revenue from contract and collaborative research (against 19% for the national industry) and allocated 64% of their expenditure to research and development related items (against 42% for the national industry).[41] This difference is further illustrated in Chart 2 where the California (San Francisco Bay Area) biotechnology industry is shown to have 64% of its workforce in research and development activities, while only 23% of the national biotechnology industry workforce is so located.

[41] "Research and development related items" includes direct R&D activities plus the purchase of R&D partnerships.

6. Financial Status by Market Orientation

The biotechnology industry is made up of a wide range of firms which serve a variety of markets and which are linked to a diversity of other industries. The financial characteristics of the firms vary between each of these sub-sectors within the industry. BIRG has grouped biotechnology firms into five types according to their market focus: diagnostics, therapeutics, agritech, suppliers and others.

Diagnostics firms are those human health care companies that design or develop products for a variety of tests for determining the presence of various health or disease states. *Therapeutics* firms are those pursuing products that require extensive clinical testing for human or animal use, and that cure or reduce the effects or incidence of disease. *Agritech* firms produce a large set of products for application in animal agriculture, plant agriculture, veterinary activities, the food/brewing industry, or for various environmental uses. *Suppliers* are those firms that produce specialized inputs for use in bioscience or biotechnology, such as biotechnology reagents, specialized biotechnology software or technical instruments for gene splicing. Some firms have been classified as *"other"* because they pursue some other type of application or because they deal with so many interrelated areas that they are difficult to classify.

The degree of concern which firms exhibit about cost factors in their operations varies between firms with different market orientations. These data were briefly examined earlier for the aggregate California biotechnology industry, but will now be re-examined, disaggregated by primary market/product type.

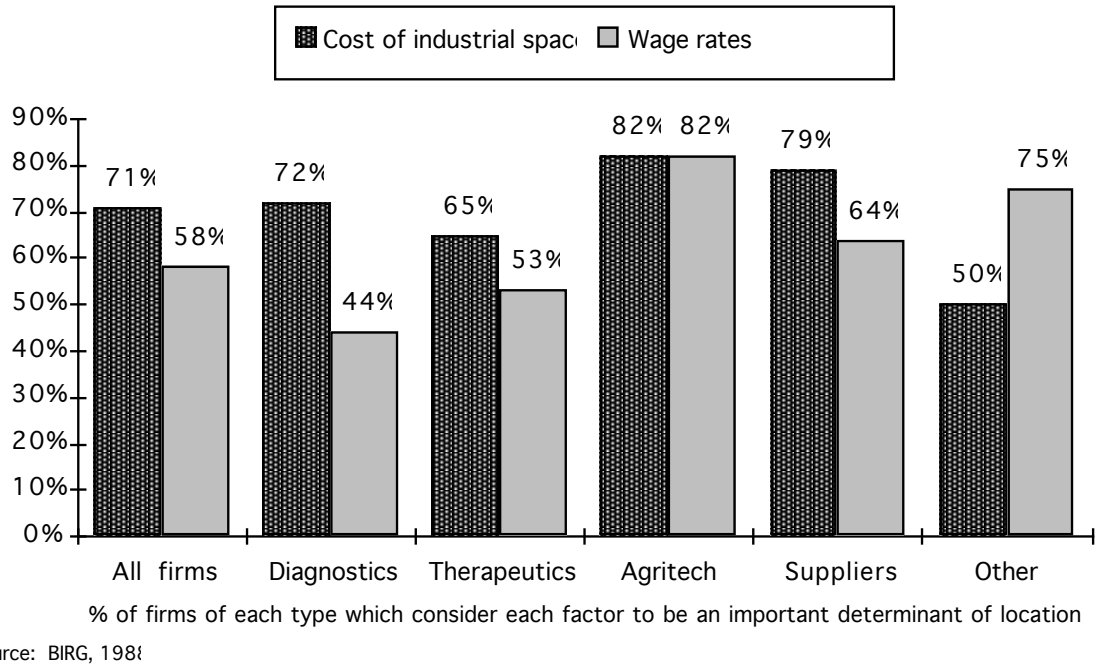
Table 3
Concern about cost factors among California biotechnology firms in different market segments, 1988

Cost factor	*% of firms of each type which consider each factor to be an important determinant of location decisions, 1988*					
	All firms	Diagnostics	Therapeutics	Agritech	Suppliers	Other
Cost of industrial space	71%	72%	65%	82%	79%	50%
Wage rates	58%	44%	53%	82%	64%	75%
Proximity to sources of finance	23%	24%	12%	27%	21%	50%
Local taxes	40%	28%	47%	36%	50%	50%
State taxes	40%	32%	41%	54%	43%	25%

Source: BIRG, 1988.

Table 3 lists the percentage of California biotechnology firms in each market

Chart 3
Concern about cost of industrial space and wages
California biotechnology firms in different market se



Source: BIRG, 198

segment which consider various cost-related factors to be important determinants of their location decisions. Proximity to venture capital or financial institutions is not

particularly important for firms of any type; and while concern about state and local taxation features more prominently, there does not appear to be any significant lessons to be drawn here about industry behavior in connection with taxation levels. Wage rates and the cost of industrial space do appear to be of special concern to firms, however, and the variations between firms of different market orientations are shown in Chart 3. Agritech firms and suppliers are the most affected by these two areas of concern about cost, suggesting that firms in these fields are further down the pathway towards regular manufacturing of their products than firms in other fields.

This conclusion is partly confirmed by Charts 4 and 5 which show suppliers to be the only category of firms, both nationally and in California, to be making composite profits. Agritech firms are shown in Chart 4 to be incurring a relatively small loss on average compared with the industry as a whole; Chart 5, however, shows this income-earning capacity of agritech firms to be less significant when measured against the asset base of the firms.

Chart 6 reveals that in actual dollars the average annual revenue of supplier firms is very high, except that in California (in contrast to the national industry) therapeutics firms have the highest average revenue earning performance. Chart 7 plots the average total assets of biotechnology firms by market orientation, revealing that at the national level, but especially in California, firms serving therapeutics market are the most substantial. Given that the annual revenue of therapeutics firms in California is already higher than that of both suppliers and agritech, we should conclude from these facts that therapeutics firms expect substantial long-term returns on their investments.

Chart 4
Net income (loss) by market orientation of firms
Comparison of California and U.S. National industry n

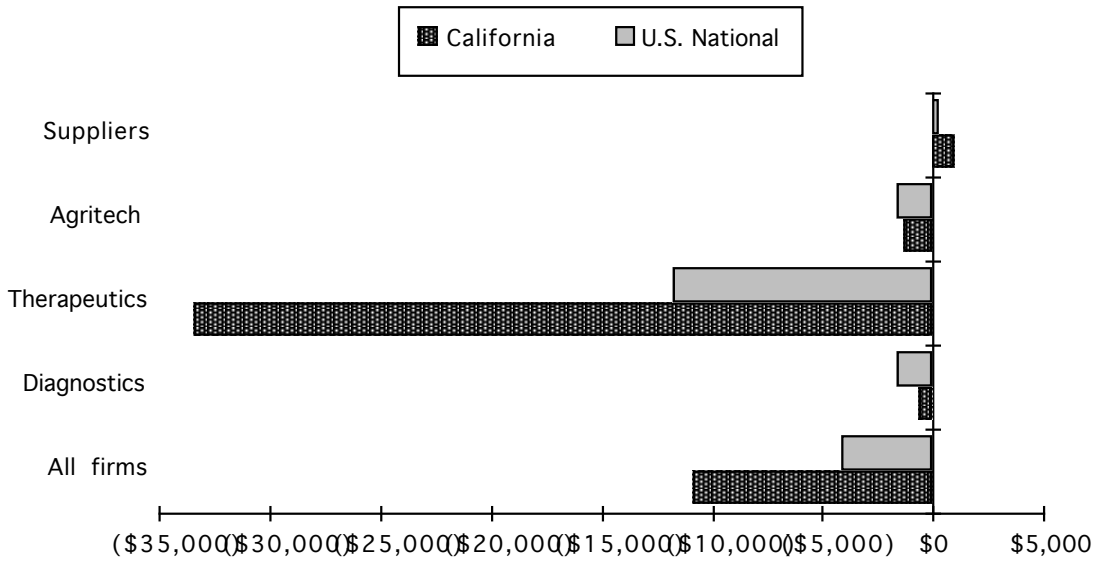
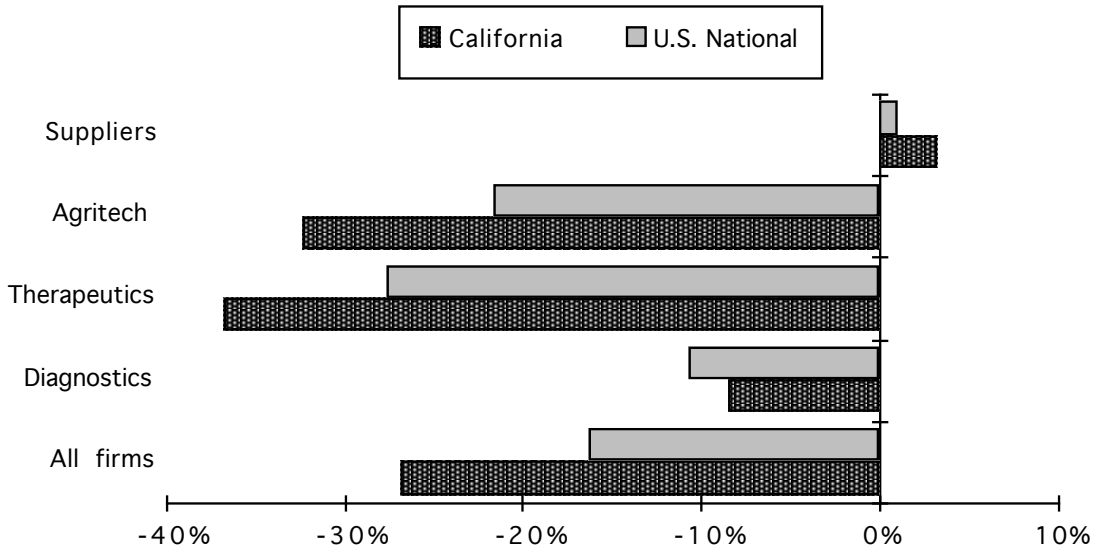


Chart 5
Return on assets by market orientation of fi
Comparison of California and U.S. National industry n



Source: Arthur Young, 1987.

Charts 4, 5, 6 and 7 together reveal a distinctive feature of the California

Chart 6
Total annual revenue by market orientation of firm
Comparison of California and U.S. National industry n

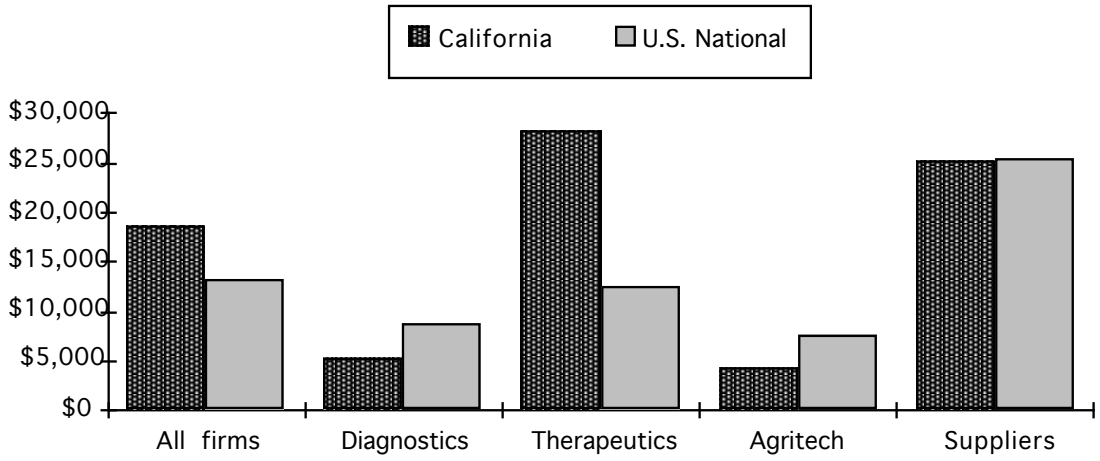
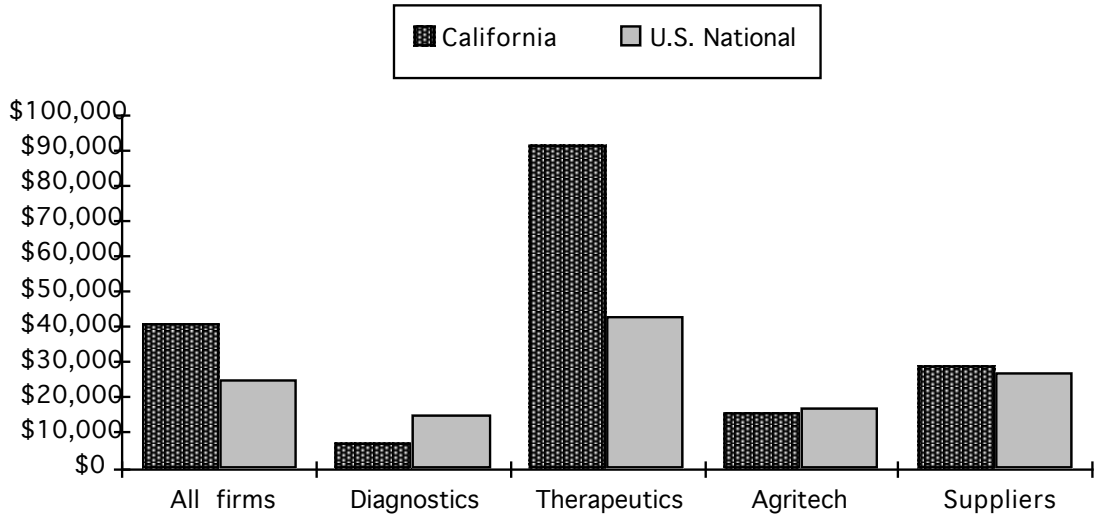
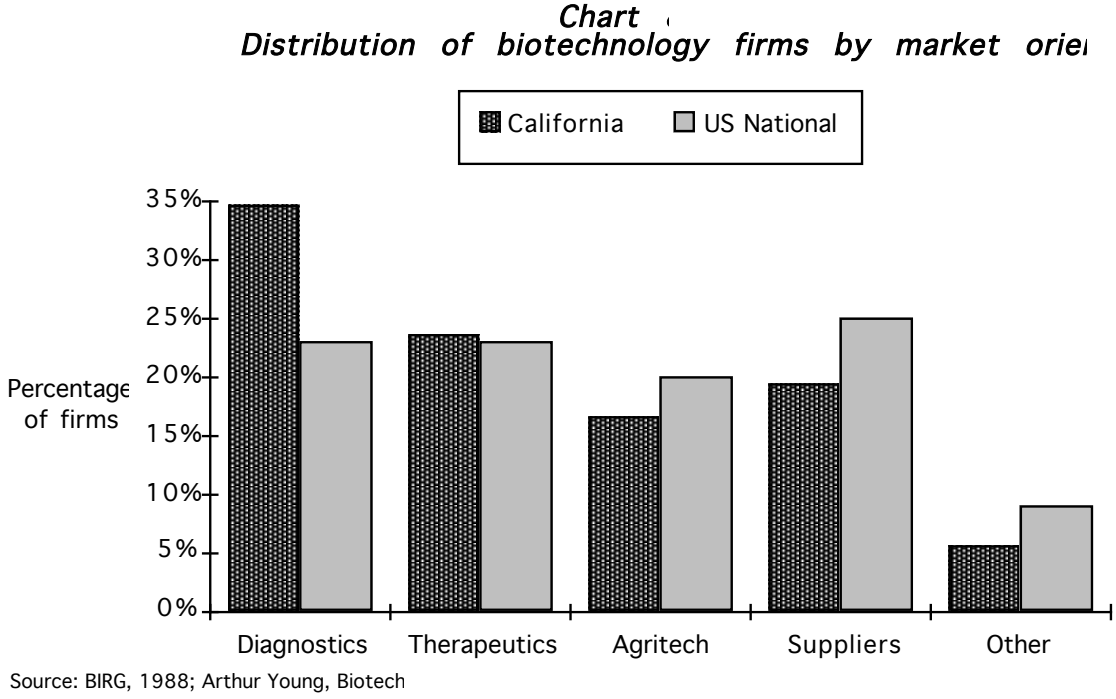


Chart 7
Total assets by market orientation of firms (
Comparison of California and U.S. National industry n



Source: Arthur Young 1987.

biotechnology industry to be its heavy emphasis on the market for the application of biotechnology in therapeutic pharmaceuticals. This is particularly interesting given the fact that, if market orientation is judged by the number of firms rather than by financial indicators, California firms place greater emphasis on diagnostics applications rather than therapeutics (see Chart 8).



Source: BIRG, 1988; Arthur Young, Biotech

Despite the importance normally attached to agriculture for the California economy, the state's biotechnology industry does not appear to place a particularly heavy emphasis on agricultural applications of biotechnology relative to national industry (this observation holds true for both the financial data and firm-population data).[42]

[42] There is evidence that, at least several years ago, investments in agricultural applications of biotechnology have declined relative to investments in health related and other applications throughout the United States (see J. R. Murray, "Patterns of Investment in Biotechnology", *Bio/Technology* [May 1983], 248-250).

7. Financial Status by Size of Firm

Biotechnology firms vary a great deal in size, from those small start-ups employing only several people, to the more established market leaders employing hundreds. The data below compare some financial characteristics of firms according to whether they are small (employing one to fifty people), medium-size (employing 51 to 135 people) or large (employing 136 or more people). According to BIRG estimates 58% of California biotechnology firms are small, 25% are medium-size and 17% are large, by these definitions.[43]

Table 4 contrasts the responses of firms of differing sizes to a question about which cost related factors are important determinants of their location decisions. The cost of industrial space is given the greatest significance by both small and large firms, the equivalent result across categories as that recorded in Table 3 for firms grouped by market orientation. Beyond this fact, however, there are significant differences between small and large firms. Whereas small firms consider wage rates to be the second most important determinant of location decisions, large firms consider this to be the least important of all. Small firms consider proximity to financial institutions and sources of venture capital to be the least significant determinant of location decisions, and while it is not a high-ranking determinant for large firms, 54% claim it to be an important determinant of their location decisions. Further, on all factors except wage rates, a higher percentage of large firms than

[43] We do not have definitive figures at this stage on the size distribution of biotechnology firms at the U.S. national level. In the national sample of firms included in Arthur Young's *Biotech 89* survey (representing the 1988 population of firms and 1987 finances), 49% were small, 24% were medium-size and 27% were large. The sample from which the financial data in this paper are derived (*Biotech 88*, representing the 1987 population of firms, and 1986 finances), consisted of 50% small firms, 27% medium-size firms and 23% large firms; the California sub-set contained 32.5% small firms, 32.5% medium-size firms and 35% large firms. BIRG's 1988 survey identified 17% of California biotechnology firms to be large (by the same definition adopted by Arthur Young). The sample of firms included in Arthur Young's annual survey, it may therefore be surmised, is biased by an over-representation of large firms.

small firms consider each factor to be an important determinant of location decisions.

These facts reveal that large firms tend to be more concerned about cost-related factors when making decisions about location. Presumably this means that large firms are relatively more concerned about cost factors in general than are smaller firms.

Table 4

Concern about cost factors amongst California biotechnology firms of different size, 1988

Cost factors	*% of firms of each size which consider each factor to be an important determinant of location decisions*	
	Small and Medium-size	Large
Cost of industrial space	73%	78%
Wage rates	34%	62%
Proximity to sources of finance	22%	54%
Local taxes	33%	70%
State taxes	34%	62%

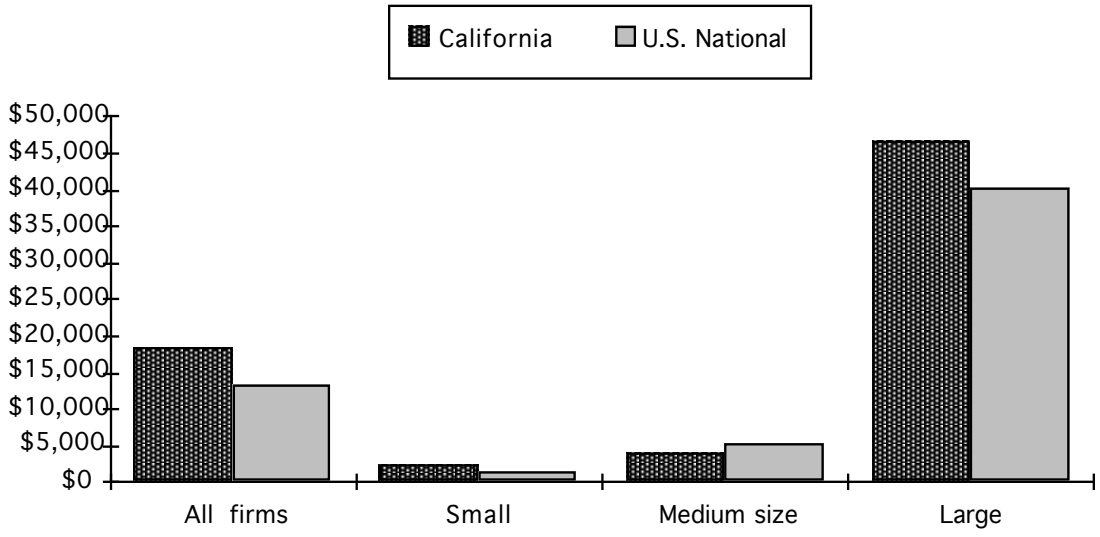
Source: BIRG, 1988.

The data in Table 4 suggest that large firms tend to be more advanced with regards to manufacturing than smaller firms, requiring major injections of capital to finance their operations. The relatively high concern about wage rates amongst smaller firms suggests a very labor intensive style of operation with the majority of attention being placed upon research, prototype development, custom-designed batch production, and heavy reliance upon human contributions. The notable concern about taxes and land/space costs among larger firms suggests a more sophisticated and capital intensive style of operation. This is in keeping with common sense expectations. The relatively high concern among larger firms about proximity to sources of finance suggests that as firms grow the nature of their

financial needs changes, demanding different kinds of financial services to those which were necessary at earlier stages.

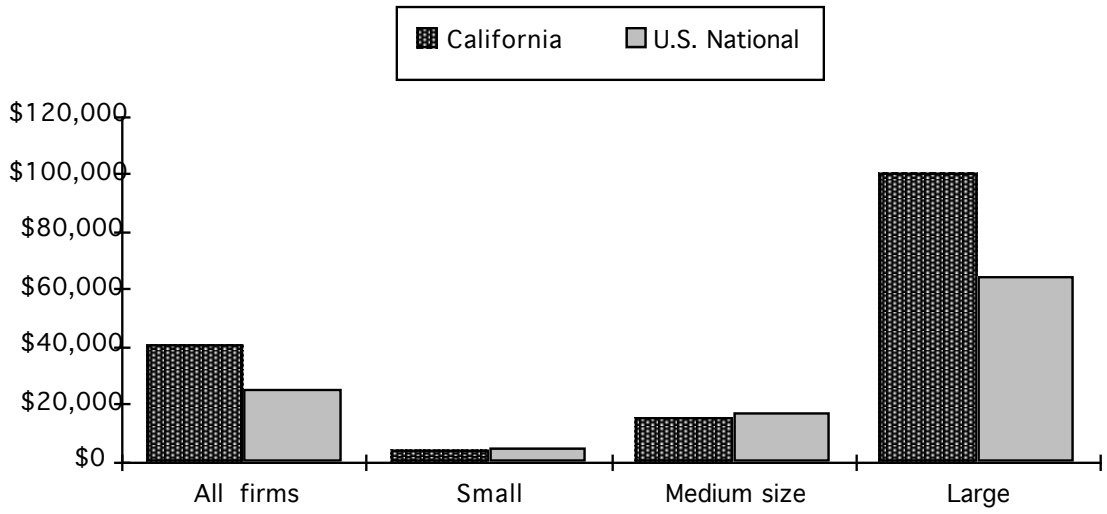
Despite the fact that large firms are in the minority they account for a sizable proportion of the revenue and assets of the biotechnology industry. As shown by Charts 9 and 10, the average asset base and annual revenue of large firms are significantly greater than those of the smaller firms. Large California biotechnology firms, furthermore, tend to be more substantial financially than their counterparts in other states.

Chart 9
Total annual revenue by size of firms ($000,
Comparison of California and U.S. National industry n



Source: Arthur Young, 19

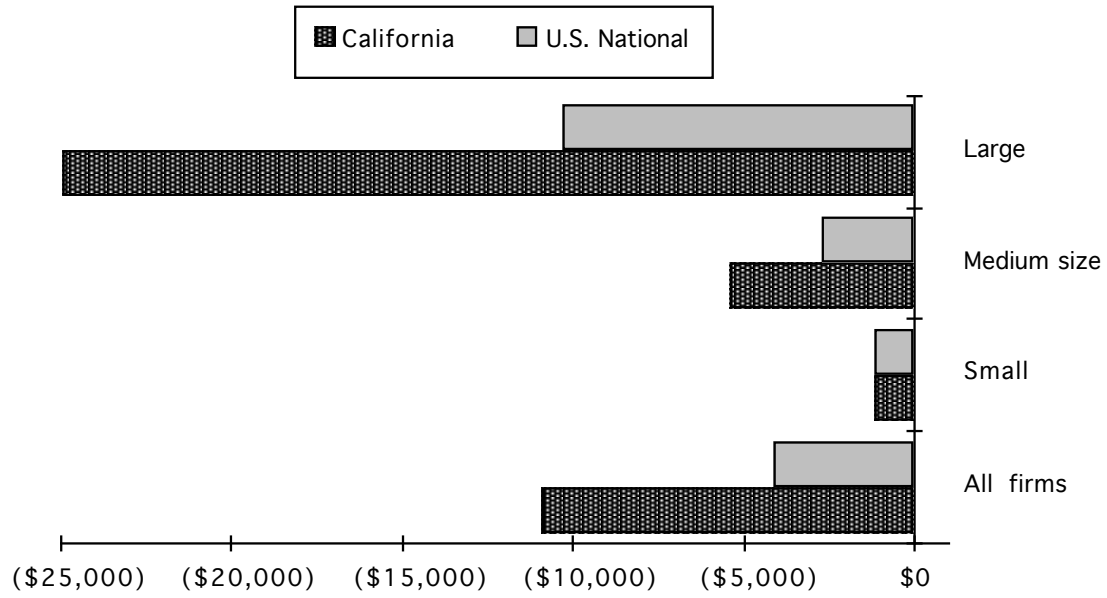
Chart 10
Total assets by size of firms ($000)
Comparison of California and U.S. National industry n



Source: Arthur Young, 19

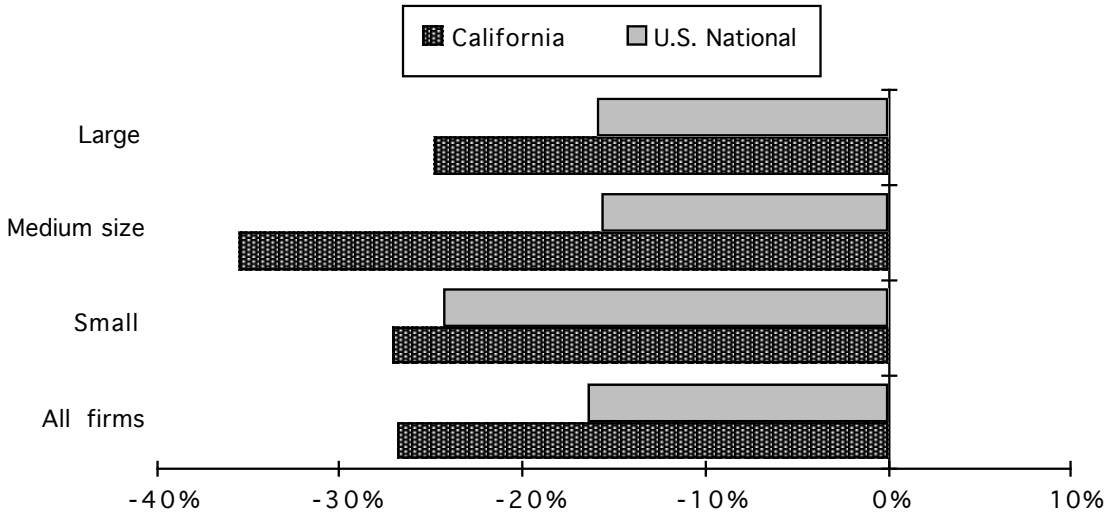
Large firms also make significantly larger losses than smaller firms, as shown in Chart 11. The most interesting feature revealed in this chart is that despite their relatively large revenues and assets the average loss incurred by California firms is markedly higher than for firms aggregated at the national level. As indicated earlier in the paper, this is probably a reflection of the relatively stronger emphasis by California firms on research activities with an expected long term payoff. A further observation is that small biotechnology firms incur roughly equivalent losses in both California and elsewhere in the United States.

Chart 11
Net income (loss) by size of firms ($000)
Comparison of California and U.S. National industry n



Source: Arthur Young, 19

Chart 12
Return on assets by size of firms
Comparison of California and U.S. National industry n



Source: Arthur Young, 19

Chart 12 presents the same figures for annual loss as provided Chart 11, but plotted as a percentage of the mean assets in each size category of firms. California

firms are also less profitable by this measure, but with the interesting difference that large firms tend to perform better than small and medium- size firms. By examining differences in the return on assets among firms of different size we have gained further evidence to suggest that, despite their relatively high losses at this stage, the larger biotechnology firms have a relatively strong financial base.

8. Cost Structure and Expenditure

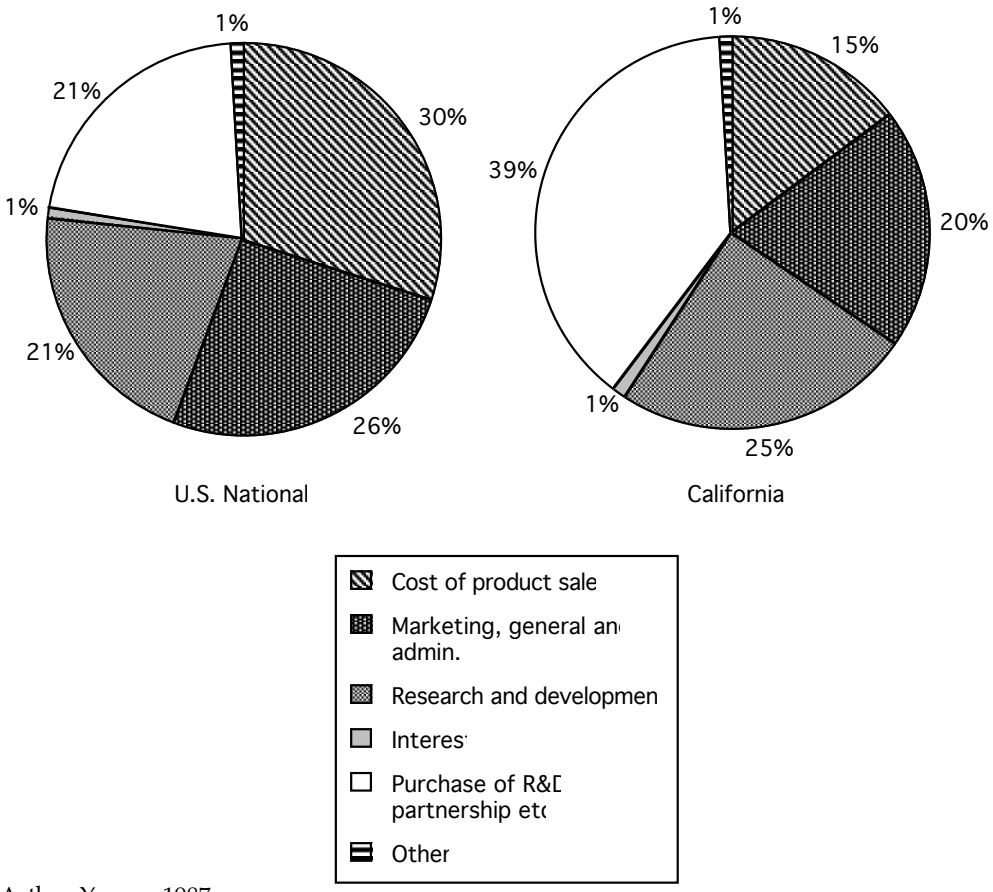
The relatively strong emphasis on research activities by California biotechnology firms, compared with other U.S. firms, is reflected in Chart 13. California firms allocated 64% of their expenditure during 1986 to the two research-related categories in the chart, against 42% for the industry nationally.

Firms elsewhere in the United States appear to be proportionally more heavily engaged in the manufacturing of biotechnology products than those in California. This is indicated by the fact that biotechnology firms nationally average twice the expenditure on meeting the cost of product sales as do California firms. A greater proportion of their expenditure (26%) goes on marketing and administration than is the case for California firms (20%).

Interestingly, about the same proportion of expenditure (1%) is directed towards servicing the interest on debts for both California and U.S. national firms, despite the fact that the national industry scores a mean debt/equity ratio 1.4 times higher than that of the California industry (see Table 2). This may be a reflection of the fact that California firms exhibit a relatively high mean level of current liabilities (see Table 2).

Chart 14 shows that the relatively low debt/equity ratio of California biotechnology firms is achieved by all types of firms except suppliers, but even here the difference between the debt/equity ratios of suppliers in California and the U.S. as a whole is not very great (1.1:1). If firms are instead classified by size

Chart 13
Distribution of expenditure in biotechnology firms, 19



Source: Arthur Young, 1987.

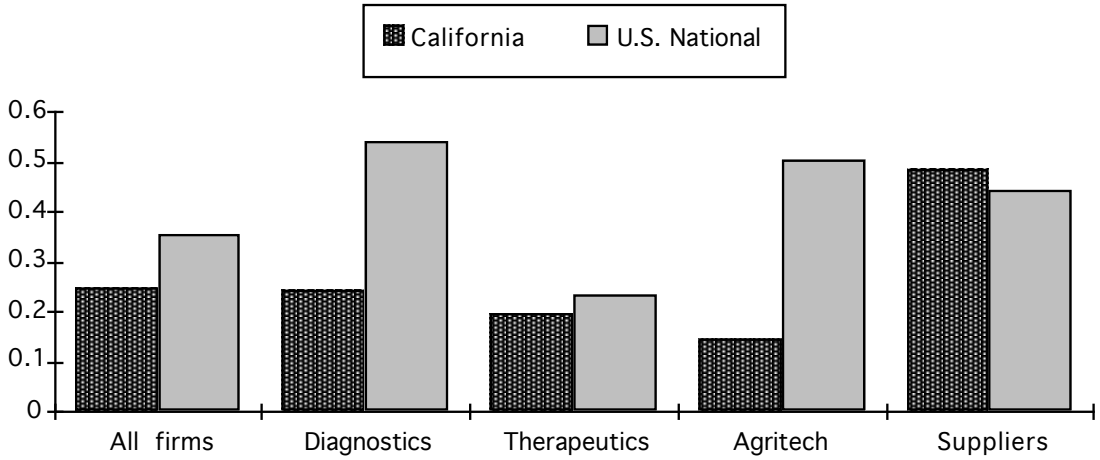
rather than market orientation then an important character difference between the California and national industries emerges (see Chart 15). There is a clear pattern in the California industry for the debt/equity ratio to decrease as the size of the firm

increases, while at the national level such a pattern is very weak, if apparent at all.[44] Furthermore, while large California firms have a lower debt/equity ratio than large firms nationally, small and medium-size firms in California show a higher bias towards debt than do the equivalent size firms nationally.

Table 5, derived from a different sample of the national population of biotechnology firms (n=124) than the data in charts 14 and 15, shows that there is a relationship between the size of firms and their tendency to be financed by equity. Large firms are less likely to have few equity holders and small companies are less likely to have multiple equity holders than medium-size or large companies. The strongest tendency to take on equity holders, across the biotechnology industry nationally, is among medium-size firms (accounting for 47% of all firms with one equity holder, and 51% of all firms with multiple equity holders). This is consisted with the picture in Chart 15. Chart 15 covers all types of firms and equity, not just those types associated with the stock market.

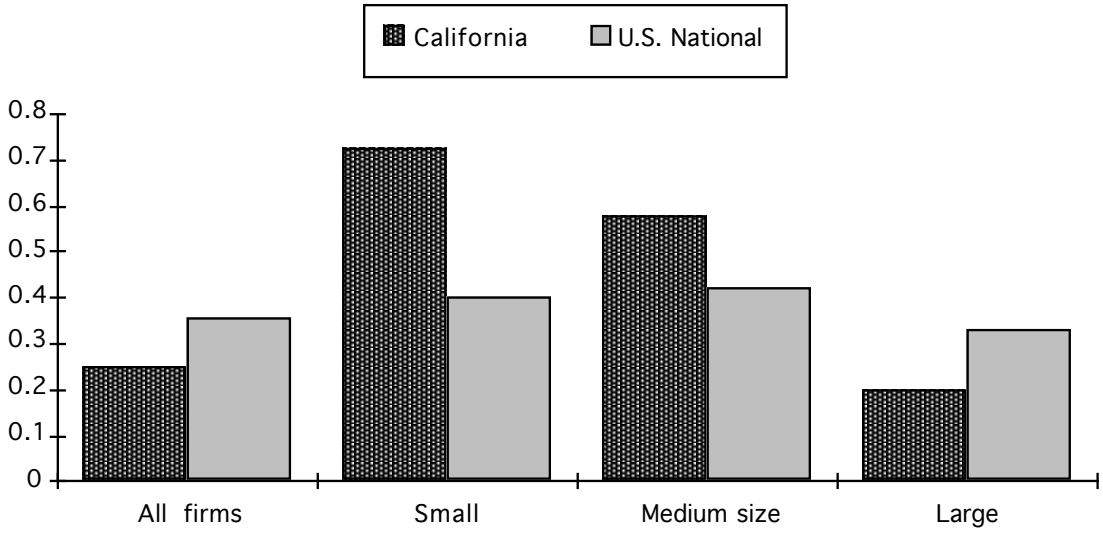
[44] The national sample of biotechnology firms described here includes the California sample. The slightly lower debt/equity ratio for large firms over small firms nationally, is probably largely a reflection of the California sub-set in the sample. If California firms were excised from the national sample the distinctions we have drawn here would probably be even more marked.

Chart 14
Debt/equity ratios by market orientation of f
Comparison of California and U.S. National industry n



Source: Arthur Young, 19

Chart 15
Debt/equity ratios by size of firms
Comparison of California and U.S. National industry n



Source: Arthur Young, 19

Together Charts 14 and 15, and Table 5, suggest that the California biotechnology industry has a relatively low debt/equity ratio due to the strong capacity of its *large* firms to obtain finance from equity holders. This relatively high dependency upon equity probably makes it more feasible for California firms to

adopt a strategy of concentrating on research type activities with longer-term pay-back periods.

The data also reveal the California industry to be more diversified in its financial structure between firms of different sizes than the national industry. The data suggest that *large* California firms would be more likely than the average firms nationally to cope with financially stringent circumstances, due to their proportionally lower dependence upon forms of financing which require continual servicing of debt. The opposite appears to be the case, however, for small California

Table 5
Equity purchased in U.S. biotechnology companies by size of firm, 1987

Extent of equity held in firms	*% of firms of each size in each equity category*			
	Small firms	Medium-size firms	Large firms	Total
No equity held	13.7%	7.3%	2.4%	23.4%
One equity holder	11.3%	21.8%	13.7%	46.8%
More than one equity holder	3.2%	15.3%	11.3%	29.8%
Total	28.2%	44.4%	27.4%	100.0%

Source: North Carolina Biotechnology Center, 1987.

firms; they would probably be less likely to cope easily in financially stringent circumstances than the average firm nationally. The restructuring which is likely to take place in the California biotechnology industry in response to financial stress is therefore likely to take a different form to that of the industry elsewhere.

9. Revenue

Despite the present low profitability of biotechnology firms, and especially those in California, and their heavy dependence upon capital rather than income as

a means of funding operations, they are exhibiting a gradual expansion in their earning of revenue. Recognizing this trend is very important in the case of the California, where so much has been staked on the long term. Underlying long term patterns, rather than short term performance or short term stock market fluctuations, are critical for evaluating the health of the industry.

During the last couple of years there have been some general signs of improvements in the income generating capacity of U.S. biotechnology firms.[45] For the leading biotechnology companies across the nation the general pattern from 1986 through to 1988 has been a very strong increase in revenues, combined with fluctuations in the magnitude of losses incurred. For example, a regular survey of twenty leading biotechnology firms revealed the following: average revenue increase of 34% from first quarter 1986 to first quarter 1987 (18 firms); average revenue increase of 42% from second quarter 1986 to second quarter 1987 (20 firms); average revenue increase of 48% from first quarter 1987 to first quarter 1988 (18 firms); and, average revenue increase of 44% from second quarter 1987 to second quarter 1988.[46] It appears that the stock market crash has had little effect on the revenue earning capacity of firms and that the high loss levels of some leading firms reflect decisions by the firms to invest heavily in product development in the hope of future revenue from product sales.[47]

A similar trend may be found in the whole industry at the national level as found among the market leaders. This is illustrated in Chart 16 (derived from Table 1). Despite popular impressions of the biotechnology industry as not having

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[45] G. Graff and J. H. Winton, "Biotechnology: Growing Greener at Last", *Chemical Week* (September 30, 1987), 20-37.

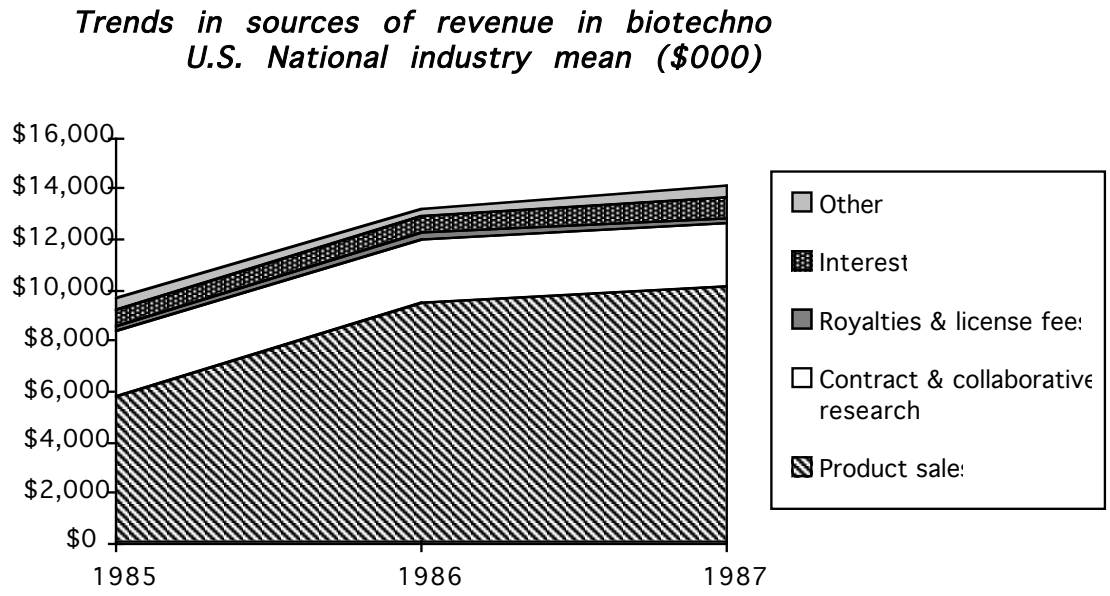
[46] W. J. Storck, "Losses Narrow at Most Biotechnology Firms", *Chemical and Engineering News* (June 8, 1987), 11; W. J. Storck, "Revenues Continue to Increase for Biotechnology Firms", *Chemical and Engineering News* (September 7, 1987), 17-18; M. Reisch, "Revenues Still Rising for Biotechnology Companies", *Chemical and Engineering News* (June 6, 1988), 19-20; W. J. Storck "Revenues Continue to Grow at Biotechnology Companies", *Chemical and Engineering News* (September 5, 1988), 9-10.

[47] *Ibid*., Storck and Reisch.

commercialized very much, Chart 16 shows the vast majority of industry revenue to be derived from product sales (72% nationally in 1987).

While the biotechnology industry as a whole still records a net loss, about one quarter of all firms at the national level had begun to record profits by 1987.[48] Considerable variation exists within the industry, furthermore, with over half of the large firms recording a profit by 1987 and half of the suppliers doing likewise (see

Chart 16



Source: Arthur Young, 1986. 1987, 1988.

Table 6). While the mean size of the loss incurred by biotechnology firms has tended to increase with the size of the firm (see Chart 11), the proportion of firms which are profitable also increases with firm size (see Table 6).

[48] G. Steven Burrill with the Arthur Young High Technology Group, *Biotech 89: Commercialization* (New York: Mary Ann Liebert, Inc. Publishers, 1988), 68-86.

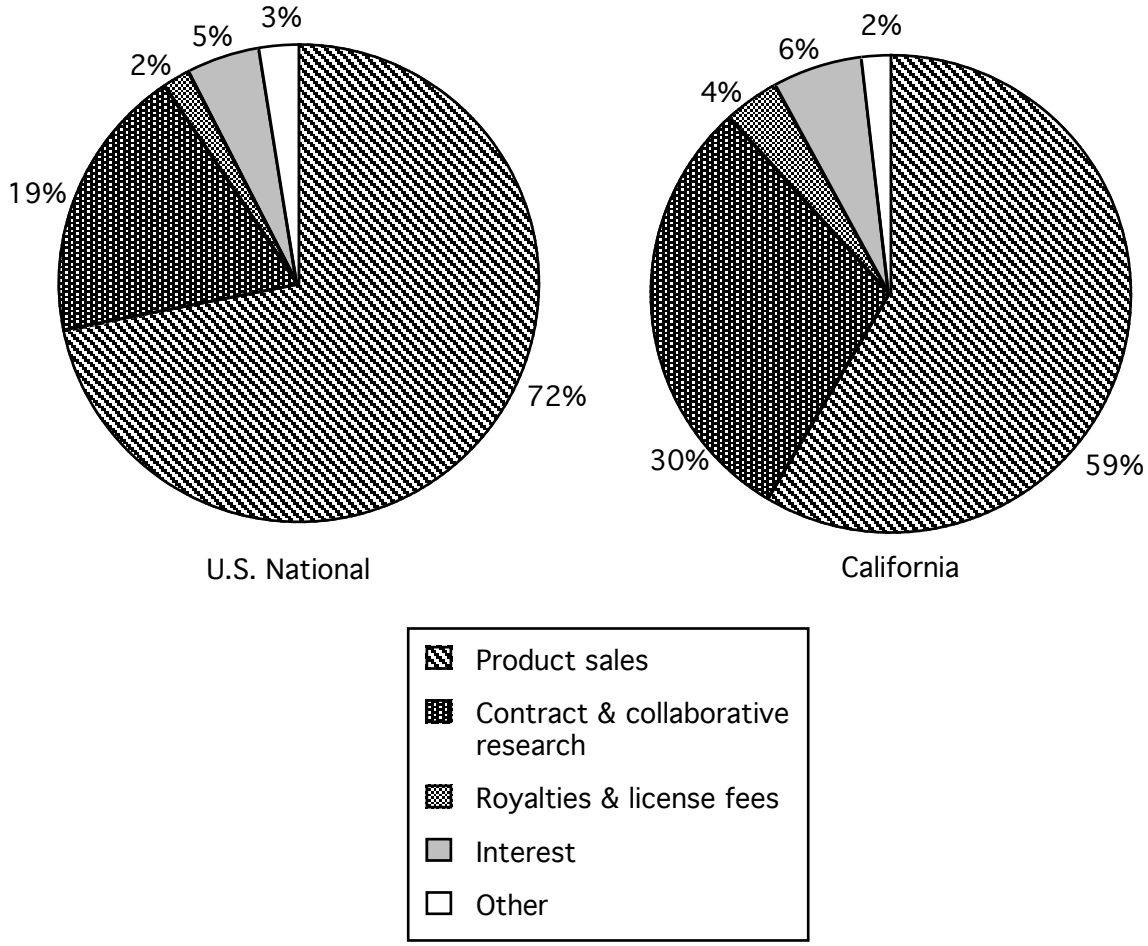
The relatively strong emphasis by California biotechnology firms on research and development activities, identified earlier in the data on expenditure, is confirmed in Chart 17 which compares the pattern of sources of revenue between the California industry and the national industry during 1986. Firms outside California obtain a relatively high amount of their revenue from product sales. It is not clear whether or not this pattern will persist or for how long.

Table 6
Percentage of U.S. biotechnology firms which are profitable, by size and market orientation, 1987

All firms	26%
Small	8%
Medium size	2%
Large	55%
Diagnostic	29%
Therapeutic	17%
Agritech	10%
Suppliers	50%

Source: Arthur Young, Biotech 89.

Chart 17
Sources of revenue in biotechnology firms



Source: Arthur Young 1987.

10. Sources of Finance

The tendency for biotechnology firms to make strong use of public financing as they grew prompted many in the industry to hope that it would be possible for the California biotechnology industry to remain independent and mature without being swallowed up by large established corporations. The grounds for such hope are now fading, however, as public funding becomes increasingly hard to obtain.

Most financial commentators observing the biotechnology industry claim that cash shortages are now causing most biotechnology firms to both cut back on some of their activities, as cost saving measures, and search for new sources of funds. In some cases this involves mergers and in others it leads to being taken over by larger established corporations. A further significant trend is for firms to form partnerships and new types of collaborative agreements, as a means of raising more funds and gaining greater market power. This is happening both between biotechnology firms and between biotechnology firms and established pharmaceutical and chemical corporations.[49] We will return to this theme later.

The biotechnology industry is widely known for the vigorous and sometimes novel use made of venture capital financing. Venture capital financing has, however, only been one of a number of methods of financing biotechnology firms. Alan Walton, of Oxford Partners, estimates that of the 120-150 public biotechnology companies presently in the United States, 50 or so have been backed by venture capital. He estimates that between June 1, 1987 and May 31, 1988, there were about 200 attempted financings of biotechnology firms, of which about 80% succeeded in raising cash outside of family or limited private resources; between 40 and 50 of the attempted financings were backed by venture capital firms. The percentage of all biotech initial-public-offerings which were for venture-backed companies has risen from about 30% in 1983 to about 60% in 1986-87.[50]

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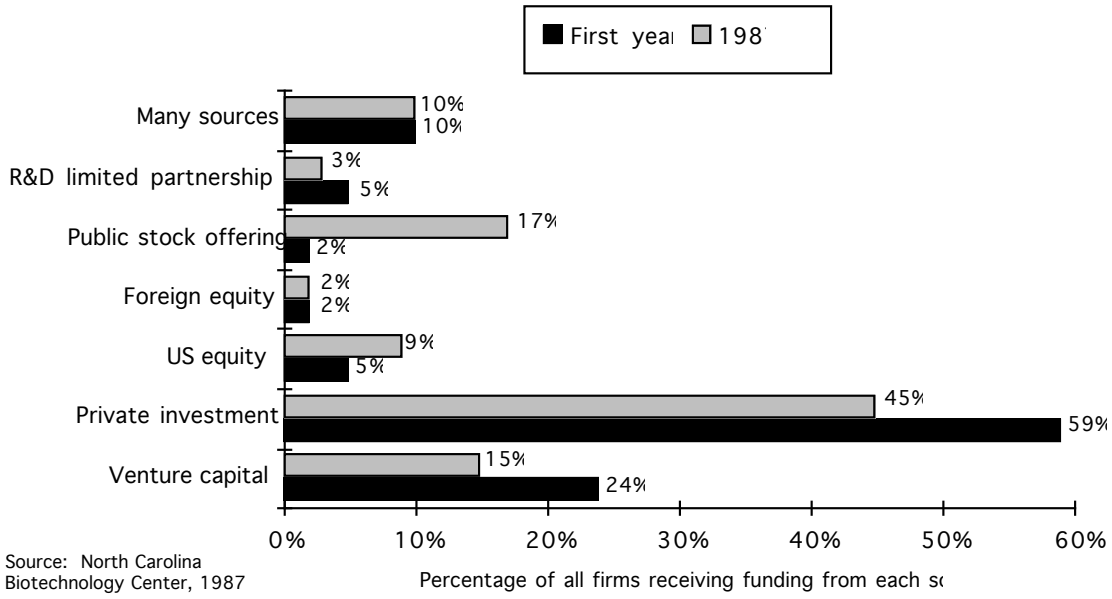
[49] See, e.g., L. M. Fisher, "Biotech Hurdle: A Cash Shortage", *New York Times* (Saturday, December 3, 1988), 1&29.

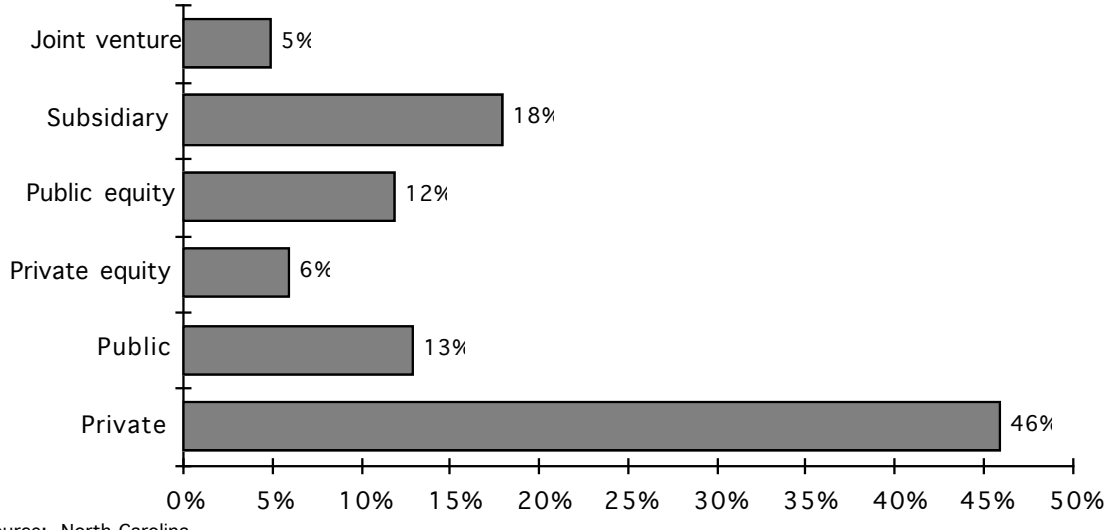
[50] Alan Walton, Oxford Partners, "A Decade of Biotechnology Investment", *BioVentureView*, 4,3 (March 1989), 24-27.

Chart 18
Primary source of funding for US biotechnc



Source: North Carolina Biotechnology Center, 1987

Chart 19
Primary source of funding
California biotechnology firms



Source: North Carolina Biotechnology Center, 19

Chart 18 shows the distribution of financing sources for a national sample of 110 new biotechnology firms, from the time of their of first year in operation up to the time of the survey (April 1987). The average year in which the firms were founded was 1981, and a funding source was designated "primary" if it constituted over half of the firm's funding.[51] Private funding is by far the single most important source of finance for firms, accounting for almost 60% of primary first year funding. By 1987 this had reduced to 45%, but was nevertheless still the primary funding source for three times the number of firms which used venture capital as their primary funding source. Despite the rising percentage of initial-public-offerings by biotechnology firms which have been venture capital-backed, the proportion of firms which rely primarily upon venture capital has been reducing (from 24% in the first year, to 15% in 1987). According to Chart 18, the only types of financing which appear to have been growing for the sample of firms over the life of their operations to 1987, were public stock offerings and other forms of equity financing.

Chart 19 shows the distribution of primary funding sources for a 1989 sample of California biotechnology firms. This data set provides no indication of the relative importance of venture capital in the firm's history of operations, but conforms to the national pattern in Chart 18, in that private financing is also the single most important source of funding for California firms. The chart also reveals that by 1989 collaboration with other firms (as subsidiaries or through joint ventures) has become the second most important means of raising finance (18% of firms gained primary funding this way).

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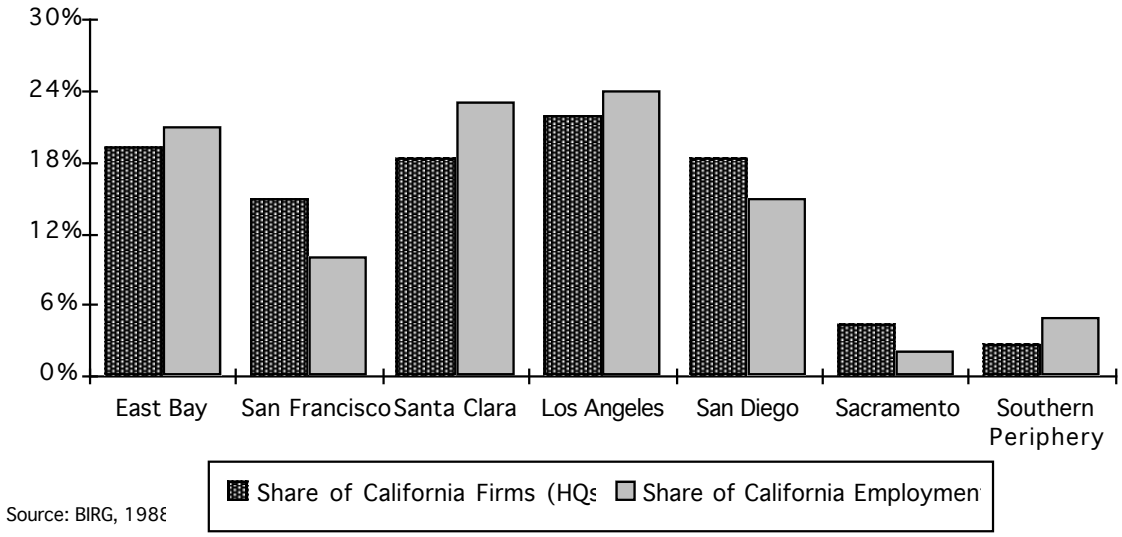
[51] The survey was conducted by the Business Studies Program of the North Carolina Biotechnology Center for the Congressional Office of Technology Assessment, and published by the U.S. Department of Commerce as *New Developments in Biotechnology: U.S. Investment in Biotechnology*, Contractor Reports, Part 1, PB88-144209 (Springfield, VA: National Technical Information Service, December 1987). The data represent answers from 119 companies for the first year and 110 companies for 1987 (of 137 companies which responded to the survey).

11. Regional Patterns in Biotechnology Industry Finance

The California biotechnology industry is not spread evenly throughout the state. BIRG's 1988 survey, which identified 114 *bona fide* biotechnology firms operating in California, together employing an estimated total of over 17,000 people, found the industry to be clustered in seven regions which we have labelled: East Bay, San Francisco, Santa Clara, Los Angeles, San Diego, Sacramento, and Southern Periphery. The boundaries of these regions are pictured in Map 1. The *East Bay* consists of the Oakland Metropolitan Statistical Area (MSA), which includes Alameda and Contra Costa counties; *San Francisco* consists of the San Francisco MSA (San Francisco, San Mateo and Marin counties); *Santa Clara* consists of the San Jose MSA (Santa Clara county); *Los Angeles* consists of the Los Angeles/Long Beach MSA and the Anaheim/Santa Ana MSA (Los Angeles and Orange counties); *San Diego* consists of San Diego MSA (San Diego county); and, *Sacramento* consists of the Sacramento MSA (Sacramento, Yolo, El Dorado, and Placer counties). *Southern California Periphery* refers the periphery of the greater Los Angeles region.

The largest conglomeration in the industry occurs in Northern California around the San Francisco Bay Area, followed by the next largest conglomeration around the greater Los Angeles region in Southern California. Northern California contains about 57% of the firms (65 firms) and about 57% of the employment (9,922 people), while Southern California contains about 43% of the firms (49 firms) and about 43% of the employment (7,404 people). Thus, the mean size of firms is about the same in both Northern California (152 persons/firm) and Southern California (151 people/firm).

Chart 20
California Biotechnology Industry
Regional Distribution of Firms and Empl



Source: BIRG, 1988

Firms in the East Bay (167 persons/firm) average about the same size as Los Angeles firms (166 persons/firm), and are larger than those in the San Diego (120 persons/firm), San Francisco (109 persons/firm) and Sacramento (67 persons/firm) regions. The metropolitan region with the largest mean biotechnology firm size is Santa Clara (187 persons/firm). Firms in the Southern California Periphery average 243 persons/firm, but the sample size is too small to draw statistically significant conclusions from this.

Chart 20 shows the regional distribution of biotechnology firms and employment in California during 1988. Los Angeles is responsible for 24% of the industry's total employment; it is followed closely by Santa Clara (23%) and the East Bay (21%). Los Angeles also contains the the largest proportion of the state's firms (22%), followed closely by the East Bay (19%), and then by Santa Clara and San Diego together at 18% each. The relative contributions of each region to employment and firm populations, as indicated in Chart 20, suggest that there is a

greater preponderance of firms in the start-up stage in the San Diego, San Francisco and Sacramento regions than in the Los Angeles, East Bay and Santa Clara Regions. While the Los Angeles region is large in terms of its absolute numbers of biotechnology jobs and firms, it is actually very weak when these variables are measured according to their relative density against the background economy in general or the "high technology" industries in particular.[52]

There are a number of interesting differences between biotechnology firms in each of the regions which are relevant to our financial analysis. Table 7 shows that, for California as a whole, the most dominant market orientation of firms is diagnostics (measured by the percentage of all firms with that primary orientation, i.e. 35%), followed by therapeutics (24%). California differs from the national pattern by this bias (see Chart 8); six of the seven California regions in Table 7 have diagnostics as one of their top two market orientations.

There are three important variations between the regions. First, the non-metropolitan regions, Sacramento and Southern California Periphery, both emphasize agritech applications. Second, the Santa Clara region is home mostly to supplier firms (Santa Clara has the strongest specialization of any of the regions, with 80% of its firms exhibiting a single primary market orientation). Santa Clara still conforms to California's general focus on diagnostics firms, however, in that this field is the second most important market orientation, accounting for 20% of firms. Third, the East Bay stands out by being the only region with its strongest market orientation on therapeutic applications of biotechnology.

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[52] E. J. Blakely and K. W. Willoughby, *The Economic Geography of the California Biotechnology Industry*, Working Paper, Center for Real Estate and Urban Economics, University of California at Berkeley (forthcoming, 1989).

Table 7
Market orientations of California biotechnology firms by geographical region, 1988

Region	Primary market orientation **(% of region's firms)** *(region's share of all firms with this market orientation)*			Secondary market orientation **(% of region's firms)** *(region's share of all firms with this market orientation)*		
East Bay	therapeutics	**40%**	*35%*	diagnostics	**33%**	*20%*
San Francisco	diagnostics	**29%**	*20%*	therapeutics	**24%**	*24%*
Santa Clara	suppliers	**80%**	*29%*	diagnostics	**20%**	*4%*
Los Angeles	diagnostics	**53%**	*32%*	suppliers	**20%**	*21%*
San Diego	diagnostics	**33%**	*16%*	therapeutics	**33%**	*24%*
Sacramento	agritech	**40%**	*17%*	suppliers	**20%**	*7%*
So. Cal. Periphery	agritech	**67%**	*17%*	diagnostics	**33%**	*1%*
California	diagnostics	**35%**	*100%*	therapeutics	**24%**	*100%*

Source: BIRG, 1988.

As discussed earlier in this paper, therapeutics firms are responsible for the lion's share of revenue and assets in the California biotechnology industry, while also being the focus for the largest expenditures on research and development, aimed at the long term. Table 7 reveals that the special market orientation of the California biotechnology industry compared with the U. S. national industry (measured by financial structure rather than firm populations) is substantially explained by the character of firms in the East Bay. In other words, from the financial point of view, it is the East Bay biotechnology industry which is most distinctively Californian in style.

The San Diego region in Southern California also shows a relatively strong emphasis on therapeutic products, with 33% of its firms having this as their primary market orientation. This is lower than the proportion for the East Bay (40%),

however, and it should also be noted that San Diego firms tend to be smaller than those in the East Bay. Investments in therapeutics in the East Bay are therefore larger than in San Diego.

We may conclude that the short term "bottom line" financial performance of the biotechnology industry is the best for firms in the Santa Clara region. Given their primary status as suppliers, the financial circumstances of Santa Clara firms will probably be relatively stable for some time yet, because the market for their products is related more to the expenditure levels of other biotechnology firms rather than to their profit levels. The flip side of this situation, however, is that the health of the biotechnology industry in Santa Clara is highly *dependent* upon the general level of activity of the industry elsewhere. It is therefore more useful to look to the finances of the industry in other regions, particularly the East Bay, for a long term perspective on the the prospects for firms in Santa Clara.

It is difficult to predict how profitable the whole industry will become in the future, but the evidence considered above indicates that, despite short term losses, the underlying financial footing of biotechnology firms in the East Bay appears to be firm. Current trends suggest that the heavy investments which have been made in biopharmaceuticals may pay off in the not so distant future. Presently, interest is persisting among venture capitalists in the pharmaceutical applications of biotechnology and there is far less current interest in financing the other biotechnology product fields such as diagnostics or agritech.[53] New investment in biotechnology appears to be focused on second- and third-generation biopharmaceuticals.[54] This suggests that mature therapeutics firms may, in the main, be able to cope financially with the delays and complications they are presently experiencing in bringing their products to the market, and a greater

[53] Walton, "Biotechnology Investment", *op. cit.*, 26.
[54] *Ibid*.

proportion may soon begin to show profits. Such a turn-around for firms would probably have a most notable effect in the East Bay.

Table 8 provides a regional break-down of the concerns of firms about cost factors when making decisions about the location of their *research and development* facilities. Firms in the Santa Clara region show by far the highest level of concern about the cost of industrial space when making decisions about locating their R&D facilities, followed by the East Bay. In the case of Santa Clara this may reflect the fact that the region's firms are commercially quite mature, with relatively high levels of attention being given to ways of maintaining competitiveness by reducing costs (this interpretation is confirmed by the fact that Santa Clara firms also exhibit the highest level of concern about wage rates). In the case of the East Bay, the heavy concern with the cost of industrial space may indicate that despite the region's special emphasis on research oriented activities it is nevertheless also quite advanced in "downstream" commercialization, in absolute terms. It may also reflect the possibility that the relatively substantial size of the research activities of the region's firms itself creates large demands for industrial space.

Table 8
Concern about cost factors as a determinant of location decisions for R&D facilities amongst California biotechnology firms in different geographical regions, 1988

Cost factor	*% of firms in each region which consider each factor to be an important determinant of location decisions*							
	East Bay	San Fran.	Santa Clara	Los Angeles	San Diego	Sacra-mento	So.Cal. Periph.	Whole State
Cost of industrial space	87%	69%	100%	67%	58%	60%	67%	72%
Wage rates	60%	69%	80%	53%	42%	60%	33%	58%
Proximity to sources of finance	33%	38%	40%	13%	0%	20%	0%	23%
Local taxes	53%	44%	40%	33%	33%	40%	0%	40%
State taxes	60%	50%	40%	33%	17%	40%	0%	40%

Source: BIRG, 1988.

The East Bay's firms exhibit the highest level of concern about taxes, at both the local and state levels, when making R&D facility location decisions. This confirms our earlier conclusion that East Bay firms are actually quite advanced in the product/innovation cycle despite retaining a proportionally high emphasis on research. East Bay firms appear to be placing attention on planning for manufacturing expansion and ensuring that they have access to affordable space to accommodate this. These financially based conclusions accord with the data from BIRG's 1988 survey which show the East Bay to be the metropolitan region with the highest proportion of its firms already engaged in manufacturing (93%), against an industry average of 82%, and a low for the Los Angeles region of 73%.[55]

While proximity to sources of finance is generally not considered by the industry to be an important influence on location decisions, Table 8 reveals that

[55] The highest percentage (100%) was scored by the Sacramento region, which is focused mostly on the city of Davis. The sample size for the region (5), however, makes it difficult to confidently draw conclusions from this.

biotechnology firms in Northern California are significantly more concerned about it than firms in Southern California. This might be interpreted as a sign that finance is harder to obtain in Northern California than in the south, but the evidence canvassed earlier suggests otherwise. Firms throughout Northern California are generally more concerned about all kinds of cost factors (see Table 8) than firms in the Southern California; their substantial manufacturing efforts combined with a strong level of investment in research indicate that the industry in the north is at a stage of development which requires large inputs of cash to sustain its commercialization process.

Table 9 provides a regional break-down of the concerns of firms about a wide range of factors when making decisions about the location of their *manufacturing* facilities (Table 8 dealt with *research and development* facilities). The only factor in the table overtly related to cost is the cost of industrial space, but it ranks across the whole state as the most important of the factors listed. This factor is important to the locational decision-making of firms for both R&D facilities and manufacturing facilities.

The prime consideration given by firms to the cost of industrial space in their decision making over manufacturing could be used to conclude that firms would be likely to relocate their facilities as they mature towards later stages of manufacturing. The second most important factor listed, however, indicates that firms also place great importance on locating manufacturing facilities close to their R&D facilities, suggesting that there are countervailing forces in the industry working to limit the tendency towards geographical dispersal over time.

Table 9
Determinants of location decisions for manufacturing facilities amongst California biotechnology firms in different geographical regions, 1988

	% of firms in each region which have considered each factor in location decisions							
	East Bay	San Fran.	Santa Clara	Los Angeles	San Diego	Sacra-mento	So.Cal. Periph.	Whole State
Cost of industrial space	87%	82%	80%	79%	67%	80%	100%	80%
Proximity to firm's R&D facility	80%	77%	80%	57%	58%	80%	67%	70%
Regulatory environment	73%	44%	60%	79%	50%	80%	100%	64%
Access to pre-existing ind. space	47%	53%	40%	86%	67%	60%	67%	61%
Proximity to markets	40%	35%	40%	36%	58%	60%	67%	44%
Availability of raw materials	40%	24%	0%	43%	25%	20%	0%	28%
Competition with pharm. co's.	13%	12%	0%	14%	8%	20%	33%	13%
Distance from Fed. reg. agencies	13%	0%	0%	21%	17%	0%	33%	11%
Other factors	27%	41%	40%	14%	58%	20%	0%	32%

Source: BIRG, 1988.

An interesting geographical character difference in the industry over this issue is also revealed in Table 9: the concern of biotechnology firms to keep manufacturing activities close to research and development facilities is significantly stronger in Northern California than in Southern California. This suggests that there tends to be intimate links between research, innovation and manufacturing for Northern California biotechnology firms. It also suggests that the spatial aspects of the maturation of the biotechnology industry will take on a different pattern in different parts of California. In the north, it is likely that the industry will remain relatively strongly clustered in its present locations as it develops, whereas in the south firms may exhibit a lower proclivity for remaining close to their geographical origins as they mature commercially.

Earlier in the paper we drew attention to the relatively high levels of loss incurred by California biotechnology firms compared with the national industry in the short term, and we subsequently suggested that this somewhat reflects the strong emphasis on research in the state, and, in particular, the notable orientation of firms in Northern California (especially the East Bay) on therapeutics products. Our regional analysis has indicated that the research expenditures of these firms appear to be closely linked to planned manufacturing ventures (a nexus most visible in the case of the East Bay). The strong emphasis on research should not be interpreted as a decision to direct resources away from manufacturing but rather to base manufacturing on strong product or process innovation. It is therefore reasonable to maintain confidence in our earlier hypothesis that the high short term losses of many California firms may be interpreted as an expression of solid investments rather than poor performance. Our analysis of firms by size, however, suggests that the long term financial prospects of *small* California biotechnology firms may not, in general, be as encouraging as either their large counterparts in the state or their small interstate counterparts.

12. Trends in the Formation of New Biotechnology Companies

From an organizational viewpoint there are two forms of companies involved in biotechnology in the United States: dedicated biotechnology firms, normally relatively small, recently formed and almost exclusively focused on new biotechnology activities; and, large diversified companies, normally long established corporations which have invested in biotechnology research in-house or which have entered the biotechnology industry through the purchase of dedicated biotechnology companies. The boom period in the United States for the formation of dedicated biotechnology companies was the first few years of the 1980s, with the peak occurring during 1981. According to the Office of Technology Assessment

(OTA) approximately 60% of existing companies were founded between 1980 and 1984.[56] Most commentators believe that this peak company formation rate will not be repeated. The OTA, for example, writes:[57]

> The "biotechnology industry," if measured by the entry of new, small companies in the field, has most likely stabilized. Some analysts would contend that, due to consolidation within the industry and the predominance of a few firms, the number of *viable* [dedicated biotechnology companies] is actually shrinking. The industry as measured by the amount of money invested by large diversified corporations and [dedicated biotechnology companies], however, is growing.

The financial climate now facing would-be entrepreneurs is more stringent than at the beginning of the decade, making it more difficult to raise funds to support biotechnology entrepreneurship. Nevertheless, there are signs that, at least in the case of California, small biotechnology start-ups are continuing to emerge at a significant level.

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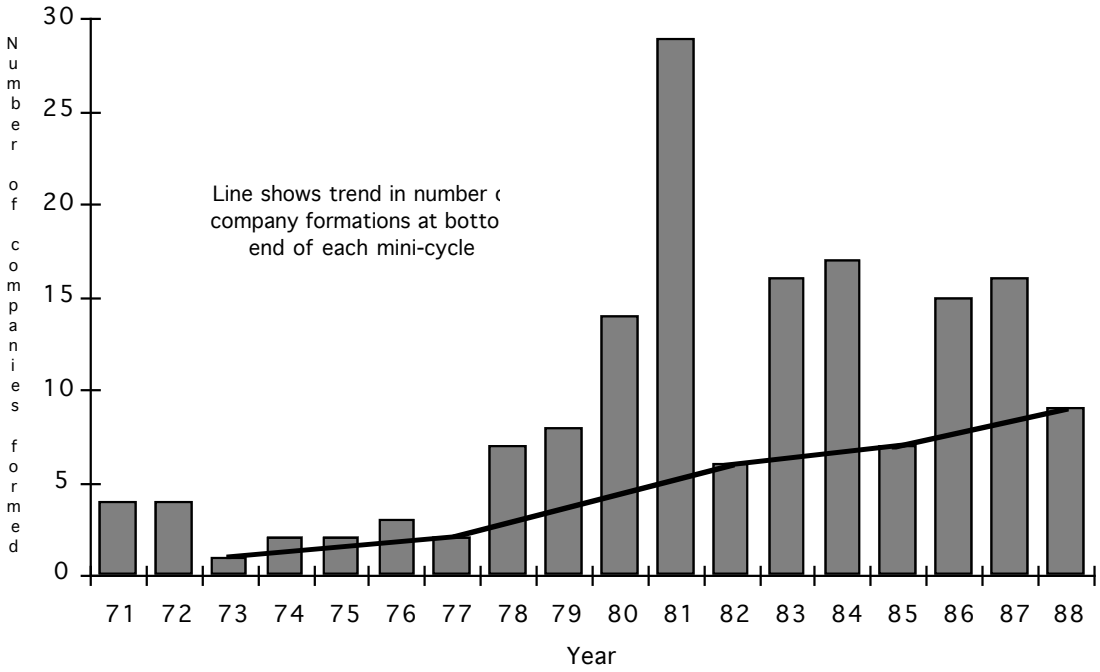
[56] U. S. Congress, Office of Technology Assessment, *New Developments in Biotechnology: U. S. Investment in Biotechnology - Special Report*, OTA-BA-360 (Washington, D. C.: U. S. Government Printing Office, July 1988), p. 78.

[57] *Ibid.*, p. 79.

Chart 21 shows the changes in the annual formation of new biotechnology companies in California from 1971 to 1988. The California pattern conforms roughly to the national pattern reported by the OTA, in that the peak year was 1981. The chart also reveals that the company formation rate appears to occur in cycles, with mini-peaks visible every three-to-four years; such peaks are observable in California in 1972, 1976, 1981, 1984 and 1987.

A dip in the company formation rate is observable in 1988, but it is not clear whether this is part of a long term decline, or simply part of the bottom level of another mini-cycle. The general opinion of national level industry observers would suggest that another significant peak should not be expected. Chart 21, however, reveals that the number of new biotechnology firms formed during the year following the peak year in each of the last four mini-cycles (1977, 1982, 1985 and

Chart 21
Formation of biotechnology companies in California,



Source: North Carolina Biotechnology Center, 1989 (raw data); BIRG (calculati

1988) has continued to increase right up to the present. It is too early to report figures for 1989, but it appears that relatively high start-up rates have persisted in California, particularly in the San Diego region.[58]

This is especially interesting in view of the October 1987 stock market crash. At first sight it would appear reasonable to interpret the decline in company formation rate during 1988 to have resulted from the crash, but Chart 21 suggests that, in the case of California, such a decline would probably have happened anyway as part of normal cyclical patterns in the industry. It appears that the biotechnology company formation rate in California is not closely connected to the stock market environment. This conclusion has also been reached by some other industry observers, such as Alan Walton, who writes:[59]

> Public perception of, and investment in, biotechnology by no means matches that in the private sector. Downturns in the public market in 1982, 1984-5, and 1988 were interspersed with strong interest in, and explosion of, new company formation in 1980-81, 1983-4, and 1986-7. Downturn in the public market has been matched by a building in the private market.

While perhaps going against certain popular perceptions of the biotechnology industry, this conclusion is entirely reasonable in view of the data presented earlier in Charts 18 and 19. At the national level the vast majority of firms (59%) have used private investment (other than from venture capital institutions) as the primary source of funding for their first year of operation, while public stock offerings provided the primary first year funding for only 2% of firms. For the California biotechnology industry during 1989, only 25% of firms (both new and established) gained their primary funding from public sources.

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[58] Informal evidence for this is available from a number of sources, e.g.: G. S. Burrill, *The Regional Biotech Industry: Risks and Rewards*, Holy Names College Symposium for Business Leaders, October 14, 1988, Oakland, California; direct investigations by A. Paul, Industrial Geography Research Group (U.C.L.A.), and Biotechnology Industry Research Group (U. C. Berkeley), 1988, 1989.

[59] Walton, "Biotechnology Investment", *op cit.*, p. 24.

While the biotechnology industry as a whole is characterized by a leading role played by university scientists as entrepreneurs, it appears that many of the newest biotechnology start-ups are spin-offs from existing biotechnology firms rather than university laboratories and departments.[60] Whether this change in the origins of biotechnology start-ups will have implications for the sources of finance remains to be seen. We should conclude at this stage, however, that the sustained base start-up rate for biotechnology firms in California will most likely create even more competition for available funding than already exists.

13. Financial Trends

Several factors have contributed to the distinctive character of the national biotechnology industry finances. One of the most widely cited is the rise of specialized venture capital institutions which, taking advantage of reductions in capital gains tax in 1978, freed up previously scarce capital for the nascent biotechnology industry.[61] This was aided by the 1981 ruling which allowed patenting of genetically engineered organisms, and the 1980 Dole/Bayh bill which allowed the exclusive licensing of biotechnology inventions which had been supported by government funding.[62] Both of these initiatives were important to the fledgling industry because the proprietary rights which new firms could now hold over their research results made their activities more attractive and less risky for potential investors. Venture capital institutions have played an important role in the young biotechnology industry, but finance from such sources has not been

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[60] This is apparent, for example, amongst the new small firms in the San Diego region (C. Hall, "Highlights of the San Diego Technology Financial Forum", *BioVentureView*, 4, 3 [March 1989], 16-18).

[61] Walton, "Biotechnology Investment", *op cit.*, p. 25.

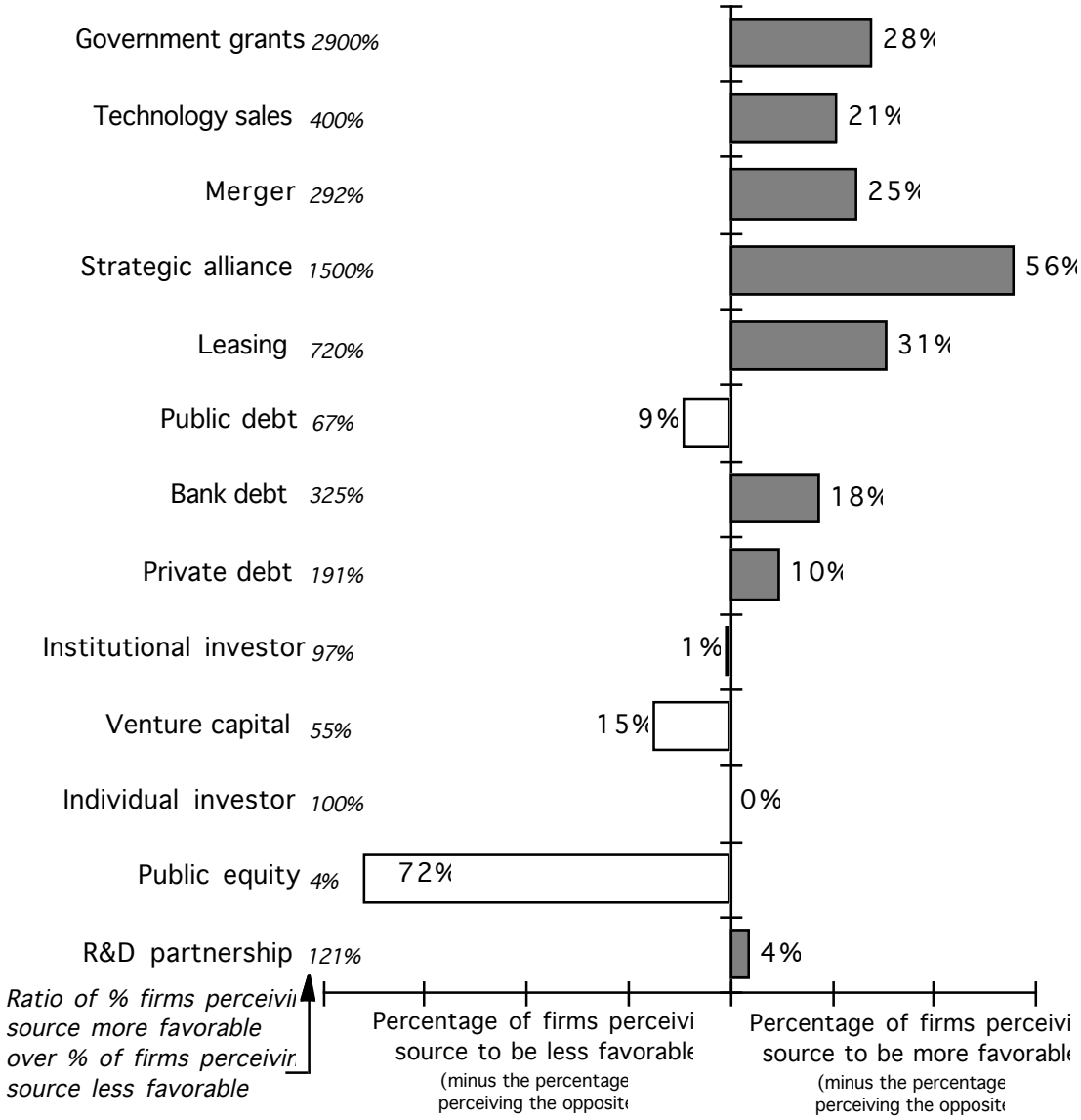
[62] *Ibid.*

responsible for such a large proportion of total biotechnology financing as may have popularly been thought.

The main historical financial trends in the California biotechnology industry, identified earlier in this paper, have been: an increasing amount of finance coming from operational revenue rather than capital, an increase in the importance of public funding, and an increase in the importance of equity financing of various forms. Most commentators now stress that the most important new sources of financing are through strategic partnerships, coalitions, mergers and various forms of inter-firm collaboration. A combination of the large number of biotechnology firms in existence, the shortage of investment capital after the stock market crash, the large amounts of cash now required by firms to finance their commercialization and scale-up plans, and the failure of many firms to live up to earlier expectations, has meant that firms have had to search for new sources of funds and new ways of managing their finances. The formation of partnerships between each other and with established large corporations is one of the main responses of biotechnology firms to this situation.[63]

[63] This theme was very prominent at a recent national meeting of biotechnology financial analysts held in New York (Session on "Optimum Strategies in a Global Market", at the *BioFinance'89* conference sponsored by KPMG Peat Marwick and BioConferences International, Inc.); see, "Analysts chart recovery strategy for cash-strapped bio-industy", *Biotechnology Newswatch* (April 17, 1989), 7.

Chart 22
Perceived Effect of 1987 Stock Market on Financing Sources of Biotechnology C



Source: Arthur Young, 1988 (raw data); BIRG, 1989 (chart).

This response is reflected in Chart 22 which presents the perceptions of the managers of biotechnology firms of the effects of the October 1987 stock market

crash on the relative desirability of various financing sources.[64] The two most significant features of this chart are that 60% of firms perceive that strategic alliances have become more favorable following the crash (with only 4% perceiving the opposite), and 75% perceive that public equity has become less favorable following the crash (with only 3% perceiving the opposite). The chart also shows observable declines in how favorable venture capital and public debt are perceived to be. Although their improved status is significantly less than that of strategic alliances as sources of finance, the following sources are also perceived as being more favorable as a result of the crash: private debt, bank debt, leasing, mergers and government grants. The fact that several times as many firms perceive technology sales as being a more favorable source of income than those which believe it to have become less favorable is difficult to interpret, but it is consistent with the increasing revenue-earning levels of biotechnology firms reported earlier in this paper.

Biotechnology firms report that they have responded at the operational level to the stock market crash by concentrating on fewer research projects and developing fewer products, but without reducing their spending. It is likely that they will market fewer products and employ fewer new staff than would otherwise have been the case, but, on the whole, it appears that consolidation of activities rather than massive cutting-back is the main practical response by firms to the finance shortages they are facing.[65]

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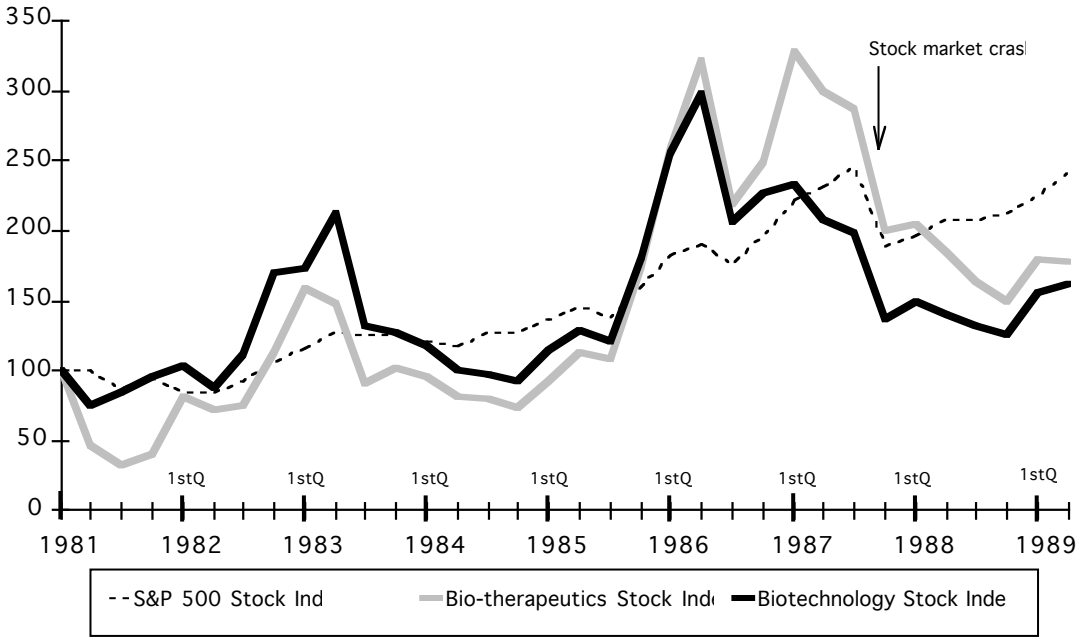
[64] The data in this chart are derived from a survey of a 1988 sample of 291 biotechnology companies from across the whole of the United States (Arthur Young, *Biotech 89*, *op cit.*, p. 43).

[65] *Ibid.*, p. 42-43.

Chart 2
Stock Market Trends for Biotechnology Firms
(Montgomery Securities Biotechnology Stock Price In



Source: Dr. Denise M. Gilbert, Montgomery Securities, San Francisco, Jul

Despite the obvious importance of the October 1987 stock market crash, on closer examination it becomes apparent that the longer term trends in the finances of biotechnology firms may have very little direct connection to this event. This is reflected in the performance of public biotechnology firms in the stock market. Chart 23 plots the Montgomery Securities stock price index for leading biotechnology firms (the thick black line) against the S&P 500 stock price index, over the eight and a half years to mid 1989. It also plots a separate index, over the same period, for those biotechnology firms from the sample which specialize in therapeutics (the thick grey line).

A dramatic dip appeared in all three indexes at the time of the crash. A recovery took place in each index soon after, but whereas the S&P 500 index had recovered by the second quarter of 1989 to near its pre-crash level, the two biotechnology indexes declined over the whole of 1988. Notwithstanding a minor

rise late in 1986, the biotechnology index experienced a general decline which commenced eighteen months prior to the crash, suggesting that there were other forces at work determining public valuation of biotechnology stocks. Biotechnology stocks were probably overpriced following heavy speculation based on exaggerated claims by companies in the early days of the industry, fuelled by several years of "biotech razzamattaz" as investors and state governments looked to the emerging industry as the new source of economic hope to replace the role once played by electronics.

The October 1987 "crash" in the biotechnology index was small relative to its total decline from early 1986 to late 1988, and it was no larger than the two earlier "crashes" it had undergone (mid 1983 and mid 1986). Chart 23 reveals the biotechnology index to be quite volatile compared with the S&P 500 index, over the whole eight and a half years covered by the chart. To some extent this may reflect the differing sample sizes, but it also suggests that the public biotechnology market is somewhat independent of the general stock market climate.[66] The attitudes of public investors in biotechnology appear to be influenced primarily by factors endogenous to the industry.

Even though a "long term" decline may be observed in the biotechnology index over the three years from 1986 to 1988, a gradual rise may be observed from 1981 to 1989 in the base level of the index (from about 75 to 126; base year 1981 = 100). Despite the hard times now facing biotechnology firms, vis-a-vis finance, Chart 23 suggests that the "base level" confidence of public investors in the biotechnology industry has not declined. The long term increase in the base level value of biotechnology stocks is even greater for therapeutics firms. Therapeutics

[66] The number of biotechnology firms incorporated into the biotechnology stock price index by Montgomery Securities has varied over time, but has remained in the low to mid twenties since 1984.

firms, furthermore, have switched from a position of lower stock prices than average for the biotechnology industry, during the first half of the decade, to higher than average prices by the second half of the decade. This suggests that the financial market has some confidence in the long-term investment strategy which we earlier identified as particularly evident in the case of California therapeutics firms; the large fluctuations in the bio-therapeutics index in Chart 23 also underlines the relatively high risks associated with this strategy.

14. Organizational Trends

A result of all the developments discussed above, in summary, is that the American biotechnology industry has now emerged from its "honeymoon" period, and is now saddled with the responsibility of grappling with the serious problems of funding gaps, product redundancy, costly commercialization, strategic marketing, and, with increasing urgency, international competition. The following quote from a leading high technology industry commentator is apposite:[67]

> The biotechnology industry is still in the toddler stage. Despite many optimistic forecasts about the potential for new products created by genetic engineering, those products are only beginning to reach the market. Some analysts predict that biotechnology may eventually become not a separate industry, but a collection of techniques to be adopted and used by other industries such as agriculture and chemical processing.
>
> Whatever its destiny, at the moment biotechnology is particularly vulnerable to the demands of cash flow. Without products on the market to generate revenue, companies have had to pay almost as much attention to raising money as they have to the technologies they are trying to commercialize.
>
> The situation has become acute in the wake of the stock market's weakness; public offerings that could have helped companies remain independent have in many cases been postponed or cancelled.
>
> As a result, biotech companies are increasingly being forced to approach larger companies seeking licensing agreements, partnerships, and joint projects.

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[67] M. H. Frakes, "Biotechnology's Double Play", editorial, *High Technology Business*, 8, 4 (April 1988), 5.

The particular ways in which firms deal with their cash shortages and financial management problems will probably be a major determinant of the differing character of the biotechnology industry between regions from hereon. The *pattern of inter-organizational relationships* among the various players in this game appears to be the key element in biotechnology firms' attempts to deal with these issues.[68]

Table 10 shows trends in the different forms of collaborations between U.S. biotechnology firms and between U.S. biotechnology firms and foreign firms. The total number of intranational collaborations between biotechnology firms increased fairly steadily from 1981 to 1986. The number of international collaborations fluctuated somewhat over the period, but remained substantial nevertheless; the table does not cover the last couple of years, but information from other sources indicates that the internationalization of U.S. biotechnology firms is presently increasing.[69] Joint ventures are proportionally the most important form of collaboration, especially at the international level. Marketing agreements also feature very prominently in international collaborations, while the purchase of equity is the second most important form of collaboration between U.S. biotechnology companies.

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[68] M. D. Dibner, "The U.S. Biotechnology Industry: An Analysis of Trends", *Australian Journal of Biotechnology*, 2, 2 (September 1988), 129-132; G. P. Pisano, W. Shan, and D. J. Teece, "Joint Ventures and Collaboration in the Biotechnology Industry", in *International Collaborative Ventures in U.S. Manufacturing*, edited by D. C. Mowery (Cambridge, Mass.: Ballinger, 1988), pp. 183-222; F. Lunzer, "Cash Crisis Creates Biotech Alliances", *High Technology Business*, 8, 4 (April 1988), 18-23; L. M. Fisher, "Biotech Hurdle: A Cash Shortage", *New York Times* (December 3, 1988), 1, 29.

[69] Arthur Young, *Biotech 89*, *op cit.*, esp. pp. 8-12.

Table 10

Collaborations Between U.S. Biotechnology Firms and U.S. Firms and Between U.S. Biotechnology Firms and Foreign Firms

Type	U.S./U.S. (plain text) / *U.S./Foreign (italics)*													
	1981		*1982*		*1983*		*1984*		*1985*		*1986*		**Totals**	
Joint venture	5	*3*	6	*22*	27	*8*	14	*17*	29	*11*	23	*16*	**104**	***77***
Equity purchase	8	*1*	7	*6*	3	*1*	8	*2*	9	*2*	13	*4*	**48**	***16***
Licensing agreement	4	*1*	4	*2*	4	*5*	6	*5*	8	*5*	4	*1*	**30**	***19***
Marketing agreement	4	*1*	0	*6*	2	*4*	5	*4*	8	*5*	13	*7*	**32**	***27***
Research contract	1	*2*	6	*3*	7	*1*	6	*3*	6	*5*	15	*4*	**41**	***18***
Totals	**22**	***8***	**23**	***39***	**43**	***19***	**39**	***31***	**60**	***28***	**68**	***32***	**255**	***157***

Source: Office of Technology Assessment, 1988.

(Unspecified collaborations were classified as joint ventures).

The Office of Technology Assessment reports that most intranational U.S. biotechnology firm collaborations occur in the human therapeutics area (29%), followed by clinical diagnostics (25%).[70] If a wider range of types of collaborations are included than in Table 10, then the proportion of agreements accounted for by the therapeutics sector may be placed as high as 45%.[71] This suggests that for the California biotechnology industry, it is probably the firms in the East Bay, and San Diego regions, which are likely to be the most active in these collaborations.

To reiterate a theme which emerged earlier in the paper, we are arguing that there are *organizational* changes taking place within the biotechnology industry in California, and elsewhere in the United States, which are substantially a response to the financial situation biotechnology firms now find themselves in. Shortages of funds, because of the need for firms to scale up their activities to commercialize,

[70] Office of Technology Assessment, 1988, *op cit.*, p. 89.
[71] Pisano, Shan and Teece, 1988, *op cit.*, p. 209.

because of the heavier competition among the growing population of firms for limited available funds, and because of the tighter investment climate, are causing firms to reorganize so that they may obtain access to new sources of funds and make feasible new ways of cutting costs.

In the pharmaceuticals area of biotechnology it may cost about $100 million for a medium-size firm with sales of $75 million/year to commercialize a new product, with about 90% of the costs occuring downstream after the research phase. Ten percent of the total costs of a bio-pharmaceutical product will probably be in research, with 40% going into development, 35% going into manufacturing, and 15% into marketing.[72] Lee Rauch, of McKinsey & Co. Inc., estimates that there will be an $8 billion gap between demand for funds and supply of funds in the pharmaceuticals dimensions of the U.S. biotechnology industry between 1989 and 1994 - unless major re-organization takes place. Rauch argues that through such measures as company mergers, some companies choosing to remain small rather than become major pharmaceuticals companies in their own right, the subcontracting of operations, and the reduction of duplication in product development between companies, this funding gap could be reduced to between $1.5 and $3 billion.[73]

It is interesting to reflect on the role of venture capital institutions in the organizational transition taking place in the biotechnology industry. The established pattern for financing the development of a biotechnology firm in the United States appears to have been that the very early start-up activities were funded from private sources, often personally connected with the entrepreneur or entrepreneurs, to be followed by the use of funds from venture capital institutions, which enabled the firm to progress beyond a very small-scale level of operations.

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[72] Rauch, *op cit.*, p. 435.
[73] *Ibid.*, pp. 436-442.

The venture capital funding would enable the firm to develop to a more substantial level of operations, while maintaining its culture of independence and entrepreneurship until such time as it reached a position where it could look to either the public stock market or major private institutional investors (pension funds etc.) for major funds to support its commercialization process.

The stock market, as indicted earlier, is generally no longer a promising source of funds for biotechnology firms. It appears that both venture capital institutions and other major institutional investors, normally used by entrepreneurial "high technology" companies as sources of major funding for "third stage" commercialization and scale-up activities, have also ceased to be readily available to play such a role. Some of the major institutional investors, it seems, have already been placing funds with the venture capital organizations for investment in biotechnology firms. Given that most biotechnology firms have been slow to realize attractive returns on investment, major institutional investors feel that they have already taken substantial risks on the biotechnology industry (mediated by the venture capitalists) and are reluctant to risk further funds without firms demonstrating a substantial track record. This is creating pressure for dedicated biotechnology companies to look to established pharmaceutical and chemical corporations, or other large industrial corporations, as sources of funds to enable their operations to continue.

Despite the current stringency in the financial market facing biotechnology firms, there is nevertheless still substantial funding available *so long as the receiving company has a significant track record or is able to offer tangible evidence of product performance*.[74] The halcyon days of being able to float on a stock issue with little

[74] E.g. during the last two years, according to Rauch (*ibid.*), U.S. biotechnology firms have raised almost $1 billion per year from public and private equity markets, debt placements, research and development limired partnerships, and strategic partnerships with other firms.

more than some bright ideas, some respected names, and good public relations consultants, have gone. Investors have already had their "fingers burnt" with hasty investments in biotechnology and are now much more informed and sophisticated in their knowledge of biotechnology and in their skill at evaluating biotechnology ventures.

Further investment may still be found by firms, however, if they present sound commercial prospects. Institutional venture capital is still available and venture capitalists appear to be playing an important role in the changes taking place in the industry, not only as suppliers of funds, but also as significant actors in the dynamics of the industry. Venture capitalists are now playing an active role as entrepreneurs in organizing collaborations, mergers and various forms of strategic partnerships between biotechnology firms. To some extent organizational changes are being adopted by firms as defensive measures, but in other cases venture capitalists are facilitating inter-company collaboration as a positive means of mobilizing funds for viable projects which would not otherwise eventuate. This provides an alternative for some dedicated biotechnology firms to being taken over by major established corporations, whether U.S. or foreign.[75]

15. Prognosis for the California Biotechnology Industry

The California biotechnology industry is something of a harbinger for the whole U.S. biotechnology industry, presently accounting for about one quarter of all the biotechnology firms in the country.[76] The next most significant states, from the

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[75] Most of the themes in the last three paragraphs have come from the authors' informal observation of the industry and from personal conversations with industry participants. Particularly helpful information has been gained from discussion with Chistina Lowell, biotechnology manager, KPMG Peat Marwick, Oakland, California, April 1989.

[76] P. Hall, L. Bornstein, R. Grier, and M. Webber, *Biotechnology: the Next Industrial Frontier*, Working Paper No. 474, February 1988, Institute of Urban and Regional Development, University of California at Berkeley (esp. Appendix Table A, pp. 30-35).

point of view of the population of biotechnology firms, are New Jersey (with 10.5% of the U.S. biotechnology firms), New York (8.6%), and Massachusetts (8.0%).[77] Many of the patterns which may be observed at the national level are also representative of the California industry. We have demonstrated in this paper, however, that in a number of ways the California biotechnology industry is distinctive.

The percentage of U.S. biotechnology companies based in California has declined from almost 30% at the beginning of the 1970s to its present level, and the location quotient of the California biotechnology industry has declined from 2.2 to 1.8 over the same period.[78] This means that the rest of the country is catching up with California in relative terms, both in the number of biotechnology firms and in the number of biotechnology jobs. In certain respects, however, the California biotechnology industry has maintained or increased its lead. For example, at the beginning of the 1970s the number of biotechnology firms in California was only three higher than the number in each of the next most populous states (New Jersey and New York), and four higher than in Massachusetts; by 1987 the gap had increased to 71 above New Jersey, 91 above New York, and 94 above Massachusetts.[79] California has a lower biotechnology location quotient than these three states, but it is important to remember that the biotechnology industry is clustered in certain local regions. If comparisons are made of the location quotients of biotechnology *regions* rather than of states, then it becomes apparent that the San

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[77] *Ibid.*, p. 14.

[78] *Ibid.*, p. 30. The biotechnology location quotient is an indicator of the density of biotechnology employment in a region, relative to the national biotechnology industry and the total economy of the local region and the nation. A location quotient of 1.0 would indicate that the region in question exhibited "average" economic competitiveness in the national context of that industry.

[79] *Ibid.*, p. 14.

Francisco Bay Area (with location quotients of over 4 and 5) has the clear lead in the industry throughout the whole of the United States.[80]

The California biotechnology industry is not only more substantial than the industry in other states in absolute terms, but its firms average higher revenues, higher assets, higher shareholder's equity levels, and higher levels of investment in intellectual property and research, than those biotechnology firms outside the state. California firms are also presently averaging larger losses than firms outside of the state, but we argued earlier in this paper that this is primarily a reflection of big investments being directed towards high-risk, high-payoff research ventures aimed at the long term, combined also with substantial investments in manufacturing. From a financial point of view, California has placed more than the average number of "eggs" in the therapeutics pharmaceuticals "basket". This is the field with the most awkward of regulatory obstacles, the potentially toughest competition from established (pharmaceutical) corporations, the longest time delays, and the biggest commercialization costs. Relatively speaking, California firms are "going for broke"!

California is also distinguished by a rich *diversity* in the types of firms which make up its biotechnology industry. It has a combination of both the most mature and financially robust firms, with the most young and financially tenuous ones. While being skewed towards the pharmaceuticals market overall, California still has more firms in each of the other biotechnology market segments than does any of the other states. The California biotechnology industry is also diverse in its industrial geography, with a different character apparent in the firms from each of the regions. There is considerable consolidation now taking place in the industry, with some of California's most established and well known firms at the forefront of this trend - yet it is also sustaining a relatively vigorous establishment rate for new firms. In short,

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[80] *Ibid.*, p. 15.

there is a rich industrial ecology amongst California biotechnology firms. This puts the state's industry in a position where its members are able to embark on some rather risky ventures without jeopardizing the prospects for the industry as a whole. The sheer size of the industry, and the maturity of some of its more established member firms, appears to reinforce a climate conducive to small scale entrepreneurship rather than detract from it.

The presence of a number of outstanding centers of research in the biomedical sciences, an attractive pool of appropriately skilled people, a fertile general financial environment, and a rich industrial ecology which enables firms to gain easy access to a wide range of technical services and specialized inputs, appears to give the California biotechnology industry an assured future, despite many obstacles. The capacity of firms to continue to raise funds from alternative sources in the face of the stock market crash and the general tightening of the public investment climate for biotechnology, suggests that the industry will remain relatively healthy, even in hard times. The continuation of high numbers of entrepreneurial biotechnology start-ups, even in what is apparently now a relatively hostile set of circumstances, suggests that the California industry will probably remain quite dynamic at the same time as it matures.[81]

The financially related evidence presented in this paper leads us to speculate on the future of the California biotechnology industry with the following observations.

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[81] Cf., Blakely and Willoughby, *op cit.*

Observation 1

We suggest that the financial difficulties now facing the California biotechnology industry will simultaneously reinforce the present trend towards greater consolidation between firms and within firms, and stimulate greater segmentation in the industry.

The logic for the first part of this observation (concerning the *consolidation* of the industry) was explained earlier: firms will continue to merge, collaborate, reduce the number of products and projects underway, and manage their assets more carefully, in order to cope with the cash shortages they now face. The logic for the second part of the observation (concerning the *segmentation* of the industry) also derives from the fact that biotechnology firms need to cope with the increasingly heavy competition for limited investment funds.

Large, relatively mature biotechnology firms appear to be able to meet their needs for massive amounts of capital to fund their commercialization by turning to the large industrial corporations (frequently pharmaceutical or chemical firms). Many of these established corporations are seeking to diversify away from their traditional products and production methods, and see the new biotechnology companies as sources of needed innovations. These larger corporations are prepared to take a long term view on the hoped-for return on their investments. While the amounts of capital needed by the growing biotechnology firms may be massive, measured against their own previous expenditures, for the large corporations, purchasing equity in the biotechnology firms (or purchasing the firms themselves) is a relatively cost-effective way of ensure that they maintain their share of the markets in which they have been operating and ensure participation in emerging new product markets. Putting some long-term risk capital into existing biotechnology firms may in fact be cheaper for them than attempting to accomplish the same achievements internally.

It is the well established biotechnology firms which are most likely to be the recipients of these big capital injections from major corporations. This is because they are the biotechnology firms most in need of large amounts of capital, and the ones most likely to reward the investing corporation with eventual windfall profits. Measured in terms of existing assets, these firms predominate in California, and they are most concentrated in the therapeutics sector.

As reported earlier in the paper, despite the institutional venture capital market having become tighter, there is still plenty of venture capital money available. Preferential access to such capital is now afforded, however, to those biotechnology firms and individuals with a proven track record. This has the net result of reinforcing the trend identified above of consolidation among biotechnology firms. Future financing of biotechnology firms, from both major corporations and from venture capitalists, therefore will most likely have the effect of rewarding the relatively well financed firms with even more finance: the "strong will grow stronger".[82]

If the preceding analysis is valid then it follows that the smaller start-up firms will have considerably greater trouble attracting development capital than did their predecessors. Should they wish to remain in business or avoid being taken over by other firms, it will become necessary for them to engage in activities which do not require such large amounts of capital and which offer relatively short pay-back periods. This will probably mean avoiding direct competition with the established firms, and avoiding the pharmaceuticals area in particular. Small firms will probably be attracted increasingly to fields of biotechnology which involve low regulatory obstacles and relatively little mandatory product trials, e.g., bio-

[82] BIRG is indebted for this insight to information gained through conversation with a number of biotechnology industry observers, especially Chistina Lowell of KPMG Peat Marwick, Oakland, California.

electronics or bio-informatics, industrial supplies, plant genetics for agriculture, energy production, environmental management, waste treatment, food processing or industrial process improvements. The diversity, size and rich industrial ecology of California's biotechnology industry makes it well placed to be at the forefront of this trend.

This trend, should it come about, represents increasing segmentation - that is, specialization - between firms in the biotechnology industry. Relatively mature biotechnology firms with substantial assets and easy access to capital will tend to specialize in the "high stakes" market areas, while the smaller, less wealthy firms will tend to specialize in the "low stakes" market areas with lower risks and faster pay-back potential.

If it indeed becomes feasible for small biotechnology firms to become profitable by specializing on the "low stakes" products, then a challenging question arises: if the small firms could make a profit in the non-pharmaceutical market areas, why wouldn't the large firms be able to do the same? Barring the possibility that some of the "low stakes" biotechnology product areas might be intrinsically better suited to exploitation by small firms than large, it follows that the more powerful, established biotechnology firms would also make a move into the currently less dominant product areas. If this happened, then the small entrepreneurial firms would be faced with very stiff competition, and given their weaker financial position, would have to develop innovative strategies for surviving, such as merging (or collaborating) with the larger firms, or discovering new market niches.

This paper showed earlier that presently the only profitable biotechnology firms, grouped by market orientation, are the suppliers (with California biotechnology suppliers being more profitable than those outside the state). This

fact should provide some stimulus to small cash-strapped firms to increasingly specialize in the direction of becoming suppliers. This, and the foregoing considerations, lead us to a refinement of our first observation: *the present financial trends in the U.S. biotechnology industry will lead to greater segmentation in the biotechnology industry, initially between firms oriented towards different market segments, but increasingly between large, well financed biotechnology firms which are oriented towards the "final markets" for a whole range of biotechnology products, and small, capital-scarce biotechnology firms producing "intermediate" products, the markets for which reside with the large biotechnology firms*. The rich industrial ecology of the California biotechnology industry may well mean that this trend will be most pronounced and rapid in California.

Observation 2

Observation 1, and its refinement, lead us to a second observation. *We suggest that the most important changes likely to take place in the California biotechnology industry during the next decade lie not so much with changes in its size, total economic importance, or direct employment levels, but with its detailed organizational structure and specialization, and with the structure of ownership and control.*

Our analysis of the financial trends in the California biotechnology industry, and its concomitant organizational patterns, leads us to conclude that the future of the industry looks relatively secure, in that there are indeed sources of capital available to finance the development and commercialization of the many soundly-based biotechnology firms in the state. What is at stake here? Not the survival of the industry - it looks destined to thrive. The control and ownership of the California biotechnology industry are the factors most under pressure as the industry progresses onto newer stages - not whether there will be employment, practical benefits from the application of new products, or new forms of wealth

generation. It is California's own stake in California's biotechnology industry that is most at stake!