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SELLING PROMISES:

AN ANALYSIS OF THE CONDITIONS INFLUENCING INITIAL PUBLIC OFFERINGS OF AMERICAN BIOTECHNOLOGY FIRMS, 1971-1993

A Dissertation

Presented to the Faculty of the Graduate School

of Cornell University

in Partial Fulfillment of the Requirements for the Degree of

Doctor of Philosophy

by

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BIOGRAPHICAL SKETCH

On January 28, 1956 Allan Ronald Ryan was born to Harry J. Ryan, Q.C. and Mary C. Ryan (née MacPherson) in Temiscaming, Quebec. His father died March 10, 1966. At that time, his mother, after a hiatus of over twenty years, reentered the workforce to support her four children: Steve, Catherine, Marilyn, and Allan. At the time none of them had yet finished their education. Over the course of the next 30 years, among them, they earned 12 university degrees and diplomas.

Allan Ryan graduated from De La Salle High School in 1972, and then spent a year on a Canada World Youth sponsored exchange program with Yugoslavia. Upon his return to Canada he entered C.E.G.E.P. at Champlain Regional College and graduated from a program in pure and applied science in 1976. After a brief period of work and travel he entered a philosophy program at McGill University and in 1979 graduated as a University Scholar with a B.A., First Class Honours. In 1980 he received an M.A. in Philosophy from the University of Toronto. In 1982 he received an M.B.A. from McGill University. After working for a year as Business Manager for a modern dance company (where he met his wife Laurel), he went to work for Canada Post Corporation. Mr. Ryan received his C.M.A. designation in 1988 from the Society of Management Accountants of Ontario.

In 1989 Mr. Ryan resigned his position as Manager of Financial Analysis at Canada Post in order to register in a Ph.D. program at Cornell. He received his M.S. in management in 1993. Mr. Ryan has held the position of Asssistant Professor at the University of Alberta since 1993. Allan and Laurel Ryan have three children: Christine 6, Steven 4, and Daniel 1.

To my sister Marilyn. You have always been there for me.

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This project would have never taken shape had it not been for the previous efforts Ralph Hybels, Steven Barley, and John Freeman made in collecting data on biotechnology firms. I thank them for allowing me to build upon their work when I created the database upon which this dissertation is based. This earlier effort was made possible, in part, by the fact that Professors Stephen Barley and John Freeman were the principal investigators for a grant from the National Science Foundation which provided seed money for mounting a range of studies of the biotechnology industry. I also thank Professor Jay Ritter for giving me an IPO time series that I used in constructing one of the graphs in this dissertation.

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I add the usual disclaimer that none of the individuals or the granting agencies and organizations that I have mentioned above are responsible for any of the inaccuracies, omissions, and other faults of the data, the argument, the results, or the conclusions of this dissertation.

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CHAPTER 1. INTRODUCTION

This dissertation is a study of the development of the population of independent American biotechnology firms in the years between 1971 and 1993. A central premise of this study is that, to develop knowledge of the dynamic forces that influence the evolution of an organizational form, attention must be directed not only to discovering the "stories" of individual organizations but also to modelling interactions among organizations at the level of the population. In the case of biotechnology I will argue that the stories and experiences of individual organizations were important insofar as they provided organizational paradigms that were widely copied. The essence of this study, however, is the examination of how environmental and population-level forces influenced the ability and propensity of firms to undergo a fundamental change in organization. The fundamental change with which I am concerned is the process by which firms underwent the transition from private to public ownership by selling their stock to the public for the first time in initial public offerings (IPOs).

THE SUITABILITY OF THE BIOTECHNOLOGY INDUSTRY FOR STUDYING IPOS

Of all of the new "industries" that have emerged in the latter half of twentieth century biotechnology is one of the oddest. The Office of Technology Assessment (OTA) goes so far as to deny that biotechnology is an industry at all. This denial of "industry status" is based largely on the observation that the ultimate product markets of biotechnology firms cannot be grouped within any traditional industry. In essence, the argument is that

since biotechnology firms do not share a common SIC code, biotechnology is not an industry. According to the OTA (1991, p. 3) biotechnology is "a set of biological techniques" that have been developed since the beginning of the 1970s and are now being applied to developing products and services in a wide range of basic industries.

The OTA is certainly correct that biotechnology firms possess widely divergent goals in terms of target markets and the types of products they are developing. In other ways, however, biotechnology firms represent a distinct organizational form and constitute a coherent organizational population that make it quite natural to describe biotechnology as an industry. Biotechnology firms are linked by three characteristics. First, biotechnology firms are made possible by a coherent set of new biological techniques that make possible the direct manipulation of processes at the sub-cellular and genetic levels. Second, biotechnology firms are unique in the way in which their early development is typically financed. With regard to financing, biotechnology firms are extreme both in the *degree* of their early, almost exclusive, dependence on large-scale equity investment, and in the *length of time* that passes before most firms introduce even a single product. For many years the operations of biotechnology startups expend massive sums on product research and produce little or no sales revenue. Third, the title "biotechnology firm" has come to have a distinct meaning for both the general public and the investment community. No matter how much diversity there is among the population of biotechnology firms, the very insistence of the public in grouping them together has practical impacts for their access to resources, their viability and their ability to influence the regulatory and political authorities which control their operations.

Some of the same features that make the biotechnology industry different from other industries also make biotechnology an ideal subject for studying the external influences on the decision to go public. If startup biotechnology firms have little choice as to capital structure because they are not able to issue debt[1] then conventional models of capital structure choices do not really apply and much of the complexity of the decision to issue equity is removed. Because of the magnitude of the financing requirements, because of the duration of this need, and because of the paucity of alternative sources of capital the biotechnology firm presents a comparatively simple context for studying the decision to go public.

THE IMPORTANCE OF THE STUDY OF INITIAL PUBLIC OFFERINGS

The focus of this dissertation is study of the process and impact of initial public offerings (IPOs) of stock in biotechnology firms. This process is important for a variety of reasons but I hold three to be paramount. First, the success of American biotechnology firms in raising money in public equity markets is widely believed to have enabled the United States to establish and maintain dominance in this new sector of economic activity. Second, the IPO engenders enduring and irreversible changes in the nature of the firms that choose to go public. The range of firm level changes include: loss of privacy, altered patterns of accountability, increased formality, altered incentive structures for employees and managers, and easier access to further capital. Going public also potentially increases the firm's exposure to takeover

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[1] Exceptions that prove the rule include Cell Products which failed after a junk bond financing arranged by Michael Milken (Bruck, pp. 116-117) and Agrigenetics which owed $60 million at the time it was acquired by Lubrizol in 1984 (*Business Week*, October 15, 1984, p. 45).

attempts and litigation initiated by shareholders, customers and competitors. Perhaps the most important change in firms that go public is that the additional investment can endow a firm with sufficient resources to support research that may lead to the development of a "blockbuster" product. Third, the IPO serves as a segregating mechanism within the population whereby the public firm is more likely to grow, to acquire other firms and to engage in a broader range of research than its private counterparts.

THE POPULATION ECOLOGY OF IPOS

Borrowing from concepts developed in the context of studies of the birth and death of organizations, I argue that counts of events affecting biotechnology firms, together with counts of the total number of firms (population density) in the biotechnology industry can be used to model competitive and legitimating forces that influence the rate at which firms launch IPOs. Regarding the IPO at the level of the population can enhance our understanding of how this event helps create and transform both industries and individual firms. The IPO is often analyzed primarily from the standpoint of the characteristics of the individual firm and the signals it generates by deciding to issue equity. Other studies incorporate consideration of the strategic postures of financial intermediaries such as underwriters. In this study, the unique features of the biotechnology industry that arise from the very ubiquity of the need for equity capital (and the absence of alternatives such as increased debt) makes it feasible to study environmental and population-level factors that influence a firm's ability and desire to go public.

Drawing on population ecology theory (Hannan and Freeman 1977, 1989; Hannan and Carroll 1992), I examine the ways in which the composition and activity of the general biotechnology population affects the degree to which individual firms choose (and are able) to make the transition from private to public ownership. In doing so, I propose extensions of the sociological constructs of legitimacy and competition that suggest that a greater degree of convergence with economic concepts of competition and efficiency are possible.

Much of the discussion that follows is rooted in a view of population-level processes grounded in Hawley's (1950) model of competitive processes which was summarized by Hannan and Freeman as follows:

> In Hawley's model, competition processes typically involve four stages: (1) demand for resources exceeds supply; (2) competitors become more similar as standard conditions of competition bring forth a uniform response; (3) selection eliminates the weakest competitors; and (4) deposed competitors differentiate either territorially or functionally, yielding a more complex division of labor. (Hannan and Freeman 1977, p. 940)

The conception of competition outlined above easily can be extended to the context of biotechnology firms competing for the "right to go public" and the consequent access to critical investment capital. First, money is always a scarce resource for any venture that faces considerable risk. Second, the success of high profile firms in using resources initially accessed through going public, when coupled with the development of a common environment (regulatory constraints, technical capabilities, and personnel availability) serves as an incentive for other firms to adopt "proven" patterns of organization and similar internal routines. Third, as time passes, winners and

losers emerge in the race for financing. Fourth, firms that fail to go public, but are able either to provide services to other firms or to sell themselves to others, start to occupy new organizational niches that accompany the development of a new division of labor within the biotechnology industry.

In this study, going public is viewed as an irreversible process that causes significant changes in the financial endowment of the firm, the internal operating routines of the firm, and the firm's overall capabilities. In the language of survival analysis, going public is regarded as an "absorbing state." Recognizing that not all firms go public, this study also considers three other alternatives: the firm remains privately owned, the firm is acquired by another firm, or the firm fails.

Firms that remain privately owned may do so for two different reasons and in two different ways. A biotechnology firm may remain private because its initial strategy made it capable of relying on internal cashflow instead of outside investment capital. Alternatively, a firm may remain private because inability to go public forces it to develop financial self-reliance. While it will be assumed that the majority of biotechnology firms are formed with a high need for external financing, this study will also allow for unobserved organizational heterogeneity related to the propensity to go public. In doing so, however, I will often assume that at least some of this heterogeneity is correlated with a variety of observable features of the organizations involved.

When private, independent firms are acquired by other firms they undergo changes that in most instances surpass even those associated with going public. Insofar as merging or being acquired often expands a firm's access to capital, this event can be seen to serve some of the same purposes as an IPO. The other impacts of being acquired are usually very different

from those associated with going public. For the purposes of this study, the acquisition of a firm is viewed as an end of the organization's history vis-à-vis the study of when and whether it goes public. While parts of larger firms are sometimes spun-off in IPOs, the factors associated with such events are inextricably linked to the features, fortunes and strategies of the parent firm. For these and other reasons, acquisition is regarded as a second "absorbing state" for the private biotechnology firm. I examine the degree to which the acquisition of biotechnology firms between 1971 and 1993 can be modelled but find no readily identifiable regularities in this process.

The final way in which a private biotechnology firm can come to an end is by outright failure. Failure is the classic and most obvious "absorbing state" and it is obvious how it keeps the affected firm from going public. In studying this event I find some indication of regularities that merit further investigation.

EVENT HISTORY METHODS

In this dissertation I introduce no new statistical techniques, but the models I estimate do demonstrate a variety of points related to survival or event history models. First, in this study I split the history of each firm into calendar quarters. In the model specifications where I employ this sub-spell duration it proves to be small enough that virtual convergence across different model estimation techniques is achieved. Second, I use bootstrap analysis (see appendix) of one of the main models to analyse the degree to which accepting the assumption of asymptotic normality of coefficient estimates is justified. With a bootstrap of 500 replications, the empirical bootstrap distributions of the parameter estimates show close convergence to the

distributions one would expect given the original model estimates, their attendant standard errors, and the assumption of asymptotic normality.

THE INSEPARABILITY OF THE IPO AND THE DEVELOPMENT OF BIOTECHNOLOGY

In 1995 there are signs that the biotechnology industry has already lived through its infancy, childhood, and early adolescence. The small startup biotechnology firm that, with the help of money raised in public stock offerings, managed to introduce some of the most innovative products of recent history is our paradigm of the biotechnology firm of the 1980s and early 1990s. Many of the firms that gave form to this image themselves no longer fit the profile. Genentech is controlled by major drug manufacturer, Cetus was acquired by another biotechnology firm and, as I write, Calgene is awaiting stockholder approval of an agreement to sell nearly half the firm to chemical and agricultural giant, Monsanto.

The biotechnology industry of the past was governed by a scarcity of personnel. In the early days of the industry the novelty of the science and lack of understanding of its potential created the need for extraordinary rewards to seduce "scientific genius" from universities where this commodity was stockpiled. As techniques and methods have become standardized the dependence of the industry on entrepreneurial risk-taking may be in the process of being superseded by an emerging dependence on large company distribution channels, controls, formality, and organization.

Whether or not the biotechnology sector continues to depend on IPOs for its growth and innovative capacity, I believe that understanding the effects organizational characteristics, environment, and the population have had on

the biotechnology IPO can teach us important lessons. Among the points that I attempt to make throughout this study is that even a financial market phenomenon such as the sale of stock through IPOs can be understood better if we step beyond an atomistic view of the organization, the entrepreneur, and actions undertaken by the organization. Financial transactions take place within a social and institutional framework that is broader than most discussions of these phenomena suggest. While I make no pretense to incorporate all elements of social and economic context into this study, the fact that it is a study of the IPO at the level of a whole population constitutes a significant innovation that broadens our understanding on what kinds of forces impinge on the financing decisions of firms.

CHAPTER 2. HISTORICAL BACKGROUND OF THE INDUSTRY AND THE SIGNIFICANCE OF IPOS

The emergence of new industries and new technologies has long captivated the interest of economists, organizational sociologists and historians. Indeed, the development of industries is a subject that almost everyone has been told is of great importance. As children we learned how the railroads and the canals shaped the development of North American commerce and the distribution of its population. As children we were also exposed to the idea that the mechanization associated with the industrial revolution reshaped social relations among the classes, inspired new ideas and led to redistribution of wealth. Finally, even as school children most of us were exposed to ideas about how ownership patterns and financial markets influence individual companies, whole industries and even the international competitiveness of nations. If we consider ideas such as these with which almost all of us are familiar, we are virtually compelled to conclude that the study of the rise of an industry is a process that academics believe must often be considered in a very broad economic, social and political context. The rise of the biotechnology "industry" must certainly be a case where, if context is ever important, the context of its development is an absolute prerequisite to understanding its current form.

The factors that were significant in the development of the biotechnology industry[2] (and that continue to shape it) are a broad array of scientific, technological, economic, institutional and political influences. An

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[2] As will be discussed in chapter 4, the term industry is used loosely. Biotechnology is unified by the science upon which it is based, not the markets that the firms will eventually serve.

argument I will make in this chapter is that the ability of biotechnology firms to resort to public equity markets for financing had a critical impact both on the industry and on individual companies. In addition, I will advance the thesis that the way in which the biotechnology sector developed and was financed had a profound and wide-ranging impact on the environment in which this took place.

New forms of economic organization and new industries are often products of their times (Stinchcombe 1965). In many cases, new kinds of organizations and new industries also place an indelible stamp on the period in which they arise and on the subsequent development of the economies and nations that serve as their nurseries. As historians reflect on the emergence of the biotechnology industry I expect that the following two points will be made: biotechnology firms bear the stamp of the times in which they arose, and the emergence of biotechnology firms led to profound transformations of the competitive environments that surrounded them. While biotechnology is a product of the last quarter of the twentieth century, it is also a symbol of what the future holds and a virtually inescapable feature of our present experience. Biotechnology has already revolutionized our capabilities in medicine, agriculture, waste treatment and criminology. The advent of biotechnology has also led to the reshaping of patent law, the reconsideration of basic tenets of ethics, and has caused many to rethink the way that high-risk, innovative businesses are financed. In a very real sense, the biotechnology industry and its environment have "co-evolved" in much of the same way this idea is developed by Baum and Singh (1994, pp. 379-402).

BIRTH OF AN INDUSTRY

In a discussion of the history of the microcomputer manufacturing industry Philip Anderson writes:

> In the beginning, there was the Altair.
>
> Not really, of course. Pinpointing the birth of an industry is difficult, for most innovations have precursors and near-neighbors. The first microcomputer represented an evolutionary branching, not wholly new, but enough of a departure to signal the emergence of a new organizational population. (Anderson 1995, p. 37)

In the same spirit we might say: In the beginning, there was Cetus. When Cetus was founded 1971 the idea of controlling new biological technologies to develop new products was novel enough to distinguish Cetus as one of the first of a new breed of companies. The fact that its founders (Bylinsky 1980, p. 149) were a microbiologist with a Harvard MBA (Ronald Cape), an M.D. with a Stanford MBA (Peter Farley), a Nobel-winning physicist who had become a molecular biologist (Donald Glaser), and a prosperous venture capitalist from Berkeley (Moshe Alafi) who was fond of referring to himself as "a poor Jewish farmer from Baghdad" (Bylinsky 1980, p. 149) was enough to make Cetus a very different kind of company. The novelty of its founders sufficed to set Cetus apart from other companies, but it was the technologies that these men dreamed of commercializing that made Cetus revolutionary.[3] Cetus was built in the anticipation of a new age of science where man's ability to control, modify and harness biological processes would be based on understanding and targeted intervention in the very basic processes of life,

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[3] According to Kenney, Cetus was originally founded to develop "superior antibiotic producing bacteria through natural selection" (1986, p. 135).

interventions that would have been impossible just a few years earlier. At the time Cetus was founded, the commercial potential of the emerging scientific understanding of DNA, cellular processes and biochemistry were just beginning to be appreciated. Soon after Cetus was founded the scope of the capabilities of the new biotechnology startups (including Cetus) would be vastly expanded by the development of monoclonal antibodies and recombinant DNA technology.

The idea of harnessing biological processes for commercial ends is by no means new. Industries such as brewing, cheesemaking, yogourt-making and baking have long relied on the cultivation and breeding of microorganisms, bacteria, and unicellular fungi. Plant and animal breeders have long taken an interventionist approach to modifying the phenotype of the organisms they were concerned with. Medical doctors since Jenner's development of the smallpox vaccine had also been experimenting with and modifying viruses. More recently, Fleming's discovery of penicillin (produced by a mold) and the subsequent identification of streptomycin (produced by a fungus found in soil) had demonstrated that living organisms could be employed in the development of new agents to fight disease. What was new about the technologies that started to be applied in the 1970s was that they were based on an understanding of cellular and sub-cellular processes and often involved the direct modification of the genetic structure of life. Two of the most basic discoveries of the age of biotechnology were recombinant DNA (rDNA) and monoclonal antibodies produced by hybridomas.

THE NEW TECHNOLOGIES

The first of the two seminal technologies that were to shape the biotechnology industry originated (in part) in the same San Francisco Bay area in which Cetus had been founded a couple of years earlier. As the story is recounted in *Recombinant DNA: The Untold Story* (Lear 1978, pp. 59-66) the collaboration between Herbert Boyer, a University of California at San Francisco biochemist, and Stanley N. Cohen, a member of the faculty at Stanford University Medical Department began in November 1972 at a late-night kosher delicatessen in Honolulu where they were both attending a conference. In this improbable setting, Cohen outlined how he believed his work on plasmids (rings of DNA found outside of chromosones) could be combined with Boyer's work with restriction enzymes (enzymes with the ability to cut string of DNA at known spots) to allow for the safe and predictable combination of DNA from different sources.

Over the course of the next year Boyer and Cohen were able to devise procedures for inserting novel genetic material into the bacterium *Escherichia coli* in such a way that the makeup of the bacterium was permanently altered. The resultant bacterium retained its ability to reproduce and it proved that the modified DNA was faithfully replicated. As Ryan, Freeman and Hybels summarize the procedure:

> In simple terms, restriction enzymes provided the means for judiciously slicing DNA, and plasmids provided the raw materials for attaching new DNA to the sliced ends, hence, recombinant DNA (rDNA). (Ryan, Freeman, and Hybels 1995, p. 334)

John Lear contrasts Cohen and Boyer's achievement with similar research conducted earlier by writing:

> But the Cohen-Boyer team had gone farther with plasmids than Jackson, Symonds, and Berg had gone with viruses, and some said that whereas the virus method of hybridizing was extremely sophisticated and tedious to duplicate, the plasmid technique was so simple that high-school students could easily learn it. (Lear 1978, p.66)

Simplicity and reproducibility gave Cohen and Boyer's recombinant techniques a commercial applicability that no previous breakthroughs in adjacent areas of biochemistry and molecular biology had really possessed.

The second seminal innovation in the race to commercialize biology came about two years later and halfway across the world at the Medical Research Council's Laboratory of Molecular Biology in Cambridge, England. Cesar Milstein and Georges Köhler created their first hybridomas in 1975. Hybridomas are essentially cells formed by the fusion of two different cells, one a myeloma (a type of tumor cell with an ability to reproduce reliably for long periods in a test-tube environment) and with a B-lymphocyte that has been conditioned to produce a specific kind of antibody. The resultant cell has the immortality of the myeloma and the antibody producing capability of the B-lymphocyte. In essence the hybridoma is a cellular factory for producing a pure form of the desired antibody. This pure form of the desired antibody is referred to as a monoclonal antibody or Mab. Like Cohen and Boyer's technique, the beauty of Milstein and Köhler's innovation was its simplicity, its reproducibility and its generalizability. In short, hybridomas had commercial potential, the potential to become cellular factories for the production of antibodies and other materials.

PATENTS

By the end of 1975, with two of the basic techniques of biotechnology having already been devised, one essential element necessary for the development of a new industry was in place.[4] What was not in place at that time, however, was the ability to claim ownership of biological innovations. This situation was already in the process of changing. Both Cohen and Boyer's rDNA techniques and Milstein and Köhler's development of hybridomas could be viewed as both commercial and scientific advances. Milstein was not oblivious to the commercial potential of hybridomas and even went so far as to advise the Medical Research Council that it might consider pursuing a patent (on their behalf, not his own). They chose not to do so (Yoxen, p. 105).

Neither Boyer or Cohen were as prescient or perhaps as bold as Milstein, they published their results and did nothing to pursue (or to suggest that others pursue) patent protection. The director of Stanford's technology transfer program was not nearly so reticent. In 1974, just before a year had elapsed from the publication of their results (at which time the ability to pursue patent protection would also have elapsed), Stanford, on behalf of itself and the University of California at San Francisco, filed the first patent application for what was eventually to become the Cohen-Boyer program. This application was kept secret until 1976 when, at a conference, Cohen

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[4] By the end of 1975 Caltech scientist Leroy Hood (Ciotti, 1985) had already started developing an automated protein sequencer that was to prove invaluable to practical biotechnology. It was to be almost ten years, however, before Cetus scientists devised the Polymerase Chain Reaction (PCR) technique for gene amplification that has also proven to be a central tool in biotechnology research (*Biotechnology Newswatch*, December 7, 1987, p.1).

responded to a rumor that someone was attempting to patent basic tools of science.[5] When Cohen revealed the actual status of the Stanford patenting effort, Boyer and Cohen were subjected to personal attack and criticism (Yoxen, p. 76). To their critics, the fact that both scientists had renounced personal interest in the patent gained them little respite from attack. In some ways, the criticism of Boyer became even more intense as his commercial interests (most specifically his connection with Genentech) served to make him one of the first biotechnology multi-millionaires. That Boyer and Cohen have never received a Nobel for their work is sometimes attributed to their commercial connections (Teitelman, p. 218). Milstein and Köhler are probably not as wealthy as their American counterparts, but in 1984 they did share a Nobel prize.

In the end, though, the decisive moment in establishing the patentability of life was to be instigated by a discovery that eventually proved to have relatively little direct commercial significance. In 1972 Ananda Chakrabarty, a scientist working in the Schenectady laboratories of General Electric, devised[6] a *Pseudomonas* bacterium that "was able to break down four of the principal components of oil" (Yoxen, p. 79). Initially, the Patent and Trademark Office (PTO) had accepted the patent application insofar as it related to the production of the bacterium and the methods of its potential use for the remediation of oil spills. What the PTO did not agree to was patent coverage of the organism itself (OTA, 1987b, p. 49).

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[5] Their objections were based both on the premise that ownership might stifle the ability of other scientists to employ essential tools but also because many believed that their success was grounded on the work of many who had made previous discoveries upon which their rDNA process relied.

[6] According to Watson and Tooze (p.489) he did so using "conventional genetic manipulations" not recombinant techniques.

The legal battles and appeals surrounding the Chakrabarty bacterium soon came to revolve around the issue of whether living things could be patented. On June 16, 1980, the U.S. Supreme Court resolved this legal debate by ruling five to four in favor of the patent applicant. This patent dispute that has entered patent history as *Diamond v. Chakrabarty*. The substance of this decision was that "the question of whether or not an invention embraces living matter is irrelevant to the issue of patentability, so long as the invention is the result of human intervention" (OTA, 1987b, p. 49). In the majority opinion, Chief Justice Burger and his colleagues held that the intent of Congress had been to have patents comprehend "anything under the sun that is made by man" (Watson and Tooze, p. 504; *Diamond v. Chakrabarty*, p. S.6).

Many view the Chakrabarty decision as the incident that opened the floodgates for the commercialization of biotechnology. Before the end of the year the Chakrabarty patent was joined by the far more commercially-significant Cohen and Boyer patent. On December 2, 1980 a patent entitled "Process for Producing Biologically Functional Molecular Chimeras" was granted to "Cohen et al." Under this, and two subsequent patents collectively referred to as the Boyer-Cohen program, Stanford collected approximately $17 million[7] in 1991 and "is expected to make $150 million by the time it expires in 1997" (Hower, 1992). The year 1980 also saw Congress pass the

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[7] If one relies on figures provided in the Office of Technology Assessment publication *New Developments in Biotechnology: Patenting Life* (OTA 1987b, p. 56), as recently as 1987 annual earnings had been only one tenth of this amount.

Patent and Trademarks Amendments Act of 1980 which removed obstacles from universities seeking to patent work funded by government agencies.[8]

WHY HAS BIOTECHNOLOGY BEEN DOMINATED BY SMALL COMPANIES?

Large American (and foreign) companies have never been blind to the commercial potential of biotechnology. In February of 1975 Merck, Roche, G.D. Searle and General Electric were all represented in one way or another when scientists gathered in Pacific Grove California for the Asilomar conference on the dangers of recombinant technologies (Rogers 1977 p. 59). As early as 1974 Monsanto had funded a joint biomedical research program at Harvard *(Genetic Engineering and Biotechnology Firms Worldwide Directory: 1985*, p. 210). As yet another example of early corporate interest in biotechnology, between 1977 and the end of 1978 Standard Oil of California, Standard Oil Company (Indiana) and National Distillers all became significant investors in Cetus[9] (*Genetic Engineering and Biotechnology Firms Worldwide Directory: 1985*, p. 76). These same companies were also contracting Cetus to perform biotechnology research for them. By 1979 other companies that had active interests in biotechnology included Koppers, Emerson Electric, Du Pont, Exxon, Schering-Plough, and Upjohn (*Business Week*, October 22, 1979, p. 160). Despite all this early interest, the majority of the product innovation within the industry has originated in the laboratories of companies

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[8] Stanford had been able to file the Boyer-Cohen patent only because the university had a specific exemption for this work.

[9] According to *Fortune Magazine* (Bylinsky, June 16, 1980, p. 149), by 1980 these three companies had purchased 65% of the company for $30 million. Some of their holdings were purchased directly from Cape, Farley and Glaser who each pocketed $2.5 million.

formed explicitly to exploit the new biotechnological advances. This raises the interesting question of why this is so.

Before the question of why small firms have dominated biotechnology can be addressed, evidence that this claim is more than a romantic fiction must first be offered. A review the history of product innovation in the area of human medical therapeutics provides some self-explanatory support for the claim. Table 2-1 presents a summary of human therapeutics approved by the American Food and Drug Administration (FDA) for the period from 1982 (when the first biotechnology-derived therapeutic was introduced) until the end of 1993. Of the fifteen types of substances, thirteen[10] started on the route to commercialization in the laboratories of biotechnology startups (sometimes in concert with researchers in universities) and not in those of established pharmaceutical firms. Of the thirty one approvals of the twenty two branded drugs that were received for twenty four different conditions, all but three approvals were for drugs which had originated with biotechnology startups. Indeed, of the thirty one approvals, nine were for drugs developed by Genentech, six for drugs from Biogen, and five were for drugs from Amgen. The involvement of the pharmaceutical houses was primarily as marketers for the drugs (twenty of the total approvals) and, with Hoffman-LaRoche's 1990 acquisition of a majority of Genentech, as purchasers of the companies that had originated the innovations.

Perhaps the dominance of the biotechnology startup is less pronounced in certain other areas of biotechnology, but the innovative

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[10] The exceptions are Ortho's OKT-3 and the haemophilus-B conjugate vaccines which were developed by an American biotechnology startup (Praxis), an established Canadian vaccine producer (Connaught), and by Merck. Whether to include these conjugate vaccines in this list is also somewhat questionable given the kind of science required for their production.

Table 2-1: FDA Approvals of biotechnology-derived human therapeutics from 1982 until the end of 1993

DRUG TYPE	MARKETING COMPANY	ORIGINATING COMPANY	CONDITION	FDA APPROVAL	SOURCES
HUMAN GROWTH HORMONE rDNA ORIGIN					
Humatrope	Eli-Lilly	Amgen	Growth deficiency in children	03/08/87	PRN 03/09/87
Protropin	Genentech	Genentech	Growth deficiency in children	10/18/85	Business Wire
ALPHA INTERFERON					
Roferon-A	Hoffmann-LaRoche	Genentech	Hairy cell leukemia	06/04/86	Henderson, 1986
Intron A	Schering-Plough	Biogen	Hairy cell leukemia	06/04/86	Henderson 1986
Intron A	Schering-Plough	Biogen	Genital warts	06/06/88	PRN
Intron A	Schering-Plough	Biogen	Aids related Kaposi's sarcoma	11/21/88	BN 12/05/88
Intron A	Schering-Plough	Biogen	Hepatitis C	02/25/91	Shenot 1991
Roferon-A	Hoffmann-LaRoche	Genentech	Aids related Kaposi's sarcoma	11/21/88	BN 12/05/88
Intron A	Schering-Plough	Biogen	Hepatitis B	07/13/92	Rosenberg 1992a

NOTE: Unless otherwise noted, all sources are for the same date (all dates in MM/DD/YY format) as the FDA approval date. PRN stands for *PR Newswire*, NYT stands for *New York Times* and BN stands for *McGraw-Hill Biotechnology Newswatch*. An earlier version of this table appeared in Ryan, Freeman and Hybels (pp. 340-341). The table format is adapted from a table that appeared in *Biotechnology In A Global Economy* (OTA 1991, p. 77).

Table 2-1 (Continued)

DRUG TYPE	MARKETING COMPANY	ORIGINATING COMPANY	CONDITION	FDA APPROVAL	SOURCES
HUMAN INSULIN rDNA ORIGIN					
Humulin	Eli-Lilly	Genentech	Diabetes	10/29/82	UPI
MAB ANTI T-CELL					
Orthoclone OKT 3	Ortho	Ortho	Kidney transplant rejection	06/19/86	PRN
HEPATITIS B VACCINE (RECOMBINANT MSD)					
Recombivax HB	Merck	Chiron	Hepatitis B prevention	07/23/86	FDA Consumer
Engerix-B	Smithkline Beecham	Biogen	Hepatitis B prevention	08/28/89	NYT, 09/09/89
TISSUE PLASMINOGEN ACTIVATOR, t-PA					
Activase	Genentech	Genentech	Heart attacks	11/13/87	Business Wire
Activase	Genentech	Genentech	Pulmonary embolism	06/06/90	NYT 06/07/90
HAEMOPHILUS B CONJUGATE VACCINE					
Hib TITER	Praxis Biologics	Praxis Biologics	Haemophilus-B (children)	12/22/88	PRN
PedvaxHIB	Merck	Merck	Haemophilus-B (children)	02/12/90	PRN
ProHIBit	Connaught	Connaught	Haemophilus-B (children)	12/23/87	PRN
Hib TITER	Lederle	Praxis Biologics	Haemophilus-B (infants)	10/04/90	PRN

Table 2-1 (Continued)

DRUG TYPE	MARKETING COMPANY	ORIGINATING COMPANY	CONDITION	FDA APPROVAL	SOURCES
ERYTHROPOIETIN ALPHA					
Epogen	Amgen	Amgen	Dialysis anemia	06/01/89	PRN
Procrit	Ortho	Amgen	AIDs related and pre-dialysis anemia	12/31/90	Antivirals Agents
Procrit	Ortho	Amgen	Chemotherapy induced anemia	1993	
BOVINE PEGADEMASE					
Adagen	Enzon	Enzon	Combined Immunodeficiency disease	03/23/90	Reuters
INTERFERON GAMMA 1-B					
Actimmune	Genentech	Genentech	Granulomatous disease	12/21/90	PRN
GRANULOCYTE FACTORS					
Neupogen	Amgen	Amgen	Chemotherapy white blood cell destruction	02/21/91	PRN
Leukine	Immunex, Hoechst	Immunex	Post transplant bone marrow infections	03/05/91	PRN

Table 2-1 (Continued)

DRUG TYPE	MARKETING COMPANY	ORIGINATING COMPANY	CONDITION	FDA APPROVAL	SOURCES
INTERLEUKIN-2					
Proleukin	Chiron	Cetus	Renal cancer	05/05/92	PRN
RECOMBINANT FACTOR VIII					
Recombinate	Baxter Hyland	Genetics Institute	Hemophilia A	12/10/92	Rosenberg, 1992b
Kogenate	Miles Labs	Genentech	Hemophilia A	03/15/93	Marketletter
INTERFERON BETA-1B					
Betaseron	Chiron	Chiron	relapsing Multiple Sclerosis	07/23/93	PRN
DORNASE ALPHA					
Pulmozyme	Genentech	Genentech	Cystic Fibrosis	12/30/93	Shogren

capacity of the biotechnology startups is still impressive. Calgene has long been the standard bearer in the area of agricultural biotechnology. With the introduction of genetically altered products such as Calgene's genetically altered tomatoes and cotton, the agricultural biotechnology startups are starting to emulate their pharmaceutical cousins. According to *Science* (Wade 1980b) the very first rDNA product introduced was likely a "DNA ligase from Escherichia Coli produced from a gene cloned by Robert Lehrman of Stanford" and introduced by New England BioLabs in 1975. The first biotechnology-derived diagnostic product approved for use in the United States was a monoclonal antibody test for allergies produced by Hybritech (an American startup). Indeed, the examples of how biotechnology startup firms were pioneers in commercializing the new biological technologies are legion.

THREATS OF LIABILITY

One reason frequently given to explain the rise of small biotechnology companies is that the large, established companies were fearful of the legal liability a biotechnology accident might create for their companies. We have only to refer back to the earliest press coverage given to the subject of recombinant technology to be reminded of the extent to which, in its initial years, in the minds of ordinary citizens rDNA was virtually synonymous with the threat of renegade manmade diseases. In 1974 the Berg open letter entitled *Potential Biohazards of Recombinant DNA Molecules* (signed by Paul Berg, David Baltimore, Herbert Boyer, Stanley N. Cohen, James D. Watson and six other leading scientists) was published in *Science* (Berg et al. 1974, p. 303). This document called for a moratorium on rDNA research until adequate

safety standards could be devised. The Berg letter brought the issue of risks to the wide attention of the media and the public around the world.

The following year, in a sequel to the Berg letter, 140 of the world's leading scientists gathered in Pacific Grove, California at the Asilomar Conference Center for a debate on how to proceed with rDNA research. The 1975 Asilomar conference, which ran between February 24th and the 27th, captured the attention of the world. One of the leading accounts of the conference was written by Michael Rogers, a writer for *Rolling Stone*, and was titled "The Pandora's Box Congress" (Rogers 1975). As Rogers tells the tale, presentations by lawyers on the subjects of risk, liability and other points of law made strong impressions on the scientists present. If scientists were preoccupied with the threat of litigation, the impact of this kind of consideration was probably even more profound in the boardrooms of corporations considering biotechnology investment.

Events over the course of the next couple of years would reinforce the public perception of biotechnology as hazard. The debate once again rose to the level of public theater when the City Council of Cambridge, Massachusetts declared a ban on recombinant DNA research until such time as a citizen's enquiry could be held to decide upon safeguards (Watson and Tooze, pp. 91-94). In 1977, anti-biotechnology activism was to rise to new heights when Jeremy Rifkin disrupted a National Academy of Sciences meeting dealing with rDNA policy (Krimsky 1991, p. 109). Rifkin[11] was to become one of the

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[11] Rifkin has proven to especially successful in opposing the use of biotechnology in food products. While drugs and diagnostics were introduced in a manner not unlike their non-biotechnology counterparts, companies such as Calgene with its FLAVR-SAVR tomato and Monsanto with its bovine somatotropin (BST), which stimulates milk production in cows, have proven to be much more exposed to public protest of biotechnology products.

constants in the debate over biotechnology policy and was to be a thorn in the side of companies involved in biotechnology research long after much of the fire of the debate had subsided.

As Barney, Edwards and Ringleb (1992) have argued, being small (and having few assets) is an advantage for a company dealing with potentially hazardous technologies. Having "deep pockets" is a disadvantage in dealing with tort risks not only because the assets exposed to litigation are more extensive but also that the likelihood of being sued rises with the belief that a company could pay damages. The presence of so-called "deep pockets" also appears to influence the actual deliberations and decisions of juries and judges. In a *New York Times* article published in 1980, journalist Anthony J. Parisi offered the opinion that, while engaging in a variety of contracts, alliances and investments, large companies had avoided direct involvement in biotechnology research for fear of litigation and bad publicity. In the same article, however, it is noted that by 1980 this fear had diminished sufficiently that the large pharmaceutical and chemical companies recently had been racing to set up their own biotechnology research operations. In promoting its Boyer-Cohen patent, Stanford had set the end of 1981 as the deadline for payment of licensing fees for companies employing rDNA technologies. By the time the Stanford deadline expired, seventy two corporations (*Biotechnology Newswatch*, December 21, 1981) had paid for rights to use this technology. Among the licensees were most of the major American pharmaceutical and chemical companies. It was evident that litigation threats alone were no longer enough to discourage large corporations from involving themselves in biotechnology. If this is so, how was it that, even after the early

1980s, the startup biotechnology firm continued to be a primary source of innovation in the biotechnology sector?

GREED, STRONG INCENTIVES AND THE BIOTECHNOLOGY IPO

I will argue that one of the primary reasons small companies continued to lead in the development of biotechnology throughout the 1980s was because of changes in American financial markets. Most particularly, the resurgence of the market for IPOs made it possible for small companies to succeed in biotechnology at the same time as it created a unique set of incentives that could make scientists richer than baseball players. In short, the conditions that allowed biotechnology companies to launch IPOs could also make university scientists captains of industry and media stars. Scientists were able to make fortunes, avoid becoming employees of big companies and also to retain the prestige of their university appointments. All this was possible because biotechnology had captured the interest of the broad investing public.

The 1970s witnessed the birth of the technologies upon which biotechnology was based. By the late 1970s, the legal cases whose resolution would form the basis of the law upon which the biotechnology industry was to rely had already been initiated. For the most part, however, the economic environment that prevailed for most of the 1970s was less than auspicious for the financing of new businesses. Throughout the 1970s public attention was focused on inflation, stagnant production, and worries about the security of energy supplies. The 1970s opened with Nixon battling a currency crisis and declaring himself a Keynesian, and closed with Jimmy Carter smarting from a second OPEC crisis and deciding to appoint monetarist Paul

Volcker as Chairman of the Federal Reserve. The 1980s, on the other hand, began with a soaring dollar. Foreign funds began to flood into the country in reaction to high American interest rates coupled with the prospect of low inflation. Even as General Motors faltered and Chrysler balanced on the precipice, the financial community was gathering for a feast. In 1980 Peter Lynch (a much celebrated mutual fund manager who was to become a folk hero of the investing public) had already assumed responsibility for the Fidelity Magellan Fund. By 1980 the 1978 re-interpretation of the "prudent man rule" already had led pension funds to begin to devote a portion of their assets to higher risk investments.[12] At this time the recent lowering of capital gains taxes had also begun to contribute to a stimulated interest in stock market and venture capital investing (Ross 1979).

While the stories of the creation of the early biotechnology firms are firmly fixed in people's minds as stories of venture capital, in fact the 1970s was a period of relative stagnation in the venture capital field. In a 1979 interview (Ross 1979), *Venture Capital* publisher Stanley E. Pratt, a prominent student of the venture capital industry, remarked that in 1978 the tide in the industry had begun to change. This remark was made against an historical backdrop of where for most of the 1970s venture capital had been scarce, financing through IPOs had been a rarity, the stock market had been lackluster, and the cost of money had been high.

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[12] On April 25, 1978 the Department of Labor proposed a change in the regulation of the Employment Retirement Income Security Act (ERISA) which constituted a recognition that prudent investment policy should not preclude inclusion of "risky investments" inside a balanced investment portfolio. This decision opened up a significant new source of funds for small companies.

Despite the fact that the 1970s was a decade of relative stagnation for the venture capital industry, it is the 1970s that produced some of the most quoted examples of the power of venture capital. The way Ken Olsen built Digital Equipment (DEC), and brought it public based on venture capital investment was the venture capital fairy-tale-come-true story of the 1960s, but by the late 1970s this was old news—the mythology of venture capital was due for renewal. By the early 1980s the DEC story began to be superseded by the story of how Genentech was born over a few beers at a Friday afternoon meeting between Boyer and Kleiner Perkins venture capitalist Robert Swanson.[13] The story of this meeting has been elevated to status of a creation myth for the biotechnology industry (Quinn, 1982; Teitelman p. 25). The central feature of the myth is the idea that venture capital was the primary source of early biotechnology financing. In fact, relatively few biotechnology firms were founded in the 1970s with or without venture capital.

Three of the firms that were founded during this period were Cetus, Genentech and Biogen. All three of these firms were founded with the direct involvement of venture capitalists (Moshe Alafi, Kleiner Perkins and TA Associates respectively), but, if one inspects the record, the bulk of the actual financing came from the pockets of large corporations. As we have already seen, Cetus received its large infusions of cash from two oil companies and a distiller.[14] By the time Genentech was founded in 1976 one of the major sources of funding for biotechnology startups was beginning to be the venture

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[13] Swanson had just moved to Kleiner Perkins from Citicorp Venture Capital Ltd. in 1975 (Quinn 1982).

[14] As of 1979, Standard Oil (California), National Distillers and Standard Oil (Indiana) had provided $30 million of Cetus' $35 million capitalization (*Business Week*, October 22, 1979).

capital arms of some of America's largest corporations. By the time Biogen was founded in 1978 it was Inco[15] that provided the bulk of startup funds and it was Inco, Schering-Plough and Monsanto that provided virtually all of Biogen's funding through the end of 1980 (Quinn 1989). If the trend had continued, biotechnology firms would have relied almost exclusively on big companies for cash, at the same time as they relied on venture capitalists for organizational impetus and for brokering the relationship with big company investors. This arrangement might not have led to the proliferation of independent firms that came to characterize the biotechnology industry. Indeed, had biotechnology firms had to continue to rely on the combination of large companies and venture capitalists one wonders whether even the existing firms would have been able to remain independent. The events of 1980 were to lead to a fundamental alteration in the dynamics of how biotechnology firms secured financing and, by consequence, would lead to a recasting of the form of organization that was favored by biotechnology firms.

THE FINANCIAL MARKETS OF 1980

Along with the story of how Genentech was dreamed up on a Friday afternoon in San Francisco, perhaps one of the most cited events in the organizational history of the industry was the Genentech IPO of October 14, 1980. The typical citation concerning this event is that the offering set "a new Wall Street record for the fastest ever price increase per share--from $35 to $89 in 20 minutes--and netted the company some $36.6 million" (Quinn 1989, p. 208). The press reveled in the event. By the following March, Boyer's face

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[15] Inco (the Canadian mining concern) had already purchased 15% or Genentech by this time and had also invested in Cetus (Bylinski, *Fortune*, June 16, 1980).

would stare out from the cover of *Time* magazine as one of the icons of the age, overshadowing even the image of Diana the princess-to-be which was relegated to a tiny corner of the same cover.[16] At the time "yesterday's" corporate America was reeling from the onslaught of Japanese and German industrial competitors and its reputation was being tarnishing by its failures. By contrast, Genentech and Cetus seemed to represent a combination of American scientific superiority, American entrepreneurial verve, and the power of the American stock market. In a stunning shift in public opinion, the American automobile and American steel manufacturers had come to stand for the "rust-belt" while American biotechnology firms were coming to stand for hopes of an American industrial renaissance. The IPO and venture capital were also beginning to be regarded as the engines that would launch these firms into the twenty first century.

The same month as Boyer's cherubic smile greeted America from the cover of *Time*, Cetus went public (March 6, 1981) and set a record for the most money ever raised in an IPO (Quinn 1989, p. 208). *Time* christened Boyer's picture with the subtitle "the boom in genetic engineering," Teitelman described the phenomenon as follows:

> It was an impressive outpouring of capital. Even more unusual was the number of academics involved in these new firms. This was a new phenomenon: never had a new industry arisen with university scientists playing such a major role. In just a few years there would be over 100 public biotechnology companies fueled by some $500 million in new publicly invested capital. The phenomenon took on a name: biomania. (p. 13)

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[16] The issue was *Time*, March 9, 1981. The cover is reproduced in Watson and Tooze (p. 523).

One interesting feature of Teitelman's book is that it documents the emergence of the instant biotechnology firm. While Teitelman doesn't call Genetic Systems an "instant biotechnology firm," the story he tells of its formation by the Blech[17] brothers is to all intents and purposes a chronicling of how firms (focusing especially Genetic Systems) were organized quickly in order to take advantage of the public's hunger for biotechnology investments.

THE IPO AS THE INSTIGATION FOR THE INSTANT BIOTECHNOLOGY FIRM

At the time the Blechs formed Genetic Systems they were not established members of the venture capital club. Instead, David Blech was a twenty-four-year-old stockbroker and sometime musician and his brother Isaac was a thirty-year-old advertising copywriter. David Blech didn't even work for an elite brokerage house, he worked for Muller & Company which Teitelman described as operating "far from the thud of big stocks like General Motors or the whirl and crash of brokerage firms like Merrill Lynch or Salomon Brothers" (p. 36). Muller was not a Kleiner Perkins, and David Blech was not a Robert Swanson, but, like Swanson, Blech was capable of seeing money "sitting on the table."[18]

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[17] Information on the Blechs is drawn from Teitelman (1989), Kleinfeld (1983) and Saunders (1983), but stories of the Blechs abound in press accounts.

[18] In an interview with Teitelman, Nelson Schneider (a pharmaceutical analyst at EF Hutton and one of the first analysts to follow biotechnology) offered the opinion that Swanson had recognized "money sitting on the table" when over 500 "money managers, investors, investment bankers and analysts" (Teitelman p. 26) crowded into a room at the Plaza Hotel in New York to hear about biotechnology.

As the story goes, Blech was first inspired by a magazine story on monoclonal antibodies. Shortly thereafter the Blechs began planning to form a biotechnology company with a view to bringing it public. Genetic Systems was founded in November of 1980, the Blechs invested about $200,000 and, on basis of having recruited one of the top scientists to lead the venture (Robert Nowinsky), were able to raise almost another $2.4 million (Genetic Systems Corporation 1981 Annual Report, Consolidated Statement of Shareholders Equity) over the course of the next seven months. Most of this early financing ($1.5 million) came from the pharmaceutical company Syntex (Teitelman pp. 42-49). On June 4, 1981 Genetic Systems went public and raised another $6 million. The shares the Blechs had purchased for about $200,000 were now worth between $12 and $24 million.[19] By the time the biotechnology market peaked in late 1991 or early 1992 David Blech's total biotechnology holdings were reputed to be as high as $320 million (Kadlec p. B4) and he had been involved in the creation or early development of over a dozen companies.[20]

The example of Genetic Systems and David Blech's subsequent leveraging of the gains generated from bringing the firm public can be seen to constitute one extreme of a process that many hold is common.[21] The Blech

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[19] The stock doubled in price the day of the offering (Teitelman p. 49).

[20] That not everyone appreciated Blech's talents, however, is reflected in suggestions that he was a master of "hype." A typical description of Blech was penned by a *USA Today* journalist the day after Blech's investment banking firm was forced to suspend its operations because of failure to maintain Securities and Exchange Commission capital requirements. Daniel Kadlec wrote: "His expertise turned into nurturing start-up companies just long enough to sell them to the public at a huge mark-up" (*USA Today*, September 23, 1994, p. B4).

[21] David and Isaac Blech followed up on their Genetic Systems success almost immediately by becoming the largest shareholders in DNA Plant Technology when it was founded in

story is one example of a story of how the IPO market influences the relations among investors, venture capitalists and entrepreneurs. As this line of argument goes, a rising stock market and the conspicuous success of the IPOs of specific companies tends to draw new participants into the pool of IPO and venture capital investors. This expansion in the pool of available capital occurs at the same time as initial public offerings are releasing risk capital into the economy as venture capitalists liquidate their holdings in newly public firms. This risk capital (both new funds and funds released by the IPOs) is then used to found new firms of the same kind that originally generated the attention as they went public. As long as investors are willing to continue buying stock of the companies involved, the cycle continues.

In the 1970s this cycle was difficult to observe because there were very few IPOs. Beginning in the late 1970s this changed very rapidly along with the massive resurgence of the mutual fund industry, the return of the IPO, and with the newly granted ability of pension funds to invest in risky stocks. Institutional investors once again came to dominate the IPO market and indirectly (although some pension and mutual fund money did flow directly into public venture capital firms) started influencing the process of venture capital formation, and, even more indirectly, influencing the process of firm creation. Whether or not this analysis is correct, one fact is well documented, the IPO market of the 1990s is a market dominated by mutual funds. Since biotechnology is still extremely dependent on the equity markets for financing

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November 1981. In February of 1982 they became major shareholders in Cambridge Bioscience (Teitelman p. 50). When Bristol-Myers purchased Genetic Systems in 1985 for almost $300 million the Blech brothers each were able to walk away with about $10 million each, a kitty that was to finance a number of other startups and turnarounds.

this makes the mutual funds extremely central influencers of the biotechnology sector.

According to Richard Spillane, Fidelity's director of research, mutual funds run by Fidelity are probably the "biggest buyers of IPOs" and provide about 10 percent of all the money raised in IPOs (Spiro and Zweig 1994a, p.88). Not only is Fidelity a dominant player in IPO markets, but, partially as a consequence, it is also owns a major portion of the whole biotechnology sector. In early 1993 Fidelity funds controlled about $1.7 billion in biotechnology stocks and thereby represent about 7 percent of the total capitalization of the industry as a whole (Laderman 1993). While no exact figures are available, at that time billions more of the industry was held by other mutual funds (Laderman 1993, p. 65). It is small wonder, then, that Robert Natale of Standard and Poor's held that the IPO market moves in concert with the purchase of mutual funds. As Natale would have it:

> It's impossible to sell an IPO to a mutual fund when there is no new money coming in. ... But when the cash is flowing, a new issue is a quick way to put the money to work. (Laderman 1993, p 65)

Edward Glassmeyer, a general partner at venture capital fund Oak Investment Partners, expresses the opinion (Alger 1993) that an active IPO market is generally followed by an upturn in venture capital investment in startups. Prominent biotechnology-watcher Steven Burrill concurs but in Burrill's opinion (Hamilton 1994, p. 88) this process is not always a beneficial one. In Burrill's account, venture capitalists have recently experienced very high returns even as investors in the public market saw their investments erode. Burrill believes (as reported by *Business Week*) that the result is as follows:

> By getting in early and then cashing out when companies go public, the venture capitalists succeed even if companies don't. The big returns they collect from IPOs let them attract still more capital. The result: Even as existing companies faltered, they kept starting new ones. (Hamilton 1994, p. 88)

At the dawn of the age of the public biotechnology the Blechs' desire to have a vehicle for a public offering shaped Genetic Systems, it is likely that the new venture capital financed companies Burrill refers to are founded on similar objectives. Companies formed with the expectation of a rapid passage to an IPO may often be tempted to spend money on research programs that will not sustained by cashflow from operations for many years to come.[22] The secret of the biotechnology financing game is often one of showing promise not necessarily showing immediate results.

In 1981 large companies were still scrambling to invest directly in biotechnology startups. In a 1981 story in *Chemical Week*, investment banker Douglas E. Rogers offered the opinion that the pool of first-rate scientific talent around which to found firms was limited, and that the amount of corporate money chasing existing opportunities was too large (and in the case of newcomers was often untargeted and haphazard). He was quoted:

> It's not a big universe. ... Today there are too many dollars chasing too few opportunities. ... I've had investors from the East say, "Can we invest $300 million right now in American biotechnology?" And I have to tell them it's not that easy. (*Chemical Week*, September 30, 1981)

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[22] The experience of Parnassus Pharmaceuticals illustrates the downside of this strategy. Parnassus had received initial financing from David Blech and was completely dependent on him for working capital. Blech had delayed bring Parnassus public as he hoped for a rebound in the biotechnology market. Unfortunately for Parnassus, Blech's operations were closed, Blech's weekly cheques stopped arriving and Parnassus had to close its doors almost immediately (Eckhouse 1994).

In keeping with the previous discussion, figures 2-1 to 2-4 suggest that, beginning in the 1980s, big corporations were no longer the only ones with

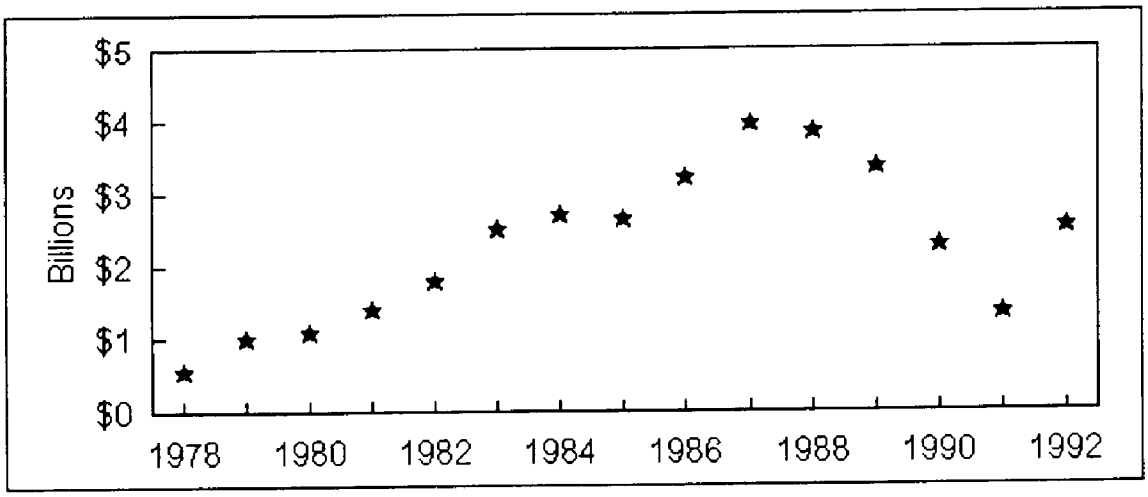

Figure 2-1: Total U.S. venture capital disbursements - 1978-1992[23]

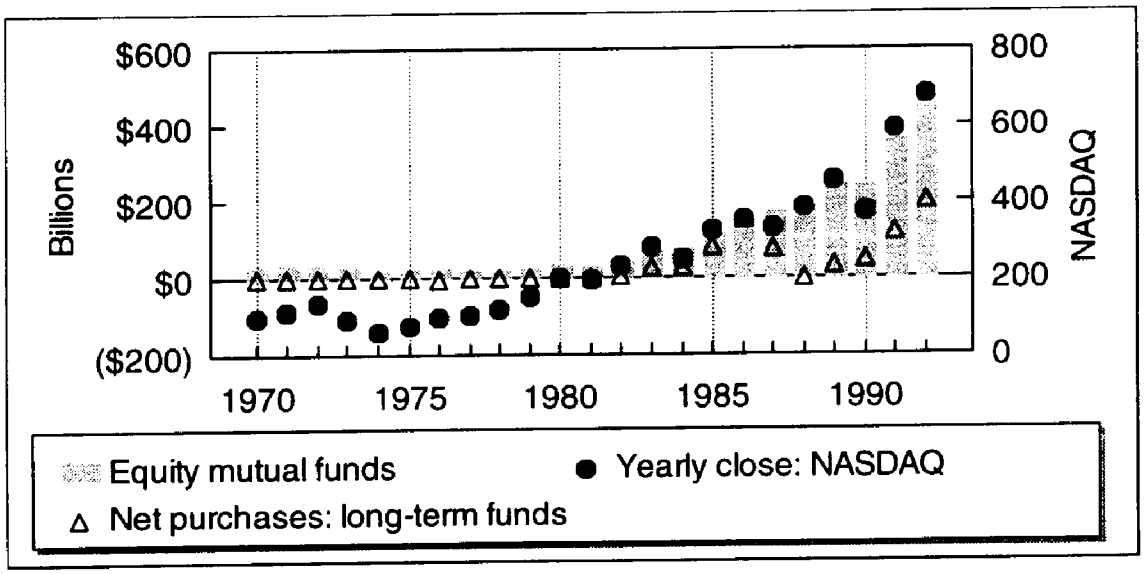

Figure 2-2: Total assets in American equity mutual funds, yearly close of the Nasdaq Composite index, and net purchases of long-term mutual funds (including bond funds)[24]

[23] Figures for 1978 to 1982 are from *Venture Capital Yearbook 1985* (p. 25), figures for 1983 to 1991 are from *Venture Capital Journal*, December 1992 (p. 33). Disbursements for 1992 are taken from *Venture Capital Journal*, June 1993 (Alger 1993, p. 31).

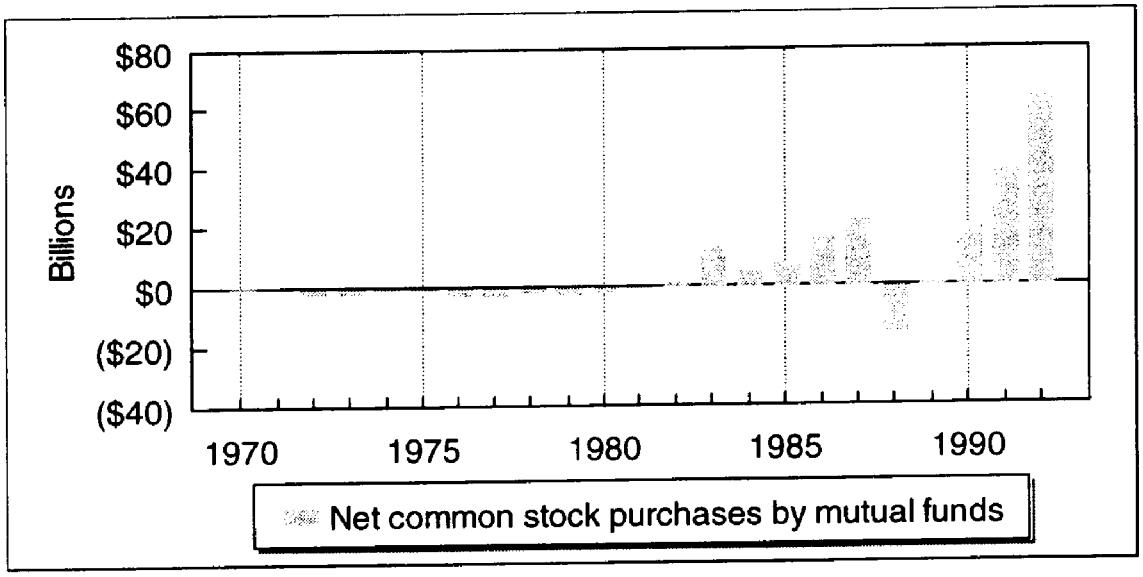

Figure 2-3. Net purchases of common stock by American mutual funds[25]

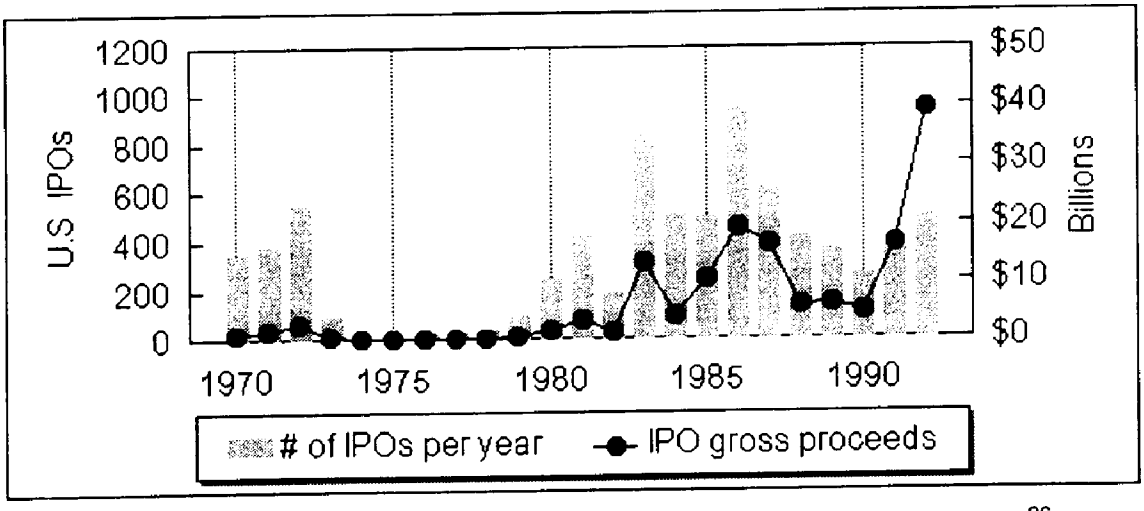

Figure 2-4: Total American IPO activity from 1970 to the end of 1992[26]

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[24] Mutual fund total net assets at the close of the year is from the *Mutual Fund Fact Book* (Investment Company Institute 1992, p. 100). Net long-term fund purchases represent net purchases of equity, bond, and income funds (Investment Company Institute, p. 108). Since the Nasdaq Composite began in early 1971 the closing figure for 1991 is actually the opening level of the index in 1971.

[25] Net common stock purchases are based on tabular information contained in the Mutual Fund Factbook (Investment Company Institute, 1992, p. 108).

[26] The figures on which this graph is based were generously provided by Professor Jay Ritter of the University of Illinois, Champaign-Urbana.

large sums of money available to invest in biotechnology. After the stagnant 1970s the level of investment by formal venture capital firms was rising (Figure 2-1). The stock market was rebounding, new investment in equity mutual funds was starting to reappear (figure 2-2), and investment in mutual funds was triggering mutual funds to buy common stocks. Most striking of all, after virtually disappearing in the 1970s, the market for IPOs started to re-emerge in 1979 and 1980.

While the graph of IPO activity (figure 2-4) clearly indicates the contrast between the 1970s and the 1980s in terms of IPOs, it doesn't show the extraordinary character of the IPO market in 1980. In an article entitled "The 'Hot Issue' Market of 1980" Jay R. Ritter reports that the "mean return on an initial public offering of common stock purchased at the offering price and sold at the closing bid price on the first day of public trading was 48.4%" (Ritter 1984, p. 215). While Ritter found that these extraordinary returns were largely attributable to a single sector, the natural resources industry, these returns do place the first day trading experience in companies such as Genentech and Genetic Systems in context. As Ibbotson and Jaffe (1975) pointed out, "hot issue" markets are a recurring phenomenon. As Ritter summarizes:

> There have been 3 or 4 periods between 1960-82 in which monthly average initial returns on unseasoned new issues have been extremely high for prolonged periods. Each of these periods was followed by a large and prolonged increase in the volume of initial public offerings. (Ritter 1984, p. 238)

While the subject of underpricing of IPOs is a very active and engaging area of research reported in the finance and accounting literature,[27] it is of relatively

[27] The two major explanations advance for this phenomenon are Rock's (1986) information asymmetry argument, and the long established hypothesis of the exercise of monopsony power by investment bankers. A detailed account of this literature can be found in a

little relevance to this study. When IPO investors have experienced a hot issue market, the IPO market as a whole grows. The fact that the Genentech IPO, one of the very first major biotechnology IPOs, was severely underpriced almost certainly had an impact on the growth of interest in biotechnology investment and biotechnology IPOs.

HOW THE IPO SHAPED COMPANY CAPABILITIES

The advent of the public biotechnology firm by no means eliminated the flow of investment capital from large companies to startups but it did offer biotechnology companies an alternative. A firm that launched a successful IPO could avoid selling itself off piece-by-piece to large companies, until control shifted completely away from the entrepreneur. High stock valuations, the opportunities public ownership offered for incentive programs based on stock performance and the prospect that further capital needs of the company might be met by returning to the capital markets all were factors the enhanced the viability of biotechnology firms. While there is no doubt that corporate alliances in the form of marketing, manufacturing, and research and devlopment agreements have always been a key source of biotechnology financing, such agreements have rarely been sufficient to eliminate the biotechnology firm's need to resort to direct sale of company equity.

The IPO not only created alternative financing for biotechnology firms, it also conferred competitive advantages upon them that were not easily

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published dissertation by Kyran McStay (1992). A very readable review of initial public offering issues (including underpricing) is provided by Ibbotson, Sindelar and Ritter (1988). An interesting recent addition to the underpricing literature is provided by Megginson and Weiss (1991) where they find that the involvement of venture capitalists "certifies" the quality of initial public offerings and reduces the degree of underpricing.

reproduced by large companies. The most critical of these was probably the advantage it gave biotechnology startups in recruiting scientific personnel. Kenney (1986) describes the rapid growth in the prevalence of commercial involvements of senior university scientists and for those who worked in their laboratories. Contrasting the ability of the biotechnology startup to attract to the difficulty large corporations had in hiring top scientists, Kenney wrote:

> Yet even with the potential salaries for professors who are willing to leave the university .... large established corporations have not been successful in attracting professorial labor. Only the provision of equity interest in startup companies combined with the ability to remain in the university convinced biology professors to become involved in private enterprise. (Kenney 1986, p. 106)

In a 1984 magazine article the same basic point is made regarding the recruitment advantage of the biotechnology startup using slightly more colorful language:

> Even though the giants are flexing their muscles, the startups are not ready to throw in the towel. They argue that the best scientists are still in their labs and that they will continue to lead the research. Indeed some of the top scientists at the small companies are pulling down salaries that would cause a revolution in a big corporate lab. "The way you attract the 'dilettante' molecular biologists is to give them academic freedom and megabucks plus equity kickers," says Nelson M. Schneider, an analyst at E.F. Hutton & Co. (*Business Week*, November 5, 1984, p. 137)

It was generally believed that the competitive advantages of the biotechnology startup would only last as long as did their ability to resort to the stock market for financing. Since many believed that stock market interest in biotechnology startups would soon wane there were some suggestions that the competitive strengths of the startups would prove to be fleeting. In 1981,

opinions offered by Scott King, an analyst at brokerage firm F. Eberstadt (New York) were cited in *Chemical Week* as follows:

> "I think it was pretty much a fad," King remarks. "I think Wall Street has other things on its mind"-- notably, the 175-point decline in the Dow Jones industrial average since mid-June. "Besides," he adds, "Wall Street has a rather short attention span. Right now, it's looking at capital goods and strategic metals." If Wall Street doesn't soon return to its fawning attitude over biotechnology stocks, a fair assumption, then these companies will most likely be forced to turn again to what for many of them has already been a fruitful source of capital: large corporate investors... (*Chemical Week*, September 30, 1981, p. 36)

What this kind of analysis failed to appreciate was that the IPO market had already stimulated the creation of a large number of biotechnology firms. The industry was becoming too large for a few large corporations to sustain the industry by themselves. The big corporations could also no longer assume that the biotechnology entrepreneurs would always be knocking on their doors for assistance. Biotechnology firms were changing, especially some of the most recent creations. One of the most striking of these new creations was Amgen. Like Genentech before it, Amgen initiated a wide range of research projects almost from the very time it was incorporated on April 8, 1980. Headed by George Rathman, a former research director at Abbott, Amgen was to secure nearly $19 million in private funding in the first year of its existence and was to embark on a research program whose promise of rewards was great but whose payoffs lay in the distant future. While Amgen was very successful in raising money from large corporations, George Rathman founded the company with the explicit rule of having

"enough investors so that no one of them would have more than a 20% equity position" (*Chemical Week*, April 11, 1984).

BIOTECHNOLOGY FIRMS AND THE HUNGER FOR CAPITAL

From the beginning, Amgen was a company that counted on being able to access the IPO market to make its program possible. As Cetus founder Cape had said several years before:

> "There is no way to pursue recombinant DNA programs on a shoestring," Cape cautions. "We can't afford to be scientific heroes but business flops." (*Business Week*, January 17, 1977, p. 76)

Amgen was not only pursuing rDNA work, it was also quickly embarking on a number of diverse projects both on its own and with its corporate partners. Even with the near-record venture financing Amgen had already received, it would need more money relatively soon. Amgen would show a net loss of nearly $1.7 million in 1982, and in 1983 (the year of its IPO) it would lose slightly over $7 million. Had it not been for public equity it might have proven difficult to sustain this level of expenditure without having to surrender more control than Rathman wanted to entertain.

One reason biotechnology firms present an excellent population for the study of how environmental factors influence the rate at which firms go public is that it can be argued that the unique nature of the business makes maintaining permanent private status very difficult. Although estimates range, there is universal agreement that introducing a biotechnology product in human therapeutics is a long and very costly process. The Office of Technology Assessment (1991, p. 74) cites ten to twelve years as being the

typical product development time for a new therapeutic agent developed by biotechnology. *Business Week* (Hamilton 1994, p. 85) cites seven to ten years as typical, and the actual record of development times for the already commercialized drugs as being basically in line with these estimates. On the cost side, Mark Edwards (managing director of Recombinant Capital, a biotechnology research firm) cites $150 million as being a typical cost for bringing a drug to market (Hamilton 1992, p. 73) while Dr. Denise M. Gilbert (vice-president of Affymax N.V., former managing director and biotechnology analyst at Smith Barney, Harris Upham & Co., Inc.) estimates (based on historical averages) the capital requirements before a firm brings a drug product to market to be between $250 million to $550 million (Burrill, *Biotech 94*, p. 16).

In the agricultural sector the costs borne by Calgene before it introduced its first biotechnology product were of a similar order of magnitude. By 1990 Monsanto's cumulative investment in agricultural biotechnology was about $800 million (Schneider, *New York Times Magazine*, pp. 26-39) and at that time they still hadn't launched their lead product, bovine somatotropin (BST).

With over 600 diagnostics products approved by the end of 1992 (Burrill 1994, p. 35) the diagnostics sector might not be seen to conform to this pattern, but, even here, annual surveys conducted by Ernst & Young between 1989 and 1993 have the percentage of firms showing a profit each year ranging from a low of 28 percent (Burrill 1991 p. 79), to a high of 38 percent (Burrill 1993 p. 50). According to the same source, the only segments of the biotechnology population that were approaching profitability during this period were firms acting as suppliers to other biotechnology firms. In this

sector about half the firms tended to show a profit each year. Some of the firms devoted to providing services and environmental remediation were also approaching profitability. At the very least, this data suggests that even for non-therapeutics firms a presumption that significant startup financing will be required is valid. In the case of biotechnology firms dealing with human therapeutics and with agriculture, the claim that can be made is much stronger: the firm will not become financially sufficient for many years. Based on the evidence of the past, the scale of investment required to bring agricultural and human therapeutic products to market will also exceed the ability of most non-public sources to finance.

The same factors that lead to the wide recognition of the insatiable capital needs of the biotechnology startup also make biotechnology a very appropriate population for studying the impact of environmental factors and strategic features of corporations as determinants of a firm's decision to go public. In a population such as this, the willingness of the original shareholding group to sell stock sends little in the way of a signal about management's assessment of the worth of the company's existing research portfolio. At the time a biotechnology startup (especially the therapeutics firm) typically goes public it usually has little in the way of financing alternatives.

Because the "assets in place" (Myers and Majluf 1984) of the biotechnology firm are intangible products of scientific research (if the company is lucky maybe some of them have received patent protection or have the prospect of being protected in this fashion) their worth is very difficult to assess. Because the passage to product introduction and subsequent profitability is still so remote, however, even insider information on company prospects may not place existing owners in a position of having an

appreciable informational advantage over an "uninformed investor."[28] The situation of the biotechnology is thus relatively unique, everyone can predict that the firm will need money. The nature of the asset base and life cycle of the company is such that significant debt financing is in most cases not available and the extent of the required financing required is of a magnitude that not even venture capital is likely to be sufficient to bring its research program to the point of fruition. From the outset, it is almost a foregone conclusion that the biotechnology firm will feel significant pressure to seek public equity financing, the only question is when and how this will occur.

That a biotechnology firm will stay independent and yet not go public is of course a possiblity. Nevertheless, few entrepreneur/scientists have the personal wealth to support a firm while the firm develops a human therapeutics product, steers it through testing and approvals, and finally prepares to market the product (or licences another company to do so). A company that doesn't go public, is not acquired, and does not fail, is most likely to be pursuing a product market strategy that allows for relatively early passage to profitability. The more quickly a firm can start earning profits, the less likely it is to need public financing. In fact, its very profitability is a sign that it is probably not pursuing costly scientific research. If such a firm is funding promising science from cashflow, however, it will face greater

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[28] Interestingly enough, a financing tool sometimes used by firms that have already gone public is something called a SWORD (an acronym created from the capitalized word of the phrase "Stock Warrant Off-balance sheet Research and Development financing"). A SWORD consists of a mature company creating a shell company which is then sold to the public. This spin-off company consists of rights to future profits from a project nearing commercialization and warrants to purchase shares in the parent company. This financing method allows the parent company to avoid some of the valuation problems associated with project financing in the presence of informational asymmetries discussed by writers such as Myers and Majluf.

informational barriers than the pure research firm because it had to get a fair price for the two very different components of the firm: the research portfolio and the part of the business that is already generating profits.

The profitable biotechnology firm is likely to be different than most of its counterparts. Early in the history of the industry, New England Biolabs was using biotechnology-based product development tools but it relied on direct sales of biological materials to researchers to build a self-sustaining business that was fully owned by the founders (Wade 1980b). One of the main sources of heterogeneity within the population as it relates to the propensity of firms to go public is likely the target market of the firm in question. Significant distinctions even exist between subpopulations of firms developing human diagnostics and those developing human therapeutics.

While the difference between a firm set up to provide materials or services to other firms and one set up to discover the cure for cancer or AIDS is obvious; the differences among other kinds of firms are less black and white. Therapeutics and diagnostics firms exhibit initial similarities in terms of personnel requirements, the identity of the regulator, the linkage to the overall size of the healthcare sector and their missions are to develop products to help the sick. The dissimilarities between diagnostics and therapeutics are also considerable. While there are some in-vivo diagnostics (Oncoscint, a monoclonal based imaging agent approved in 1992, is an example) most diagnostics are in-vitro and as such are subject to much less stringent approval processes. Many diagnostics are also quicker to develop than therapeutics, although diagnostics that first require identification of a gene can be just as time-consuming. Finally there is not the emotional appeal attached

to developing a diagnostic product that there is to developing a therapeutic. As Teitelman writes:

> You did not succeed in diagnostics with one home-run product; it required lost of singles. Babe Ruth always got more votes than Ty Cobb. (Teitelman 1989, p. 107)

WHAT ALTERNATIVES EXIST FOR A PRIVATE COMPANY?

Even if we accept that biotechnology firms (subject to the caveats about the differential needs by target market strategy) are likely to need external equity for an extended period, the question still arises how this is to be achieved. Writing in *Management Review* Gail Dutton reports on an interview with Steven Burrill as follows:

> "Death is unattractive, so firms finance," he adds. "The power has moved from the companies to the investors, and the paradigm that all good science deserves money no longer applies." With this power shift, financing has become more creative and firms are more willing to accept lower values. (Dutton 1995, p. 40)

Along with Burrill, most readers will probably agree that firm failure is a fate to be avoided, and that securing external financing is probably desirable and required. Initially, one might consider seeking venture capital or capital from what are commonly referred to as "angels," but often the strings attached to such financing is considerable.[29] In comments reported in Ernst & Young's *Biotech 94: Growth of an Industry*, Shaman Pharmaceuticals president Lisa A.

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[29] The range of sophisticated sources of financing beyond the boundaries of "formal" venture capital firms is extensive enough that splitting the world of startups into venture-financed firms and non-venture-financed firms is more problematic than it might first appear. Is receiving funds from Kleiner Perkins, Caufield and Byers venture financing and receiving funding from Bill Gates former partner Paul Allen not venture financing?

Conte claims that the time and effort managing relations with public shareholders might actually be lower than the effort required to manage relationships with venture capitalists. Even if venture capital is secured, however, it is unlikely to be sufficient by itself. Finally, even in the rare case where venture capital could fully fund the company until product launch and profitability, a company financed with venture capital must eventually contend with the harsh reality that venture capitalists generally have an "exit strategy" for liquidating their investments.

Barry (1994) describes the options open to the venture capitalists in terms of "exit strategies as follows:

> Venture capitalists may exit an investment in a number of ways. The most common avenues for exiting a successful venture are via an IPO or a merger. In other cases, exit may occur through liquidation or share repurchase. It appears that exit via IPO is the most profitable form, although that does not mean that investments that are harvested via merger would have been better served by an IPO. (Barry 1994, p. 12)

Barry's assessment of the relative attractiveness of exit strategies is echoed in the pages *Venture Capital Journal*. Associate editor Lisa Vincenti writes: "It is the exceptional deal that gives venture capitalists more in a sale than they would get in an IPO" (Vincenti 1994, p. 38). For similar reasons the original shareholders of a biotechnology company probably have the same ordering of financing alternatives as venture capitalists have of "exit strategies."

In the biotechnology industry there is another factor that makes the outright sale of the company to another company a less attractive alternative, namely, the difficulty of retaining key personnel after mergers. The situation in the biotechnology industry is similar to an example employed by Oliver E. Williamson in *The Economic Institutions of Capitalism*. Williamson tells the

story of Tenneco's (which he describes as the nation's largest conglomerate) acquisition of Houston Oil and Minerals Corporation in 1980. Tenneco wanted its new subsidiary to retain the aggressive posture it had had as an independent. With this goal in mind, Tenneco offered various inducements to retain key exploration staff, management and production personnel. Despite Tenneco's efforts, within a year all these units had been decimated by departures of key personnel. Williamson assesses the situation as follows:

> The offers by independent producers which evidently have fewer or different burdens and restraints, of "stock options, production bonuses and, especially, royalty interests in the oil they discover—[incentives] that the majors have been unwilling to adopt' (Getschow 1982, p. 1) were principally responsible for the unraveling. Despite their best efforts, large firms are not always able to replicate small firms in all relevant respects. (Williamson 1985, p. 158)

The fact that the experience of companies acquiring biotechnology companies has sometimes been similar no doubt suppresses the level of outright takeovers in this sector. Examples of key departures from acquired firms include Nowinsky's departure from Genetic Systems in order to found ICOS. After Hoffman-LaRoche acquired majority ownership of Genentech they also lost key personnel. The most prominent departure from Genentech was that of David Goeddel, the "leader of Genentech's development of human insulin, human growth hormone and tPA who left to found Tularik" (Ryan, Freeman, and Hybels 1995, p. 351).

THE DECISION TO GO PUBLIC

Many practical guides (e.g., Wat 1983; Arkebauer 1994; Ernst and Young 1993; Halloran 1979) exist to guide the entrepreneur through the

process of deciding whether or not to go public and how to proceed if an IPO is the selected alternative. In general there is considerable consensus among these sources as to what constitute the "pros" and "cons" of going public. In a recent issue (December 1994) of *Management Accounting,* James B. Hare provided a listing of these considerations. Hare's summary includes most of the points that are typically advanced relating to the decision to go public. Using Hare's listing as a guide, the advantages of going public are popularly taken to include:

1. The IPO provides an "immediate influx of capital."
2. Unlike debt, equity capital doesn't need to be repaid. More equity improves your future borrowing capacity.
3. Raising additional capital in future public offerings is simplified.
4. "Public companies tend to more valuable than comparable private companies, thanks in part to increased liquidity, information about the company that is easier to obtain and is more dependable, and a readily ascertainable stock (and hence company) value." (Hare 1995, p. 26)
5. IPOs cause less ownership dilution than financing alternatives like venture capital.
6. Increased visibility and "enhanced reputation" may provide spillover benefits for other areas of the firm's activities.
7. The IPO enhances the firm's ability to use stock incentives with "vendors, suppliers and employees."
8. A public firm can use company stock to "effect mergers or acquisitions."

9. Going public provides shareholders with a more liquid asset, eases shareholder estate planning and stock can be used as collateral.

In a similar vein Hare enumerates the disadvantages of going public as follows:

1. The cost of going public is high. Underwriters typically charge upwards of 7 percent of gross proceeds (for most of the biotechnology firms a more typical charge was 10 percent). Printing, auditing and legal fees add significant fixed costs.[30]
2. An erosion in the market or other factors could leave the company with either costs but no proceeds or reduced proceeds.
3. The process is time consuming and strenuous.[31]
4. The firm and the firm management lose much of the privacy that they have formerly taken for granted. Salaries, strategies, company performance, lawsuits and a wide range of other issues now have to be disclosed for all to have access to.
5. With the sale of stock more parties must be consulted in or informed of decisions. If enough stock has to be sold, shareholders could wrest control of the company from its founders and managers. Related issues that Hare mentions are reduced flexibility, pressures to pay dividends or increase stock prices and the need to maintain contact with investors and analysts.

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[30] In his analysis of the costs of going public Ritter (1987) discusses how significantly the fixed cost component of going public can affect the desirability of small offerings.

[31] Malone (1991) provides an excellent account of the process from the perspective of company management.

6. The ongoing costs such as those associated with investor relations, audit charges, legal costs, director's indemnification.
7. The monetary and psychological impacts of managing in the face of volatile stock prices and restrictions on sales of stock by insiders.
8. "No turning back. Once you're public, you're probably public for good. Taking a company private is difficult and costly." (Hare 1995, p. 27)

Review of the considerations outlined above combined with recollection of the unique attributes of the biotechnology startup vis-à-vis providing high-powered incentives for staff provide strong anecdotal support for a central premise of this study: going public is an organizational transition that is fundamental, irreversible and touches virtually all aspects of an organization's operations.

ORGANIZATIONAL ROUTINES AND RESOURCE DEPENDENCE

If we follow Nelson and Winter (1982), and choose to view the firm as a collection of routines, then it is difficult to deny that the changes engendered by an IPO constitute a key life event that alters the face of the firm. Being public creates a whole range of new organizational routines that revolve around accounting, shareholder relations, relations with financial regulators, and handling inquiries from reporters. These changes in routine don't even include the massive changes in routines that can be brought about as a consequence of having resources. The unusual nature of the financing available to biotechnology firms also makes the biotechnology population a particularly interesting exception to the rules of selection which Nelson and Winter applied within their simulations of selection processes affecting firms.

The possibility that firms such as biotechnology firms might lose money for years without failing was not lost on these writers. They wrote:

> The model assumes that firms that lose money tend to decline. While this seems plausible, it ignores the possibility (remarked on but not explored by Friedman) that such firms might be sustained by resources "from the outside." Temporarily, at least, an individual firms may be sustained by funds supplied by stockholders or creditors rather than by customers. (Nelson and Winter 1982, p. 158)

In fact, in the biotechnology industry it is often the firms that have committed the most money to research, and hence lose the most money, that are most successful at raising money in IPOs. If modelled in a Nelson and Winter type of simulation it might very well turn out that firms that embark on early "go for broke" research strategies may actually enhance their longer term survival and growth prospects.

A key tenet of resource dependence theory as developed by Pfeffer and Salancik (1978) is that the degree to which an organization is dependent on a given resource directly influences the degree to which that firm organizes itself to ensure access to that resource. In a review of resource dependence theory Pfeffer (1982) raises the point that this process is complicated by the fact that organizations invariable are confronted with incompatible and varied demands from different social actors. Pfeffer (1982, p. 195) illustrates this point with the following quote:

> An organization's attempts to satisfy the demands of a given group are a function of its dependence on that group relative to other groups and the extent to which the demands of one group conflict with the demands of another. Three factors are critical in determining the dependence of one organization on another. First, there is the importance of the resource, the extent to which the organization requires it for continued ... survival. The

> second is the extent to which the interest group has discretion over resource allocation and use. And, third, the extent to which there are few alternatives, or the extent of control over the resource by the interest group, is an important factor determining the dependence of the organization. (Pfeffer and Salancik 1978, pp. 45-46)

While it is sometimes argued (Aldrich 1979; Freeman 1982) that small organizations have little ability to control the environments that they face, even small firms can use the IPO as a tool to alter the balance of power between investors and company management. Under the tests outlined by Pfefffer and Salancik there is little doubt that equity financing is a critical resource. If a firm is dependent upon a few large companies or venture capital firms there is little question that the firm and its management will be subjected to significant external control. Assuming that management wants to minimize external control of its decisions there are some mechanisms available such as selling its research expertise, selling options on future distribution rights to its products under development, and outright sale of rights to its technology. While all of these transactions might limit the direct intervention of outside parties in company management, to one extent or another they also amount to a sale of the company's birthright.

The IPO addresses problems of resource dependence in three ways. First, the number of shareholders typically increases once a company goes public. Second, because mutual funds are important shareholders in IPO firms, and mutual funds typically cannot demand representation on a company's board of directors (Laderman 1993, p. 64) company management is accountable for results, but is not subject to day-to-day interference. Third, being public makes alliances, mergers, and further stock issues more straightforward and controllable. The IPO causes a shift in the degree to

which sharp boundaries exist between the firm and its environment. By creating new connections with investors, underwriters, bankers, analysts and journalists the IPO directly alters the degree to which the firm influences its environment. The public firm is also much more visible, firm management is more likely to be consulted by government commissions, and the firm is liable to get more attention from the media. While visibility and disclosure will not always enhance a firm's ability to raise cash (bad news is disseminated as well as good news) shares of a public firm (that is not the target of a hostile takeover) will tend to be owned by investors who agree with current management's vision of how the company should be run.

THE IPO AS AN IRREVERSIBLE CHANGE IN AN ORGANIZATION

One of the claims I make in this dissertation is that going public causes significant, enduring, and irreversible changes in an organization. It is the "life altering" impact of the IPO that makes it a fundamental change in organization rather than just a change in financial structure. Much of the previous discussion in this chapter has addressed the importance of the changes that the IPO causes. What has been glossed over thus far is the question of why the impacts of the IPO are irreversible. I will now address this omission.

There are at least seven different ways in which it can be said that changes brought on by an IPO are irreversible. These are:

1. The public firm usually has greater financial resources than when it was private. Newly invested funds are often reserved for research initiatives. To deliver on its promises the firm must hire additional staff, expand its facilities, and generally start to commit itself to greater fixed expenses. An organization engaged in specialized

activities such as biotechnology can rarely undergo reversal of such growth without incurring considerable material and reputational losses.

2. While it is possible to "go private," such actions are usually financed by means of leveraged buyouts. Until the firm enters a phase where it is producing sustainable profits it is unlikely that debt financing to support a management buyout will be available. Even if a reversion to private status were navigated successfully, it would probably have to be accompanied by a change in corporate strategy that reduced the firm's commitment to research.
3. Companies that go public usually have to cope with changing from being "small" to being "big." This is so even when in objective terms the firm remains relatively small. This growth often causes problems. In the extreme, going public can even set up a sequence of events that can lead to the demise of the company (e.g., Southern Biotechnology). Malone (p. 234) writes: "what used to be scarce, money, is abundant, and the challenge becomes not to over-indulge every pent-up whim."
4. Whatever information is revealed about the corporation in disclosure statements required of public companies can never be retracted. Secrets, once revealed, can never be made secret again. Disclosure of information relating to some research programs can even lead some competing firms to alter their plans.
5. Routines, once established, are not easy to eradicate. A public firm develops considerable formality in its legal, financial, and public relations operations. The organizational apparatus that supports

these operations is difficult to make less formal (and less costly) without having it become disfunctional.

6. If many workers are shareholders, a reversion to private status would also cause a large shift in the structure of employee incentives and compensation.
7. Once a company is public it cannot control who buys parts of the company. Although hostile takeovers are virtually unheard of in this industry (probably because the worth of the company is based on staff who might leave in the face of a takeover), such a possibility becomes possible if more than 50 percent of the stock is sold to outsiders.

SUMMARY: IPOS, THE FIRM, AND THE POPULATION

In this chapter I have tried to develop two key ideas. The first of these is that the emergence of a population of publicly-traded biotechnology firms is one that altered the conditions for all biotechnology firms. The creation of a population of public firms led to a revision of the position the biotechnology industry occupied within a community of organizational populations that includes venture capital firms, underwriters, mutual funds, large diversified corporations, and other biotechnology firms. The second key idea of this chapter is that going public permanently alters the capabilities of the affected corporation. In conclusion, I argue these two ideas suggest that differential abilities of firms to go public will serve to segregate the population of biotechnology firms sufficiently that in the end at least two distinct populations of organizations will emerge. These populations will be distinguished on the basis of size, power, and products and many of these differences will be

traceable back to changes in individual firms as they reached the crossroads of deciding whether or not to go public.

CHAPTER 3. METHODS

This chapter discusses the statistical methods used to analyze the data on IPO rates of American biotechnology firms. The sources of this data and its specific qualities will be discussed in the next chapter. Specifically this chapter deals with the general applicability of event history models, the definitions of hazard rates (and related concepts), functional forms used to model hazards, the mechanics of "spell-splitting," and the complications associated with modelling competing risks.[32]

EVENT HISTORY METHODS

Event history methods (Tuma and Hannan 1984) are applied in a variety of contexts in the social sciences. In recent years these methods have been applied to everything from the analysis of the duration of spells of unemployment (Flinn and Heckman 1982) to the determinants of teenage pregnancy (Hogan and Kitagawa 1985). Within the context of organizational sociology, an increasingly common application of these methods has been in the study of organizational founding and failure. Many of these studies of organizational vital rates found their original inspiration in theoretical work (Hannan and Freeman 1977) which linked organization founding and failure to the density of the populations in which the organizations were resident. This branch of study is often referred to as population ecology. The study of IPO rates of firms can be approached in a similar fashion to the study of the failure

[32] In writing this chapter I found Barron's exposition (1992, pp. 38-54) of the methods he had employed to be very helpful. Especially enlightening was his discussion and illustration of the "spell-splitting" procedure.

of organizations. Partially because I pay particular attention to the role population density plays in a firm's passage toward going public this current study falls firmly in the evolving tradition of population and organizational ecology. In addition, since the nature of the problem is similar to that of the study of organizational failure, it is also the case that the same event history models that are applied by population ecologists are applicable here.

HAZARD RATES AND RELATED CONCEPTS

In order to study the rate at which events occur, and to relate the occurrence of these events to properties of the units being observed, and their ambient environments we first have to become acquainted with certain basic concepts. First, the idea of when an event occurs is made clearer if we introduce the idea of splitting duration into segments in which an event either occurs or does not occur. Let $t_0=0$. We can then characterize the duration as consisting of a time axis with n segments such that $0=t_0<t_1<t_2<....<t_{n-1}<t_n$. Each segment has length $\Delta t= t_n-t_{n-1}$.

We now apply this to our discussion of the prevalence of an event by specifying a random variable T that is the amount of time that passes until the occurrence of the event of interest.[33] The probability that this event occurs within any section of the time axis is thus the probability that a state transition takes place in the time between t_m and t_{m+1} given that it has survived in that state until time t_m is:

$$Pr(t_m \leq T < t_m + \Delta t | T>t_m) \text{ where } t_m + \Delta t = t_{m+1}. \qquad \text{Equation 3-1}$$

[33] The substance of the discussion around equations 3-1 to 3-10 is drawn from Petersen 1991 (pp. 274-279). More detail and supporting proofs can be found in Petersen's paper.

This concept is coupled with the specification of the probability that the event has *not* occurred during this same interval, which is given as follows:

$$\Pr(T \geq t_{m+1} \mid T \geq t_m) = 1 - \Pr(t_m \leq T < t_{m+1} \mid T > t_m) \qquad \text{Equation 3-2}$$

where $t_{m+1} = t_m + \Delta t$.

From the preceding two equations one can derive the probability that the event has not occurred prior to t_n by applying the rules of conditional probability. This probability expression is written as:

$$\Pr(T \geq t_n) = \prod_{m=0}^{n-1} \Pr(T \geq t_{m+1} \mid T \geq t_m) \qquad \text{Equation 3-3}$$

where $t_0=0$ and $t_{m+1} = t_m + \Delta t$.

In a similar fashion, once again applying the rules of conditional probability, we have the probability that the event does occur within the interval between t_n and t_{n+1} as being:

$$\Pr(t_n \leq T < t_n + \Delta t) = \qquad \text{Equation 3-4}$$

$$\Pr(T \geq t_n) \text{ X } \Pr(t_n \leq T < t_n + \Delta t \mid T \geq t_n)$$

$$= \prod_{m=0}^{n-1} \Pr(T \geq t_{m+1} \mid T \geq t_m) \text{X} \Pr(t_n \leq T < t_n + \Delta t \mid T \geq t_{n-1}) .$$

We now use the equations developed above to introduce some of the central concepts of event history methods. We begin with the idea of the

instantaneous hazard rate.[34] For any given firm in the population, the hazard rate for going from state *i* to state *j* (given measurement of duration in continuous time and letting the interval in which an event can be observed approach zero) is defined as

$$r_{ij}[t_m \mid \mathbf{X(t)}] = \lim_{(\Delta t \to 0)} \frac{PR[t_m < T_j \leq t_m + \Delta t | T_j > t_m, \mathbf{X(t)}]}{\Delta t} \qquad \text{Equation 3-5}$$

where **X(t)** is a vector of covariates. In words, when an event can occur at any point in continuous time the hazard rate is the instantaneous rate at which an event occurs at a given time t, conditional on the values of relevant covariates and the event not having occurred prior to that point.

From equation 3-5 we have the probability of an event (initially specified in equation 3-1) as Δt becomes small being:

$$Pr[t_m \leq T < t_m + \Delta t \mid T \geq t_m, \mathbf{X(t)}] \qquad \text{Equation 3-6}$$

$$= r[t_m \mid \mathbf{X(t)}]\, \Delta t \quad \text{where } \Delta t \text{ is small.}$$

Note that for notational simplicity the subscripts for origin and destination states have been dropped. Inserting equation 5-6 into equation 5-2 and we have:

$$Pr(T \geq t_{m+1}) = 1 - r[t_m \mid \mathbf{X(t)}]\, \Delta t \text{ , where } t_m + \Delta t = t_{m+1} \qquad \text{Equation 3-7}$$

Now inserting 5-7 into 5-3,

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[34] In most of the remaining chapters the hazard rate will be identified by the kind of rate actually being estimated. For the most part this will be the IPO rate and will be identified as such.

$$\Pr(T \geq t_n) = \prod_{m=0}^{n-1} \{1 - r[t_m | X(t)]\Delta t\} \qquad \text{Equation 3-8}$$

and inserting 5-8 into 5-4 gives

$$\Pr(t_m \leq T < t_m + \Delta t) = \prod_{m=0}^{n-1} \{1 - r[t_m | X(t)]\} \times r[t_m | X(t)]\Delta t \qquad \text{Equation 3-9}$$

Since the preceding two equations presuppose that time is absolutely continuous, we can now take the limit of 5-8 as Δt goes to zero (recalling that Δt by definition has length $t_n - t_{n-1}$) as the number of intervals $\rightarrow \infty$. This yields the famous relationship of the survivor function[35] S(t):

$$S(t) \equiv \Pr(T \geq t_n) = \lim_{\Delta t \downarrow 0} \prod_{m=0}^{n-1} \{1 - r[t_m | \mathbf{X(t)}]\Delta t\} = \exp 0 \left[-\int_0^{t_n} r[u | \mathbf{X(t)}](u)\, du \right]. \qquad \text{Equation 3-10}$$

The complement, $F_j(t) = 1 - S_j(t)$ is "simply the cumulative distribution function or the probability that an individual experiences the event by time t" (Teachman and Hayward 1993, p. 345). Finally, it can be shown, either by differentiation of the cumulative distribution function, or by dividing both sides of 5-9 by Δt and taking the limit, that the probability density function $f_j[t|\mathbf{X(t)}]$ can be characterized as the product of the hazard rate and the survival function. In any case it is clear that by specifying the hazard rate one can then derive expressions for the survivor function, the probability density function, and the cumulative distribution function.

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[35] This definition of the survival function can be found in Kalbfleisch and Prentice (1980 p. 6), and Teachman and Hayward (1993, p. 345). The general proof of the equation can be found in an appendix to Petersen (1986, pp. 319-320). The proof for the special case of a constant hazard rate is straightforward.

For the most part, the models constructed here of IPO rates (and of failure and acquisition rates) are based on a log-linear function which relates observed covariates **X(t)** to the hazard rate. Given the nature of the problem being studied, one nice feature of log-linear models is that they do not admit negative rates. The simplest of such log-linear functions is the exponential model that assumes the hazard rate r(t) is constant over time. This exponential specification of the hazard rate is represented as follows:

$$r(t)=\exp[\beta' \mathbf{X(t)}] \qquad \text{Equation 3-11}$$

where β is a vector of coefficients and **X(t)** is a vector of exogenous variables assumed to influence the rate. This fact that this exponential model assumes constant hazard rates through time initially appears to conflict with one of the central objectives of this study is to relate IPO rates to a variety of changing environmental conditions. This apparent conflict will be resolved in a moment when it is shown how this simple model can be used to deal even with complex rates that change over time.

A second commonly encountered specification of hazard rates is Cox's proportional hazards model (1972) which uses partial likelihood methods to estimate hazards. A feature of this specification is that although it allows for hazard rates to vary over time, no specific parametric assumptions are required about how the "baseline" hazard varies over time. In this study, however, one of the issues of interest is if there is a specific pattern of changes in the rate at which firms go public as they age. Without modification, Cox's proportional hazard model would not allow us to get an idea of the impact aging has on IPO rates. As with the exponential model outlined above, however, the applicability of this model can be extended to

include the impact of changing covariates. The means of making these extensions will be described below.

The specific form of the Cox model is

$$r_{ij} = h_{ij}(t)\exp[\beta' \mathbf{X}] \qquad \text{Equation 3-12}$$

where $h_{ij}(t)$ is an unspecified nuisance function that varies with time but that is constant across individuals, β is a vector of coefficients and **X** is a vector of covariates. Hopkins makes the following observation:

> Notice that no parametric model is assumed for the underlying hazard function. This model implicitly contains two assumptions. The first assumption is the multiplicative relationship between the underlying hazard function and the log-linear function of the covariates (the proportionality assumption). Thus the ratio of the hazard function for two individuals with different sets of covariates does not depend upon time. ... The second assumption is that the effect of the covariates upon the hazard function is log-linear. (Hopkins 1990, p. 769)[36]

Unlike the exponential model which is estimated using maximum likelihood methods, the Cox model is estimated using partial likelihood methods outlined by Cox (1972). The insight of the Cox model is that, given proportionality, one can take the ratio of the hazards that an event will affect any individual at any point in time given that an event occurs to some individual lead to an expression which does not involve $h_{ij}(t)$. Paraphrasing Hopkins (1990 pp.

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[36] In fact the implications of the first assumption are neither as onerous nor as forgiving as one might assume. As soon as one introduces time-dependent covariates proportionality no longer applies so this assumption is really not as restrictive as it might appear. Conversely when we include age of the firm among the time-dependent covariates we in fact have to make parametric assumptions about aging. Nevertheless, within the sub-spell, no assumptions have to made about the impact duration has on the hazard, and indeed the hazards are proportional within this very limited sense.

760-761): the conditional probability that individual k with covariate vector $\mathbf{X}_k$ experiences the state transition of interest at time t_k, given that a single response occurs at t_k and given the risk set R_k (those at risk immediately before the event), is the ratio of the hazards:

$$\exp(\beta'\mathbf{X}_k) \Big/ \sum_{l \in R_k} \exp(\beta'\mathbf{X}_l) \qquad \text{Equation 3-13}$$

As Hopkins then continues, multiplying these conditional probabilities together for all of the *m* distinct response times gives the partial likelihood function (Cox 1975):

$$L(\beta) = \left\{ \prod_{k=1}^{m} (\exp(\beta'\mathbf{X}_k) \Big/ \sum_{k \in R_k} (\exp(\beta'\mathbf{X}_l) \right\} \qquad \text{Equation 3-14}$$

Various adjustments to the basic likelihood outlined above are made to make allowance for ties in the response times. The partial likelihood models estimated in this study are all estimated using the implementation contained in the PROC PHREG program distributed by the SAS Institute. Discussions of the specifics of the maximization process can be found in documentation supplied with many survival analysis programs.[37]

A third means of estimating hazard rates is to rely on non-parametric methods. Given that no previous studies can be relied on guide us in the specification the effect aging has on IPO rates a method that allows for a crude representation of how hazard rates vary over time is valuable. One

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[37] One such source is Rohwer 1991 (pp. 56-58). A short discussion is also included in Hannan and Freeman (1989, p. 198) and in Hopkins (1990).

such method is the life-table or actuarial method whereby the time axis is broken up into intervals of often arbitrary duration and the hazard is estimated on the basis of the probability of an event within each interval. In order for this life-table method to work, each interval must contain a sufficient number of events to allow for accurate estimation of the probabilities. One shortcoming of this and other non-parametric methods such as Kaplan-Meier and Aalen estimators is that they do not allow for the estimation of the impact of covariates (except for the specification of discrete strata within the data) on the rates being modelled. The life-table estimator of the hazard rate is based on the following values.[38]

I_i = intervals of discrete duration, i= 1, 2 ...., q; $[t_{i-1}, t_i)$,

$D_i = t_i - t_{i-1}$ duration of interval I_i,

E_i = the number of firms with events in interval I_i,

and

C_i = the number of censored observations within interval I_i.

These values are then used to define N_i (the number of organizations entering interval I_i) and R_i (the "risk set" or set of organizations at risk of an event in interval I_{i+1}). The first of these is recursively defined as $N_1 = N$ (the original number of organizations) and $N_i = N_{i-1} - E_{i-1} - C_{i-1}$. Finally, R_i, the risk set for in interval I_i, adjusted for the fact that some organizations are censored within the interval[39] is defined as follows:

$$R_i = N_i - C_i / 2. \qquad \text{Equation 3-15}$$

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[38] This discussion is broadly modelled on that contained in Rohwer 1991 (pp. 33-34) and that in found in SAS/Stat User's Guide, 1990 (pp. 1044-1045).

[39] The common practice of assuming that, on average, half of the censored observations are present throughout the interval is adopted here.

The conditional probability of an event in interval I_i is thus:

$$q^* = E_i / R_i, \qquad \text{Equation 3-16}$$

and finally the hazard rate and its standard error are estimated as follows:

$$r_{ij}(t) = (2\,q^*) / [D_i\,(2-q^*)]. \qquad \text{Equation 3-17}$$

and

$$\sigma[r_{ij}(t)] = r_{ij}(t)\sqrt{1-\left\{\frac{D_i\,h(t)}{2}\right\}^2 \Big/ R_i q^*}\,. \qquad \text{Equation 3-18}$$

Life table estimates of hazards will be used as a first crude tool of picturing the behavior of the IPO hazard as the firm ages. These crude pictures of hazards will be combined with other methods to suggest a simple parametric representation of how the hazard changes with firm age.

SPELL-SPLITTING

The main modelling enterprise of this study relies on the specification of how hazard rates are affected by the values of covariates that change with the passage of time. Many of these covariates change continuously but others are values that can easily be taken to describe conditions over a discrete period of time. While the actual IPO occurs on a given day and can thus be seen as occurring at a specific point in continuous time, the process of preparing for the IPO takes place over a period of months. Given these considerations, it is desirable to define time-varying covariates in such a way that they can be taken to describe conditions over a period prior to the IPO. The period considered most appropriate over which to measure variation in

time varying covariates was the calendar quarter. This selection is a natural one because of the nature of quarterly company financial reporting (which in the vast majority of cases coincide with calendar quarters) and also because relevant economic data are released on a quarterly basis.[40]

A method commonly employed in event history studies is a process referred to as "spell-splitting" whereby the simplifying assumption is made that covariates that change with time change only at discrete points. In this process the full "spell" (the period between the organization's formation and the occurrence of an event or the end of the observation period) is divided into disjoint sub-spells that collectively constitute the full life history of the individual firm. In effect this approach treats covariates that change with time as if they were step-functions where the values are updated at the beginning of each sub-spell. This "spell-splitting" methodology is described in Tuma and Hannan (1984), Petersen (1986), Rohwer (1991), and Blossfeld, Hamerle and Mayer (1989) among others. In this study, all variables are updated at the beginning of each calendar quarter and retain these values throughout the quarter that constitutes the "sub-spell." Firms which experience no event during the course of the sub-spell (in this case the quarter) are treated as if they were right-censored at the end of the quarter.

This method can be applied in a straightforward fashion as long as the hazard does not change over the course of the spell, in which case the exponential specification of the hazard can be used throughout. In order to allow for the possibility that the hazard does vary within the calendar quarter, some models employing this spell-splitting methodology are also estimated

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[40] Though it must be admitted that the release dates for this information precede the ends of calendar quarter by a month so the match is not perfect.

using the Cox partial likelihood model described above. In fact, IPO rates do appear to vary over the course of the calendar quarter. As can be seen from Figure 3-1 there appears to be a pattern to the within-quarter distribution of IPOs. While is possible to speculate as to the reasons for this variation (holidays, working schedules of underwriters, impacts of availability of quarterly results, etc.) none of these factors is of particular relevance to this study. In any event, the effect of this within-quarter variation of IPO rates on the covariates of interest is checked by running both exponential models and partial likelihood models. Some of the latter are reported for comparative purposes.

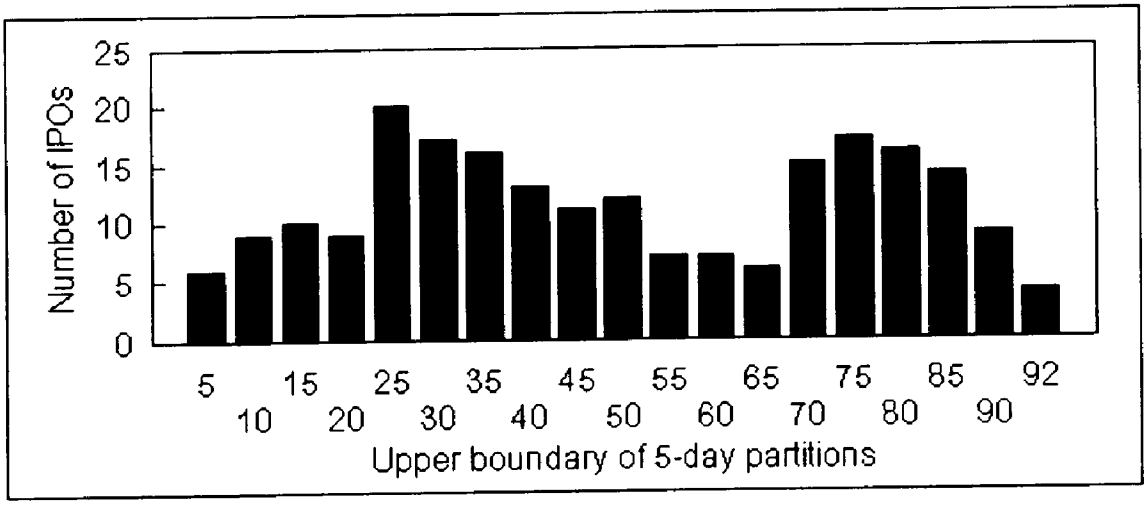

Figure 3-1: Within-quarter distribution of IPOs

In the spell-splitting method the likelihood is constructed as a product of survivor functions for individual sub-spells and the probability density function for the last sub-spell (if the full spell ends in an event). Following Hannan and Carroll (1992 p. 244) this likelihood function is represented as

$$\mathcal{L} = \prod_{i=1}^{I} f_i(t)^{\delta_i} S_i(t)^{1-\delta_i} \qquad \text{Equation 3-19}$$

where δ_i equals one if the "time of the mortality of the organization (that is uncensored); and it equals zero otherwise" (Hannan and Carroll 1992, p. 244). In the case of the exponential model the coefficients can be estimated using maximum likelihood. I estimated all parametric models with SAS PROC LIFEREG (SAS Institute, 1990). When using Cox's partial likelihood model,[41] spell-splitting procedures analogous to those described above are equally applicable (Rohwer 1991, pp. 67-70).

COMPETING RISKS AND CAUSE-SPECIFIC HAZARDS

The passage from private to public status has a specified and observable duration, and it can be argued that the process is influenced by a variety of measurable external factors and is likewise affected by observable features or measurable dispositions of the individual firms. As in event-history models of organizational failure, the study of the propensity of firms to go public is complicated by the fact that events other than IPOs can terminate the firm's existence as an independent, privately-financed entity. In the case of studies of organizational mortality, the main competing risk to consider is absorption by another firm through merger or acquisition. In the case of IPOs, the firm can exit its state as a privately financed entity by one of three general classes of event: failure, acquisition and IPO. Hence failure and acquisition can be regarded as competing risks to IPO.

In estimating the hazard of IPO, a cause-specific modelling of the specific hazard of IPOs is employed. As demonstrated in Kalbfleisch and

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[41] The Cox model can be sensitive to the existence of ties and spell-splitting leads to an increased number of "within sub-spell' tied durations. In the models reported in this study, however, the results proved to be invariant over the alternative computational approaches to treating ties (all four methods available in SAS PROC PHREG were tested).

Prentice (pp. 168-172), if a sufficient number of observations exist on the "cause-specific waiting times, the joint distribution can be estimated arbitrarily closely without the assumption of latent waiting times and independence of competing risks" (Hannan and Carroll 1992, p. 245) and maximum likelihood methods can be used to estimate the hazard of the event of interest. In employing this modelling approach, organizations that exit the risk set by an event other than the one being studied (in this instance an IPO) are treated as right-censored observations. For purposes of completeness, to get a better picture of the data as a whole, and to assess the possible validity of the stronger assumption of independence of competing risks, results of running models of the two other specific risks (failure and acquisition) are also presented at the end of chapter 5. All the hazards reported in this study can thus be seen as cause-specific rates (for event j).[42] Following Hannan and Carroll 1992, p. 245) we consider a "joint distribution of a random variable (T,Y), where T_i still denotes time of mortality or right censoring and Y_i denotes the type of mortality observed to occur to the ith organization." Modifying Hannan and Carroll's notation slightly, the cause-specific hazard rate (for cause j) is defined as

$$r_{ij}[t|\,X(t)] = \lim_{(\Delta t \to 0)} \frac{PR(t + \Delta t > T_i \geq t,\, Y_i(T_i) = j \,|\, T_i > t)}{\Delta t} \qquad \text{Equation 3-20}$$

In our case, the IPO rate is estimated by treating spells ending in acquisition or failure as right-censored observations. Since IPOs are used to right censor observations in the competing risk models of failures and acquisitions, these

[42] Please note the change in notation compared to the equation 3-5, here i stands for the organization rather than the origin state.

models should be understood to represent failures and acquisitions of private firms only.[43]

EVALUATING THE EFFECTS OF AGING AND PERIODS USING PIECE-WISE CONSTANT EXPONENTIAL MODELS

Because there are few prior studies that can serve as guides for either the specification of how age affects IPO rates or how various periods affected the IPO rates of biotechnology firms in particular, an investigative modelling approach was employed to guide model-building in both these cases. The approach in question is commonly referred to as a piece-wise constant exponential model. In this approach dummy variables are used to identify age categories (or historical periods). Within these categories or periods the hazard rate is constrained to be constant within the category (or period) but across categories can vary in any fashion suggested by the pattern of events in the actual data. This method is extremely flexible and allows the IPO rate to assume virtually any shape over time or across age categories. In both cases these models are used primarily to validate parametric assumptions about the structure of the hazard rates, if supported by this analysis the more parameter-parsimonious models are then employed in the balance of the analysis. The only constraint on the application of this method is that the periods and age categories have to be constructed so that at least some events occur within each period or category.

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[43] Preliminary examination of failure and acquisition rates of all firms, including subsidiaries, indicates that the basic findings related to these events is similar when the event studied is not confined to departures from private status.

CHAPTER 4. SOURCES AND DESCRIPTIONS OF THE DATA EMPLOYED

In this chapter I describe the steps I took to ensure that I secured information on as great a proportion of the firms within the biotechnology population as was possible. As opposed to many other types of studies, the normal practice within the organizational literature on population ecology is to strive to estimate all models on the basis of data for all members of the population concerned. This emphasis on comprehensive data collection arises out of a concern that bias will be introduced into models if some kinds of firms (possibly those that have survived) are more likely to be identified if one employs less rigorous data identification procedures. This chapter also outlines various general characteristics of the data that are central to understanding the IPO process and the environment in which they they place.

IDENTIFYING THE POPULATION

The task of enumerating the universe of American biotechnology firms over the full study period was difficult because no single rule for identifying a firm as a biotechnology firm has been adopted either by researchers or by the financial and business press. The lack of agreement over how to identify biotechnology firms is underscored by the fact that contemporaneous estimates of how many biotechnology firms are active in America often differ by considerable margins.

Two possible explanations exist for these divergent opinions over how many biotechnology firms are active. The first is that there is substantive disagreement over what qualifies a firm to be considered a "true" biotechnology firm. The second is that different sources vary in their success

at finding all the firms that fit their definition of biotechnology firms. The success of any individual or institution at coming to know of the existence of a particular firm might vary with geographic proximity to the firm, the research focus of the firm and the extent of the firm's affiliation with other firms and institutions involved in biotechnology research. In practice, both definitional disagreements and practical difficulties of identification of firms appear to contribute to the discrepant groups of firms identified by different authorities as being the population of American biotechnology firms.

In order to allow for the likelihood that different sources might vary in their success in identifying the existence of any given biotechnology firm, nine different directories of biotechnology firms (published between 1985 and 1993) were employed to identify and categorize firms. The nine directories coded[44] were: *Bioscan 1988* and *Bioscan 1990*; *Genetic Engineering and Biotechnology Firms Worldwide Directory, 1985* (GEBW 1985); *Genetic Engineering and Biotechnology Yearbook, 1985* (GEBY 1985); Mark Dibner's *Biotechnology Guide, U.S.A. 1988* (Dibner 1988) and *Biotechnology Guide, U.S.A. 1991* (Dibner 91); appendix A to *New Developments in Biotechnology: U.S. Investment in Biotechnology* (OTA 1988, p. 25-34); *1993 GEN Guide to Biotechnology Companies* (GEN 1993); and *Sixth Annual GEN*

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[44] With the exception of *New Developments in Biotechnology: U.S. Investment in Biotechnology, Biotechnology Guide, U.S.A. 1991* and *1993 GEN Guide to Biotechnology Companies* all of these directories had previously been used as sources of company information for the Biotechnology project under the direction of Stephen Barley at Cornell. The addition of these three sources led to the expansion of this predecessor database by about 342 firms. In addition, all company entries that were inherited from the Barley database were recoded so that each piece of information from each source directory (founding dates, home state, technology focus, etc.) was recorded as a distinct data item so as to allow for identification of discrepancies among directories, to allow for a better audit trail of source information and generally to allow for easier verification of information by maiking it easier to return to source directories for clarification.

guide to Biotechnology Companies (GEN 6). Coded as a separate source were companies listed by Mark Dibner as dead or missing in *Biotechnology Guide, U.S.A. 1991.* All nine directories I employed were widely circulated and all made claims to wide or exhaustive coverage of the American biotechnology industry.

In addition to identifying firms by using these specialized directories, some firms were added to the database after a review of the business and technical press. Particular efforts were made to identify firms that either failed or were absorbed early in the history of the industry and that, as a consequence, were not mentioned in directories. An example of such a firm is Armos, Inc., whose history and failure is documented in Kenney (pp. 173-174, 181-182). Similar efforts were directed towards identifying firms that appeared only at the very end of the study period and were particularly likely to have been overlooked by even the latest of the directories employed. An example of such a firm is Myriad Genetics, Inc., a firm which was founded in 1992 and rose to prominence in 1994 when it was granted a patent to a gene for breast cancer.

CATEGORIZING FIRMS BY RESEARCH FOCUS

To allow for fact that there are different definitions of what constitutes a biotechnology firm, all firms considered eligible for inclusion in the study database were further categorized as to what kind of biotechnology activity the firm was engaged in. At a gross level, this categorization was expressed by assigning a primary activity class to each firm. The categories employed were: human therapeutics, human diagnostics, agriculture (including veterinary), toxic waste treatment, drug delivery, other applications and

unknown focus. Since many firms were active in more than one of these areas of activity, a rule had to be developed to assign such firms to a single category. In most instances the primary focus of firms was readily apparent from listings in directories and other accounts of the firm's activities. In other cases the rule was generally to assign a firm to the category of greatest regulatory oversight and capital requirements accoding to the following rules. If the firm is active in human therapeutics, then categorize it as a therapeutics firm. If a firm is not a therapeutics firm but is active in human diagnostics, then categorize it as a diagnostics firm. If a firm is neither a therapeutics firm or a diagnostics firm but is active in agricultural or veterinary research, then categorize it as an agricultural firm. These three rules allowed for virtually all firms to be assigned to a single category of firm.

The meaning of some of the remaining categories of firms bears further explanation. Drug delivery firms included firms whose focus was not the production of active therapeutic agents themselves but rather the development of novel means of drug delivery that depended on new technologies. This category includes firms whose research lies in liposomes and in transdermal drug delivery. Some argument can be raised that these firms are not properly biotechnology firms in the first place but, in practice, these firms were, and are, widely identified as being biotechnology firms. Toxic waste treatment firms are those firms whose treatments are dependent on the utilization of bioremediation techniques derived through biotechnology research. Firms categorized under "other applications" included the following: firms utilizing biotechnology in food preparation; firms engaged in chemical manufacture, testing laboratories such as those testing for DNA matches (most often used for determining paternity and for forensic identification); and

firms actively employing biotechnology to produce products but whose activities were not themselves directed at the specific target markets otherwise identified (e.g., Research Genetics, Inc. which does custom rDNA and monoclonal antibodies for research use only by other firms and institutions). Firms included as biotechnology firms of "unknown focus" were firms asserted to be active in biotechnology by directories or other sources but about which insufficient information was available to assign them to a specific category. Firms in this last category might reasonably be regarded as having somewhat dubious standing as biotechnology firms. Many of these firms appear to have risen to the attention of compilers of directories by virtue of their relationships with other biotechnology firms (often when they were acquired by other firms).

The categorization scheme outlined above allows for easy contraction and expansion of the definition of "biotechnology firm" to suit different purposes. It also serves to describe essential heterogeneity among the firms being studied. Firm capital requirements and the expected duration of negative cashflow from operations almost certainly vary according to what kind of product is being developed. Being able to build models that distinguish between a firm engaged in developing new human therapeutic agents and a firm developing in-vitro diagnostics should improve the quality of the results obtained relating to the likelihood of IPOs. It should be noted, however, that the overall definition of biotechnology firm is much narrower than that which is often employed. In this study, firms whose fortunes are dependent on biotechnology but whose core business does not employ the

new technologies are not themselves considered biotechnology firms.[45] Thus a wide range of firms selling instrumentation, fine chemicals, glassware, laboratory equipment, and other materials essential to biotechnology research are not counted among biotechnology firms. In addition, firms providing consulting and engineering advice to biotechnology firms but which do not produce products themselves were similarly excluded from consideration.

The relative numbers of the various categories of firms in the American population at the end of the study period can be seen in tables 4.1 and 4.2. These tables emphasize the fact that although therapeutics firms form only about a quarter of the population of independent, private firms, therapeutics firms constitute nearly 60 percent of the 1993 population of independent, public biotechnology firms. This discrepancy supports the general suspicion that firms in these categories display differential needs and propensities to go public. Given the dominance of therapeutics, diagnostics and agricultural firms there is also reason to suspect that it might be these kind of firms that form the core of the public perception of biotechnology firms. If this suspicion is justified then employing a more restrictive definition of biotechnology firms might conform more closely to the implicit definition of biotechnology firms that has been adopted by the financial markets.

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[45] In the coding of firm classes conducted under the direction of Stephen Barley and Ralph Hybels, firms that were coded BO (for Biotechnology Organizations) and MBO (for Maybe Biotechnology Organization) were included in this core grouping and firms coded SG (for Suppliers of Goods) and SS (for Suppliers of Services) were excluded. In coding I conducted of other directories I tried to employ the same categorization philosophy as that developed by the original Barley project group. Further detail on coding of firm classes can be found in Barley, Freeman and Hybels (1989).

Table 4-1: Independent non-public population at the end of 1993

Type of firm	Count	Percentage
Therapeutics	114	24.8%
Diagnostics	108	23.5%
Agriculture	29	6.3%
Toxic	20	4.4%
Other	144	31.4%
Drug delivery	4	0.9%
Unknown	40	8.7%
Total	459	100.0%

Table 4-2: Population of public firms at the end of 1993

Type of firm	Count	Percentage
Therapeutics	106	58.9%
Diagnostics	35	19.4%
Agriculture	14	7.8%
Toxic	2	1.1%
Other	13	7.2%
Drug delivery	9	5.0%
Unknown	1	0.6%
Total	180	100.0%

COVERAGE OF THE VARIOUS DIRECTORIES

In order to assess the adequacy of our means of identifying participants in the industry and the relative strengths of the various sources of firm information, a comparison of these sources was conducted to see if what degree of consistency could be found in enumerations of the population and what particular strengths and weaknesses prevailed for each directory. Table 4.3 shows the number of independent biotechnology firms listed in each directory (each directory also included subsidiaries and firms which for this study were categorized as suppliers of goods and services rather than biotechnology firms) and (reading across) what percentage of these firms were also listed in each of the other directories.

Table 4.4 presents a similar analysis but this time the coverage of each directory is broken out by the percentage coverage each directory achieves for each category of firm. In both tables it is apparent that coverage of the industry in the two directories authored by Mark Dibner is broader (possibly due to a less exclusive definition of biotechnology) than that of other directories. The listing of defunct firms found in Dibner's 1991 directory is also the source of many of the firms of unknown focus, many of which are only found in this single listing. Although not apparent in these particular tables, the directory *Genetic Engineering News 93* (GEN 1993) is the sole source of many of the firms which appear late in the study period but is a poor source of firms that had been active earlier in the history of the industry. In general the *Bioscan* listings were also found in other directories, signalling that *Bioscan* uses a definition of biotechnology that is among the most restrictive of the directories employed in this study.

Table 4-3: Degree of overlapping coverage among source directories

	#	1. OTA 1984	2. Dibner 1988	3. Dibner 1991	4. Dibner defunct	5. GEBW 1985	6. GEBY 1985	7. GEN 6	8. GEN 1993	9. Bioscan 1988	10. Bioscan 1990	Only Entry
1. OTA 1984	225	100%	87%	73%	12%	62%	60%	58%	44%	64%	63%	.4%
2. Dibner 1988	267	73%	100%	72%	15%	54%	54%	54%	45%	61%	59%	1%
3. Dibner 1991	491	34%	39%	100%	0%	26%	26%	28%	47%	32%	47%	26%
4. Dibner 1991 (defunct firms)	97	27%	40%	1%	100%	30%	31%	8%	2%	24%	13%	46%
5. GEBW 1985	198	0.71	0.73	65%	15%	100%	77%	47%	36%	69%	60%	7%
6. GEBY 1985	194	0.7	0.74	65%	15%	78%	100%	45%	37%	68%	62%	4%
7. GEN 6	166	78%	87%	83%	5%	57%	53%	100%	60%	65%	71%	0%
8. GEN 1993	316	31%	38%	74%	1%	22%	23%	325	100%	28%	46%	21%
9. Bioscan 1988	212	68%	76%	74%	11%	65%	62%	51%	42%	100%	80%	1%
10. Bioscan 1990	285	50%	55%	80%	5%	42%	42%	41%	50%	60%	100%	6%
In none of above	79											

Table 4-4: Percentage of firms of each research focus found in each source directory

	#	OTA 1984	Dibner 1988	Dibner 1991	Dibner defunct	GEBW 1985	GEBY 1985	GEN 6	GEN 1993	Bioscan 1988	Bioscan 1990
Therapeutic	260	23%	30%	63%	5%	20%	19%	21%	46%	25%	41%
Diagnostic	196	29%	31%	70%	5%	28%	29%	21%	37%	32%	38%
Agriculture	62	35%	40%	68%	8%	37%	40%	24%	34%	35%	42%
Toxic waste	29	28%	34%	62%	1%	10%	21%	14%	34%	21%	28%
Other	209	33%	40%	60%	1%	30%	26%	23%	42%	24%	26%
Drug delivery	14	29%	29%	43%	0%	21%	21%	7%	29%	21%	50%
Unknown	74	4%	5%	0%	64%	0%	1%	1%	1%	3%	11%
All firms	844	27%	32%	58%	11%	23%	23%	20%	37%	25%	34%

DEFINITION OF FIRM BIRTHS

Depending on context, a variety of definitions of firm birth could be sensibly advanced. In cases where licencing is an essential step in establishing operations the date on which the licence is granted has been used in studies (e.g., Baum and Oliver's 1991 study of child care service organizations). In *Organizational Ecology*, Hannan and Freeman give the following account of the various definitions they have employed for organizational birth.

> Our empirical materials differ in how they define the time of starting. For labor unions, it is the date of a national convention that writes the charter for a new union or the date on which a merger between unions is ratified at national conventions. For semiconductor manufacturing firms, the starting date is the date of entry into the production and sale of semiconductor devices. For newspaper publishers and restaurants, it is the date of start of business (publishing newspapers or serving meals). (p. 149)

A final reasonable definition of organizational birth is the incorporation date of the firm. While use of incorporation dates as start dates for firms is common, one prior study which employs this data is Ranger-Moore, Banaszak-Holl, and Hannan (1991). It is this last definition of organizational birth that has been employed in this study.

Several arguments can be advanced in favor of using incorproration dates as start dates in this particular context. First, self-reports of start dates of independent firms included in the industry directories strongly tended to correspond to dates of firm incorporation. This tendency was in most cases only violated in cases where firms had been involved in some kind of business combination that allowed respondents to use either the start date of the legal entity as a starting point or to use the date on which the physical or

organization unit in question first came into existence. Full knowledge of the organizational history of a company allowed for the reconciliation of self reported start dates and the legal incorporation dates in all but a handful of cases. Second, the perceived risk of biotechnology coupled with organized opposition to its use (e.g., Jeremy Rifkin's various endeavours) likely serves as a strong inducement to limit liability by means of incorporation. This latter consideration is in keeping with the argument presented earlier that the very existence of the small biotechnology firm was influenced by corporate America's reluctance to place substantial assets at risk (Barney, Edwards, and Ringleb 1992) by dabbling in technologies that might unleash dangerous organisms that would lead injured parties to seek legal redress for damages. Third, since the event of interest in this study is the act of going public and in order to do so a firm must be incorporated, firms that might later expect to resort to going public might also be expected to incorporate at the earliest available opportunity.

NAME CHANGES AND REINCORPORATIONS

In researching information on firm incorporations, every effort was made to record all relevant information on the history of a firm's legal existence. Since it is a well known fact that firms do not always incorporate themselves in their state of primary operations or that of their head office, care was taken to record both the dates on which companies were incorporated and those on which foreign corporations were registered. In cases where the original appearance of a firm in its home state (in most cases an unambiguous designation of the state in which it was primarily active determined by information included in directories and other information

sources) was as a foreign corporation, the date of its original incorporation in another state (usually Delaware) was also sought and recorded. Since firms also frequently reincorporate themselves (usually in another state, with the most common state of reincorporation being Delaware) care was also exercised to ensure that reincorporation dates were not conflated with incorporation dates.

Finally, since many firms change names over time, and since the same firm might appear in different directories under different names, all information on legal name changes (and dates thereof) was recorded and employed in ensuring that multiple listings for single firms were not included in the database. With a similar motivation, any information on company tradenames and abbreviations of company names were also recorded when available.

The primary source of company incorporation information was from direct query of state records. Records for a number of states, including the two most prominent states for biotechnology firm startups, California and Massachusetts, were available for on-line query through the Lexis-Nexis database (the number of states accessible through Lexis-Nexis has since been expanded significantly). All of the remaining states provide for public access of records by telephone or written queries of incorporation data. Details of how to secure such public access data were obtained by referring to listings of state agencies found in *INC. Yourself* (McQuown, 1992). Delaware records were also accessed via a public access computer terminal in the offices of the Secretary of State offices in Dover, Delaware to ensure that confusions engendered by similar names and multiple incorporations could be

minimized by collecting that full and accurate corporate histories were recorded for all firms which were identified as biotechnology firms.

Knowledge of which state a firm was incorporated in was also important, since there is evidence that a firm's choice to incorporate or reincorporate in a state other than its home state conveys information about a firm's strategic intentions. Romano's 1990 survey of the state competition debate in corporate law highlights that the many of the considerations that would influence a company to choose to charter itself in another state most often resolve around questions of regulating the relations between management, directors and shareholders. The simpler the present and expected governance structure of the firm the less likely that there is any particular advantage to be gained by choosing to incorporate in another state. Romano's observations relating to her research on the concomitants of reincorporation support both this contention and put the issue of choice of state in which to incorporate into a transaction cost context.

> My data on reincorporations support this contention: Firms reincorporate when they are preparing to initiate a discrete set of transactions, the most frequent being a public offering, a merger and acquisition program, or defensive maneuvering against takeovers. A number of legal rules that vary across the states, including the conditions for shareholder voting and appraisal rights, affect the cost of engaging in such activity. For instance, corporation codes may limit merger voting and appraisal rights of the acquiring firm's shareholders, which reduces acquisition costs. They may also regulate takeovers or make charter amendment flexible, reducing the costs of resisting a bid. Finally, different organizational rules, including the requirements for shareholder meetings, written consent, and board communication, both ease the transition to, and reduce the cost of operating, a newly publicly traded firm. (Romano 1990, pp. 225-226)

Tables 4.5 and 4.6 summarize the incorporation choices of firms coupled with how many of the different classes of firm have subsequently gone public. These tables suggest that incorporation in Delaware is associated with the subsequent financing choices made by the corporation. A tabular summary of the 20 states in terms of counts of biotechnology firms is represented in table 4.7. The importance of California and Massachusetts as centers of biotechnology research is readily apparent, especially when their percentage share of the independent biotechnology population is compared to their share of the U.S. population (derived from the *Statistical Abstract of the United States: 1994*, table 26).

DEFINITION OF GOING PUBLIC AND SOURCES OF INFORMATION

Since the motivation for this study was to examine the factors affecting the likelihood that a firm would make a major change in form, the definition of an IPO needed to be kept consistent with this mission. In keeping with many of the discussions and studies of IPOs found in the finance and accounting literature (Ibbotson, Sindelar, and Ritter), this study excludes the very smallest public offerings from consideration.[46] These small offerings, referred to as Regulation A offerings, involve much less stringent oversight by the Securities and Exchange Commission (SEC) and other regulators than larger offerings, typically attract much less attention from the financial community (industry directories such as the *Investment Dealers Digest* do not include them in their financing summaries), and because of fixed costs of the offerings

[46] The number or firms affected by this exclusion is only eight. Identification of six of these eight firms as biotechnology firms is questionable, and only one of which (Earl-Clay Laboratories, which failed in 1988) was without doubt an active firm universally recognized as being both legitimate and as a core biotechnology firm.

Table 4-5: Incorporation choices of biotechnology firms

Home State	Only Home State Charter	Delaware Reincorporation	Delaware Incorporations	Total # of Firms
Unknown	0	0	5	5
AL	1	1	2	4
AZ	1	0	3	4
AR	1	0	0	1
CA	163	27	50	240
CO	10	5	4	19
CT	4	1	10	15
DE	0	0	1	1
DC	2	0	1	3
FL	9	1	5	15
GA	6	0	4	10
HI	1	0	0	1
IL	11	2	5	18
IN	5	1	1	7
IA	8	1	0	9
KS	2	0	1	3
LA	3	0	1	4
ME	5	1	3	9
MD	30	5	15	50
MA	46	9	37	92
MI	16	0	0	16
MN	12	0	0	12
MO	3	2	2	7

Table 4-5 (Continued)

Home State	Only Home State Charter	Delaware Reincorporation	Delaware Incorporations	Total # of Firms
MT	2	0	1	3
NV	5	0	0	5
NH	0	0	1	1
NJ	23	2	19	44
NM	5	0	0	5
NY	28	1	15	44
NC	18	3	3	24
ND	0	1	0	1
OH	12	0	2	14
OK	2	0	1	3
OR	10	0	0	10
PA	23	1	7	31
RI	0	0	2	2
TN	8	0	1	9
TX	33	3	11	47
UT	2	3	2	7
VA	8	0	2	10
WA	19	1	6	26
WI	12	0	1	13
Total	549	71	224	844

Table 4-6: IPO activity by incorporation status

Home State	IPOs Home state Charter	IPOs Delaware Reincorporation	IPOs Delaware Incorporation	Total IPOs
Unkown	0	0	0	0
AL	0	0	0	0
AZ	0	0	0	0
AR	0	0	0	0
CA	31	12	28	71
CO	2	4	1	7
CT	0	0	4	4
DE	0	0	0	0
DC	0	0	1	1
FL	3	0	2	5
GA	0	0	3	3
HI	0	0	0	0
IL	0	0	1	1
IN	0	0	1	1
IA	0	1	0	1
KS	0	0	0	0
LA	0	0	1	1
ME	0	1	2	3
MD	5	0	7	12
MA	8	4	16	28
MI	4	0	0	4
MN	5	0	0	5
MO	0	1	1	2

Table 4-6 (Continued)

Home State	IPOs Home state Charter	IPOs Delaware Reincorporation	IPOs Delaware Incorporation	Total IPOs
MT	0	0	1	1
NV	0	0	0	0
NH	0	0	0	0
NJ	4	2	13	19
NM	3	0	0	3
NY	8	0	6	14
NC	2	1	0	3
ND	0	1	0	1
OH	1	0	0	1
OK	1	0	0	1
OR	1	0	0	1
PA	2	0	4	6
RI	0	0	1	1
TN	1	0	0	1
TX	0	1	5	6
UT	0	2	0	2
VA	1	0	1	2
WA	3	0	4	7
WI	0	0	0	0
Total	85	30	103	218

Table 4-7: Twenty states with the largest number of independent biotechnology firms compared with those states' shares of the U.S. population

Home State	Total # of Firms	Percentage of total firms	Cumulative Percentage of total firms	Percentage of U.S. Population	Cumulative Percentage of U.S. Population
CA	240	28.4%	28.4%	12.1%	12.1%
MA	92	10.9%	39.3%	2.3%	14.4%
MD	50	5.9%	45.3%	1.9%	16.4%
TX	47	5.6%	50.8%	7.0%	23.4%
NY	44	5.2%	56.0%	7.0%	30.4%
NJ	44	5.2%	61.3%	3.0%	33.4%
PA	31	3.7%	64.9%	4.7%	38.1%
WA	26	3.1%	68.0%	2.0%	40.2%
NC	24	2.8%	70.9%	2.7%	42.9%
CO	19	2.3%	73.1%	1.4%	44.2%
IL	18	2.1%	75.2%	4.5%	48.8%
MI	16	1.9%	77.1%	3.7%	52.4%
FL	15	1.8%	78.9%	5.3%	57.8%
CT	15	1.8%	80.7%	1.3%	59.0%
OH	14	1.7%	82.3%	4.3%	63.3%
WI	13	1.5%	83.9%	0.7%	64.0%
MN	12	1.4%	85.3%	1.8%	65.8%
GA	10	1.2%	86.5%	2.7%	68.5%
VA	10	1.2%	87.7%	2.5%	71.0%
OR	10	1.2%	88.9%	1.2%	72.2%
	=====	=====		=====	
	750	88.9%		72.2%	

and their high risk are typically very costly sources of small amounts of equity capital. More germane to the question, however, is the fact that these offerings engender few of the changes in the affected organization, its management, and its relationship with its environment that their larger counterparts do. Although the threshold of gross proceeds over which more stringent oversight becomes applicable changed twice in the study period,[47] the working definition of an IPO employed throughout was an offering generating gross proceed in excess of $1,500,000.

Various sources were employed to identify the dates and details of IPOs. In the first instance, all issues of the biannual *Investment Dealer's Digest Directory of Corporate Financing* between 1979 and 1994 were examined for mention of financing activity by any of the firms in the database of biotechnology firms.[48] Data on offering date, offering size, underwriting (if any), and offering costs were recorded. In most instances this initial identification of IPO date was followed by examination of either prospectus information or information in the first annual reports or 10K following the offering. Examination of these primary documents served to expand the information of firm activities for categorization of firms into the aforementioned activity classes. Data on the firm's previous financing and operatiing activities were also secured from these primary sources for use in other studies not

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[47] In 1979 the amount was increased from $500,000 to $1,500,000 and in 1992 it was increased from $1,500,000 to $5,000,000.

[48] In this review and in all other data collecting exercises any firm that was not in the database of biotechnology firms but sounded as if it might be a biotechnology firm was subjected to further investigation to ensure that firms weren't being excluded in error. This further research almost invariably revealed that these firms were engaged in activities other than biotechnology as defined for this study.

reported on here, including examination of the valuation of unseasoned equity of biotechnology firms.

Other directories that were systematically consulted for information on firm financing activity (in general providing more detailed information than that available in IDD's *Directory of Corporate Financing*) were various editions of *Moody's: OTC Industrial Manual* and firm data included in *Standard and Poor's: Corporate Record.* As a final check that coverage of biotechnology IPOs was complete, various online databases and back issues of magazines such as *Bio/Technology* were reviewed for any joint mentions of IPOs and biotechnology firms.

For the most part, once information on an IPO was secured, no further interpretation had to be conducted. Exceptions were cases where different sources differed and in the case of firms that used a "best efforts" offering.[49] In all cases of disagreement over dates (usually only a day or two difference among sources) further research in all cases resolved the disagreement in favour of one source or the other. In the case of best efforts offering one could choose to record either the offer date when the sales effort begins or the closing date when the offer is either withdrawn or the shares actually begin trading. In most respects, the closing date of a best efforts offering conforms most closely to the IPO date for underwritten offers and hence this date is used for all best efforts offerings. Up to 30 of the 218 IPOs identified

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[49] Best efforts offerings are offerings whereby an underwriter makes no guarantee that the offer will be sold and over a specified period of time attempts to sell the shares at a negotiated price. If the underwriter fails to sell at least an agreed to minimum portion of the offering by the closing date of the offer, the offering is cancelled and no shares are sold. Unlike a "firm commitments" offer in which the underwriter "underwrites" the shares, most of the risk of a best efforts offering is borne by the issuing firm. Best efforts offerings are usually smaller and utilized by less reputable or less "attractive" firms.

were best efforts offerings (when I could find no confirmation that an offer was underwritten I recorded as being a best efforts offering until further information was secured, so this number is almost certainly overstated), for the most part the offerings involved were small and involved less prominent firms.

DEFINITION OF FAILURE AND LIMITATIONS OF INFORMATION

While use of incorporation dates provided a relatively unambiguous definition of firm founding, the definition of firm failure was somewhat more problematic. In the case of failure, like founding, a number of different choices of how to operationalize the event are available to a researcher. Hannan and Freeman (1989, pp. 149-150) list formal dissolution, resource contraction, loss of participation, disorganization and cessation of operations as being among the possible subprocesses that might be taken to signal organizational death. In their overall discussion of definitions of mortality (1989, p. 149-151), Hannan and Freeman also discuss the problem of "lingering death." As they describe the concept, sometimes a firm or an organization may remain legally alive while its activities have shrunk to a shadow of what they once were or even after any real activities of the firm have actually come to an end. In this same discussion, Hannan and Freeman speculate that the extent of this problem varies according to the kind of organization and the cost and benefits of legal dissolution. In the case of biotechnology firms it is easy to imagine where the cost of maintaining the firm could drop to the cost of maintaining its corporate status if facilities were closed and employees were laid off. At the same time, an incentive to maintain legal standing might exist if owners believed that residual intellectual property or patents might still retain some value.

While in some respects defining organizational death as the date at which the last employee was laid off, the date the last phone was disconnected, or the date the last physical facility was vacated would best conform to our intuitions of whether or not the firm was alive, unavailability of information on such events precludes their use. While it does not really address the problem of lingering death, the persistence of legal standing as an incorporated entity was taken to be the defining characteristic of life. Various means of losing corporate status exist, but, with the exception of voluntary dissolution of the corporation, in all state jurisdictions various time limits exist within which corporations must file reports, replace resident agents, and pay franchise taxes or face suspension or involuntary dissolution. To allow for cases where carelessness or other factors lead to temporary suspensions and subsequent revivals, the operational definition of death was taken to be revocation of corporate status that wasn't revived or reversed within six months. In keeping with the practice in other population ecology studies and the discussion of mortality in Hannan and Freeman, bankruptcy and Chapter 11 reorganization were taken to result in the emergence of a distinct organization even if the corporation didn't disappear altogether. Bankruptcies and Chapter 11 reorganizations were thus counted as organizational deaths.

FIRMS FOR WHICH DATA WAS MISSING

Despite all search efforts incorporation dates for some firms that were included in the database could not be found. There are a variety of explanations for the failure to find these dates. These explanations include:

- The firm never existed. This might be the case when firms were included because of name confusion (Selgene instead of Celgene, Conviron instead of Convirons). This might also be the case where plans to form a firm are reported in the press but are never acted upon or where the legal names selected for the enterprise differ from those initially considered.
- The firm is identified by an abbreviation which is not registered as an official name or as a "Doing Business As" (DBA).
- The firm was never incorporated because it is an operating division of another firm.
- The firm is foreign and does not do business in the United States.
- The state records are no longer retained in an accessible format. Some states like Colorado and Maine purge their computer databases of defunct or inactive companies on a regular basis and will conduct a paper search only upon request and payment of fees. Some states also appear to be less diligent about retaining information of prior names of corporations than are others.
- The company has chosen to operate as an unincorporated entity.
- If the company has chosen to launch a "backdoor IPO," unravelling a company's corporate history from that of the public shell company it acquired can be difficult.

All of these explanations account for some of the 114 firms for which no incorporation data could be found. Fortunately, for all but a few of the entities in question, there is good reason to doubt their status as independent biotechnology firms. On average, the 844 firms for which incorporation data was found and which were included in analyses appeared in 2.8 of the nine directories coded. If firms listed by Dibner as deceased are included as

appearances then the average rises to 2.91 appearances per firm for which incorporation data was found. By contrast, on average the 114 firms for which incorporation data was not found appeared in only 1.04 directories each. If appearances in Dibner's lists of defunct firms are included this average rises to 1.39. In fact, of these 114 firms, 54 (47%) appeared in no directories at all and 34 (30%) more appeared only in Dibner's list of defunct firms. The comparable percentages for the firms for which incorporation data was available were 9.4 percent and 5.2 percent respectively. The relatively high percentages of mystery firms that are found in Dibner directories is explained in part by the fact that this directory places heavy reliance on the business press for its entries. This indirect identification of firms allows for more error to be introduced than if inclusion always required other confirmation of the organization's existence. In addition, among the firms for which incorporation data was available but which were listed in fewer directories, the explanation for this lack of coverage was much more likely to be explained by their being too young to have been covered by the directories in question.

Of course, some of the firms for which incorporation data could not be obtained were generally acknowledged to be true biotechnology firms. Among these, Nakanishi International Enterprises is mentioned in four directories and Indiana Biolab is mentioned in 6 directories. Of these, the first is known to be a plant propagation firm engaged in plant cultivation from single cells and operating as a sole proprietorship. Information on the latter suggests that the company was formed prior to 1971. The incorporation dates of two other firms, Cyanotech and BioHumanetics were not included because both firms engaged in reverse takeovers of public shell companies early in their existence and subsequently recorded their founding dates as the

dates on which the public shell companies were founded. Five further firms that made frequent appearances in directories as biotechnology firms were Immunex, Inc. (not Immunex Corp.), Atlantic Antibodies, Inc., Applied Genetics, Inc., Verax Corporation and Clonetics Corporation. All of these corporate histories could probably be discovered by searches of corporate records in several states that now only can be found in paper files. For the moment, however, this information has yet to be secured.

Of the remaining companies, many appear to have first been counted among biotechnology firms when they were acquired by or entered into agreements with firms that were known to be engaged in biotechnology. Of this grouping some almost certainly were formed prior to 1971. Others whose credentials as biotechnology firms are weak might also have chosen to operate as unincorporated entities. For small firms engaged in low risk activities there may have been little cost to this decision, even though it appears to have been an option selected by very few of them.

FIRM ACQUISITIONS AND IDENTIFICATION OF FIRMS AS SUBSIDIARIES SINCE BIRTH

Since the universe of firms being studied excluded biotechnology firms that were founded as subsidiaries of other companies, and counted merger or acquisition as one of the competing risks in survival models, securing accurate data on both founding status and subsequent changes is ownership was of paramount importance. In the construction of the database of firms, all biotechnology firms including subsidiaries and joint ventures were recorded along with independent firms. In addition, all known subsidiaries of biotechnology firms were entered into the database even when the activities

of the subsidiary were not known with certainty. One of the most difficult challenges of the data collection exercise, however, was determining whether a firm identified as a subsidiary of another firm had always been so. If a firm were falsely assumed to have been a subsidiary from birth, two sources of error would be introduced into model estimates. First, failure to include the firm in the risk set would lead to an overestimation of the rate of IPO occurrence for all periods during which the firm persisted as an independent entity. Second, false identification of a firm as a subsidiary from birth would lead to an undercounting of the number of firms which exited the risk set by acquisition or merger.

We resolved ownership ambiguities about inclusion of firms in three ways. First, specialized directories and databases of mergers and acquisitions (*Mergers & Acquisitions*, *Mergerstrat*, and *Mergers and Acquisitions Report*) were searched for for any mention of any of the biotechnology firms in the database including those identified as subsidiaries, joint ventures or divisions of other companies. Second, any available corporate histories of the parent companies (e.g. Moody's manuals, Standard & Poors manuals and company annual reports and 10Ks) were searched for any mention of events involving the subsidiary in question. Third, general searches of the databases such as the news databases on Lexis/Nexis were searched for any mention of firms whose histories hadn't been verified by other means.

In keeping with the practice of directories such as *Mergers & Acquisitions*, wherever possible the date used for acquisitions was the date the merger or acquisition was finalized rather than the date it was announced. Utilization of the date the merger or acquisition became effective avoided the

problem of how to count announcements of mergers and acquisitions which were subsequently cancelled for whatever reasons.

OTHER DATA AND THE CONSTRUCTION OF COVARIATES

Covariates included in the models in general were measured at the end of the calendar quarter preceding the quarter in question (in some cases, such as IPOs and stock market levels, the level of the covariate in question was included for the two preceding quarters). Covariates of event counts such as births, deaths, IPOs, and acquisitions were constructed by counting all such events that affected non-subsidiary U.S. biotechnology firms. The quarterly closing level of the Nasdaq Composite index was secured from various issues of the *Nasdaq Fact Book and Company Directory.* Companies founded during the first quarter of 1971 (the first quarter Nasdaq was in operation) were assigned a value of 100 for the level of the Nasdaq Composite at birth, 100 for the first sub-spell for the level of the Nasdaq lagged one quarter and a missing value for the first sub-spell for the Nasdaq composite lagged two quarters. CPI figures and prime rate figures were obtained from U.S. government statistical series U0M320 and U0M019 found in files BCIH-07.dat and BCIH-12.dat downloaded from the Economic Bulletin Board at the University of Michigan.

THE POPULATION ECOLOGY OF THE INITIAL PUBLIC OFFERING

This chapter has focused on the nature of the data collected for use in this study. The care taken to identify all American firms that have ever been active in biotechnology as well as the effort expended in discovering and recording all the major life events of corporations was necessary for the kind

of analysis that I contemplated employing. In the next two chapters I will use this data to relate features of the firm and its environment to its propensity to go public. While many issues will be examined, the central concern of these chapters will be to assess the extent to which the firm's decision to go public is influenced by its social and political environment as captured by the size and activities of its reference populations. This discussion will be heavily influenced by the concepts of competition and legitimation as championed by population and organizational ecologists (e.g., Hannan and Freeman 1989).

CHAPTER 5. IPO RATES OF NON-SUBSIDIARY BIOTECHNOLOGY FIRMS, 1971-1993

This chapter is an analysis of the factors that influenced the rate at which American biotechnology firms went public in the period from the beginning of 1971 to the end of 1993. The basic working assumptions of this chapter are that all subsets of this population of firms responded to a set of common environmental forces, and that firms in this population generated similar signals of their strategic intentions. In chapter 6 both of these assumptions will be relaxed. First, I argue that institutional and economic forces such as legitimation, competition and general macroeconomic conditions influence a firm's ability to raise money in IPOs. Then, I argue that forces internal to the firm influence the firm's propensity to go public. The nature of these internal factors is a composite of objective factors such as aging and declared market strategy and strategies that are inferred from conditions that prevailed at the time of the firm's birth coupled with the choices the firm made as to state of incorporation.

INSTITUTIONAL PROCESSES, LEGITIMACY, AND DENSITY DEPENDENCE

Of the 218 IPOs included in this study, at least 191 (pre-IPO financial data on about 6 firms could not be found) were mounted by firms that had shown a loss in the fiscal year prior to the IPO. In addition, of the 218 IPO firms 195 had negative balances in retained earnings at the time they went public. These figures suggest that the confidence needed to generate investor interest in these offerings was not engendered by a history of past

profitability or by the strength of their balance sheets. Even more than for most IPOs, the process by which biotechnology firms were judged suitable candidates for investment had to be based on predictions of events and estimation of probabilities about which very little relevant data was available. Information on a firm's research programs and information on the quality of its staff does provide usable information for gauging a firm's prospects, but the existence of such information does not eliminate the extensive uncertainties caused by the lack of performance data and dependable information on the size and potential profitability of target markets.[50] As such, the financing environment of biotechnology firms bears at least a superficial resemblance to the environments which institutional theorists have taken to be particularly sensitive to judgments regarding the "legitimacy" of the constituent organizational forms.

The situation facing firms in a new industry who seek public equity financing is somewhat akin to the general situation facing the founders of a new organization. In founding a new business the founders usually face the reality that the firm relies on parties external to itself such as customers, bankers, and suppliers to ensure its success. In large part, predictions of the company's prospects for securing and holding the confidence of external parties are used as inputs to the founding decision itself. A new company is often in the position of operating in a new industry, of employing new technologies or of operating in a fashion that departs from established norms. If any of these conditions hold the firm will often face difficulties in securing the

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[50] For a discussion of the pitfalls of market forecasting in the biotechnology industry see Teitelman (pp. 190-191) and Kupor (1991, pp. 266-267). For a discussion of the lack of investor discrimination at times biotechnology is "hot" see the comments by stockbroker Richard Bock quoted in *Business Week* (Hamilton 1992, p. 66)

confidence and understanding of third parties. The difficulties the firm experiences in this regard are sometimes direct outgrowths of normative dissonance arising out of its very novelty. The firm's youth and the public's unfamiliarity with the nature of its business can asssume primacy over issues such as whether it possesses the technical abilities needed for conducting the business at hand.

In recent years organizational sociologists have been turning to the concept of legitimation to help explain the dynamics of population growth. Theoretical discussions of the concept distinguish between two related ideas of how legitimation emerges. This distinction has recently been summarized by Baum and Powell (1994) in the following fashion:

> The writings of the new institutionalists highlight several factors that contribute to the legitimacy of an organizational form or practice. Zucker (1977) treats institutionalization as a process, emphasizing legitimacy is a cognitive phenomenon, reflected in taken-for-granted assumptions. Meyer and Rowan (1977) and DiMaggio and Powell (1983) stress that legitimacy is embedded in relational networks and normative codes of conduct. Thus they view institutionalization as both a process by which certain activities come to be regarded as obligatory and a state in that widely shared norms and values are buttressed or even mandated by cultural, professional, and political expectations or laws. (p. 1)

While it is not clear that all institutionalists would accept the distinction drawn above as anything more than a distinction between levels of analysis, Baum and Powell continue by borrowing from Aldrich and Fiol (1994) an labeling the two conceptions of legitimacy "cognitive legitimacy" and "sociopolitical legitimacy." Baum and Powell claim that population ecology theory, as exemplified by Hannan and Carroll (1992), stresses the cognitive conception of legitimacy as having the most direct application to the study of

population dynamics. The degree to which a given organizational form is "taken-for-granted" and regarded as "natural way to effect some kind of collective action" (Hannan and Carroll, 1992:34) has direct implications for creation and survival of both individual firms and of populations of firms. Under this view, population density does more than signal that a kind of organization has access to important resources and has the potential to become embedded in established inter-organizational networks. As expounded by Hannan and Carroll, growth in population density also creates the availability of such resources and networks. This creation of resources occurs because familiarity with an organizational form breeds acceptance, and acceptance increases the likelihood of exchange and support.

An argument based on economic or efficiency considerations can also be formulated whereby it is asserted that the very proliferation of firms of a certain type lowers the costs of doing business with such firms. The larger and more concentrated the niche which a given form of organization occupies comes to be, the more feasible it becomes for a supplier of goods or services to develop capabilities for serving this niche. As the cost of servicing the special needs of the niche drop, competition among suppliers can also lower the cost of doing business for firms in the emerging niche. Similarly, the cost and risk borne by customers and investors can decline as it becomes feasible for third party providers of information and product certification to do so and be assured of a sufficiently large market for their services.[51] Finally, Ed Penhoet, co-founder, chairman and chief executive of Chiron, argues that the

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[51] The rise of specialized legal firms, consulting firms specializing in biotechnology patenting and FDA applications, and even landlords who rent out well-equipped laboratories to small firms all illustrate the many ways that an industry that has traditionally lost money has been a source of profits to many other kinds of firms.

proliferation of firms actually simplifies life for the startup firm by making for "easier access to resources than in previous years" (Moran, Reuters, May 29, 1995). Penhoet's rationale for making this claim is summarized as follows:

> Namely, more players in the market means smaller, less endowed firms can call upon other companies to conduct some research or manufacturing for them. (Moran, *Reuters*, May 29, 1995)

Both the cognitive view of legitimacy and efficiency considerations related to the emergence of threshold populations of firms support the idea that population density has the potential to serve as a central influence in making an organizational niche attractive and viable.

Juxtaposed to this conception of legitimacy as an outcome of population growth is a conception of legitimation as an outcome of forces which, by their nature, are external to, though not necessarily independent of, the focal organizational population. Thus the passage of laws, and the emergence of supporting institutions (whose genesis might not be directly related to the growth of the focal organizational population) could be taken to be central influences in determining the degree to which an organizational form becomes viable and hence such organizations are attractive to found. Partially because the two forms of legitimacy deal with different levels of analysis and partially because the environment and the organizational form underwent rapid change in the early 1980s in the case of biotechnology it is probably hard to untangle the growth of cognitive legitimacy and sociopolitical legitimacy. As was discussed in chapter 2, the period spanning 1980 and 1981 was one of multi-dimensional change in the world surrounding the biotechnology industry. It was also a period of rapid growth of the population

of biotechnology firms and of the financial and other material resources necessary for firm survival.

COMPETITION AS AN OUTGROWTH OF POPULATION DENSITY

If we are to argue that the growth of the population of biotechnology firms makes it easier for firms to go public because of enhanced legitimacy and the growing abundance of relevant resources in the environment, we must also acknowledge the obvious fact that investment financing is a scarce resource for which firms must compete. At certain points in the recent history of biotechnology, enthusiasm reached such a fever pitch that virtually any firm related to biotechnology could attract investors (see Teitelman for a popular account of "biomania"). Even though available capital has sometimes seemed to exceed the supply of high-quality investment targets, it is also the case that there is ample evidence that this has not always been the case. One of the early stars of biotechnology, Agrigenetics, was acquired by Lubrizol. Shortly before the sale Agrigenetics had had to withdraw an IPO when the market suffered a decline (*McGraw-Hill's Biotechnology Newswatch*, October 15, 1984, Volume 4, Number 20; Pg. 3). The struggles of another agricultural biotechnology firm to secure financing, International Plant Research Institute (IPRI), are well documented (Dwyer 1983, pp. 316-320). IPRI eventually experienced takeover by Bio-Rad, Chapter 11 bankruptcy, and eventual rebirth as Escagen (Escagen prospectus, January 21, 1987). As one inspects the back issues of magazines such as Bio/Technology a topic frequently covered is the shortage of equity capital and the competition for financing (e.g., Klausner 1983, pp. 646-647).

Given that there has been a shortage of investment capital for at least some biotechnology firms some of the time, it is natural to assume that the greater the number of firms in the population the greater the competition for funds will be. This competition takes many forms. First, the greater the number of firms the greater the degree of overlap among the research programs of the firms in the industry and hence the greater the selection of potential investment vehicles available for an investor interested in any given area of research.[52] Second, as the population grows, the institutional resources of the financial community are increasingly likely to be rationed. These resources include venture capital, underwriting, legal services and even the availability of analysts to cover the newly public firms (Hamilton 1994, p. 84; Kupor 1991, pp. 266-269). All of these resources are rationed not just on the basis of available capital but also by the availability of knowledgeable manpower. The very novelty of biotechnology initially made it difficult for the investment community to deal with the biotechnology sector because so few of individuals had a sufficient grasp of both the financial markets and the scientific issues dealt with by these new companies. Third, as the number of firms rises, the question of whether it is better to support continued expansion of established firms or to invest in yet another startup becomes manifest. This is particularly so as many of these firms return to the markets for further rounds of financing. In summary, there is substantial reason to believe that growth in the number of firms will lead to increased

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[52] Overlapping research programs and the competition they cause have long been a source of concern to investment professionals interested in biotechnology. In an interview Daniel H. Case, one of the managing directors of Hambrecht & Quist, predicted that this kind of overlap would lead to consolidation among smaller firms. Case was of the opinion that "the market's far enough away and sometimes so small, that six companies really shouldn't try to accomplish the same thing (Burrill 1989, p. 137).

competition for funds and diminished ability of firms to raise money through IPOs. This competition emanates both from other not-yet-public firms and, perhaps even more intensely, from firms that are already publicly traded. Figures 5-1, 5-2, and 5-3 depict the size and composition of the biotechnology industry over time.[53]

MODELLING EFFECTS OF DENSITY DEPENDENCE

The preceding discussion of legitimation of organizational forms and competition among firms suggests a number of hypotheses that relate the prevalence of IPOs to the forces of legitimation and competition. First, borrowing from the population ecology literature on organizational founding, I hypothesize that the prevalence of IPOs will rise with overall population density because of increased acceptance and legitimacy of the organizational form.

$$L_t = \lambda_t \exp(\alpha N_t) \qquad \text{Equation 5-1}$$

In the above equation L_t is legitimacy of the relevant biotechnology population at time t, and N_t is the population at time t. If legitimacy does lead to an increased ability to raise financing and if legitimacy is related to population density we would expect α to be positive, thus the first hypothesis related to the impact population density will have on IPO rates is:

H5-1: $\alpha > 0$

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[53] Subsidiaries and firms after they have become subsidiaries through takeovers and mergers are not included in these populations. The slight decline in the total population in the 1990s is partially a result of acquisitions and failures. It may also be a result of failure to identify some of the newest firms.

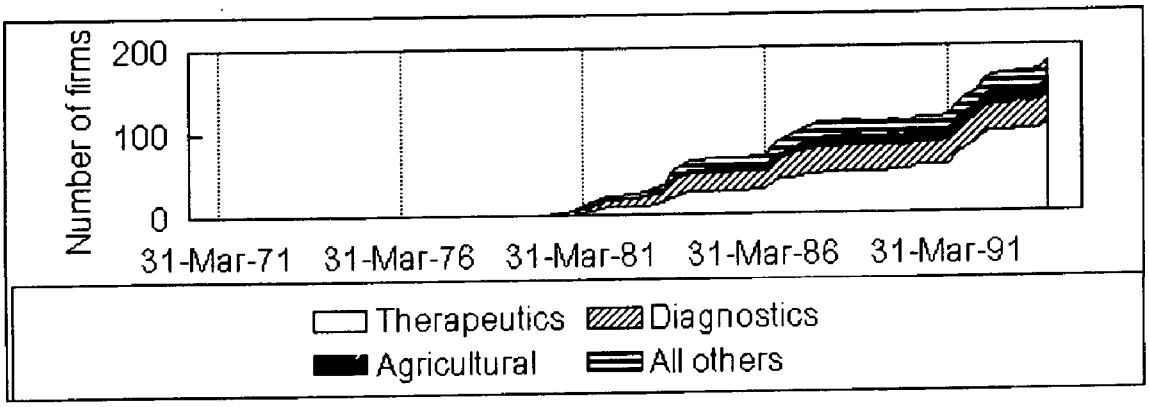

Figure 5-1: Population of non-subsidiary publicly traded biotechnology firms

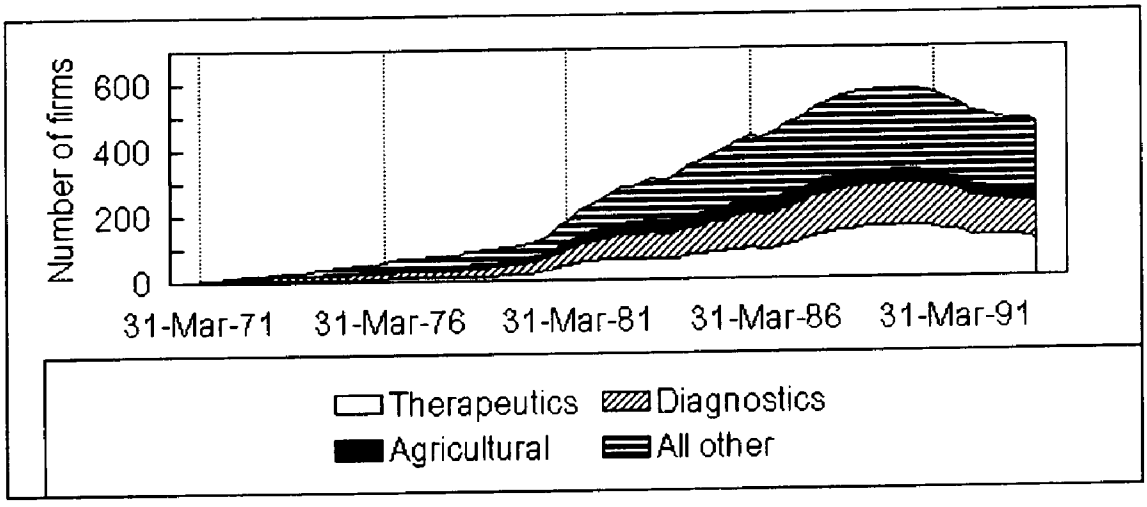

Figure 5-2: Population of private, non-subsidiary biotechnology firms

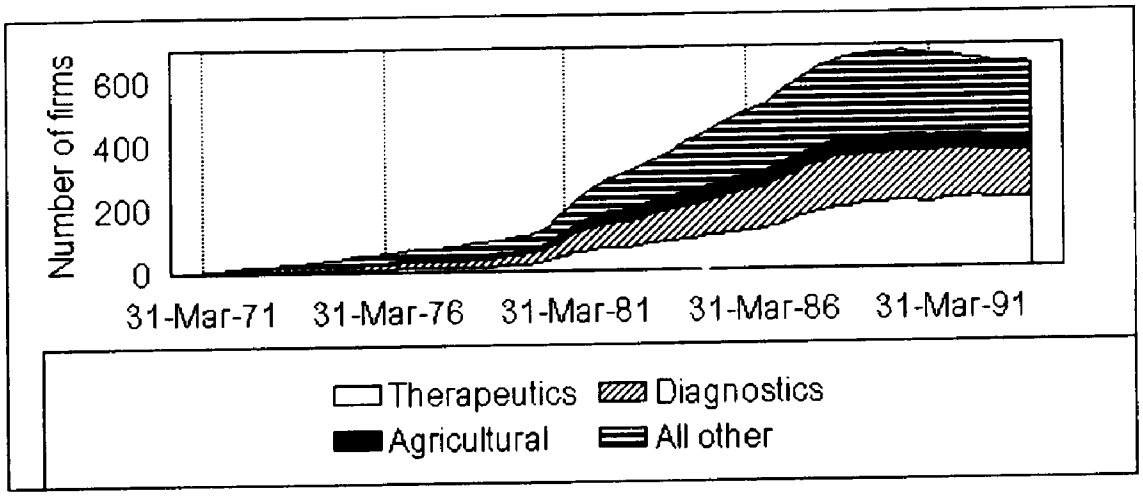

Figure 5-3: Population of all non-subsidiary biotechnology firms both public and private

As a variant on this theme, I also investigate the idea that, if the organizational population is divided into two subpopulations, one being firms that are already public and one that is composed of firms that have yet to go public, the same legitimating process might be observed with each of these subpopulations. The functional form that will be adopted to model this relationship is the simplest of various models whose merits are discussed variously by Hannan and Freeman (1989), Hannan (1991), and Hannan and Carroll (1992) whereby legitimacy is related to population density. Because of the variety of possible ways IPO rates might respond to subpopulation densities, however, these response patterns are not embedded in formal hypotheses. The issue of choosing among incompatible models of how IPO rates respond to population density is addressed later in this chapter.

Once again borrowing directly from the population ecology literature on firm foundings and failure, it is hypothesized that once a given population density is achieved (the population's carrying capacity), the forces of competition will come to overwhelm the impact of legitimacy and further increases in population density will depress the ability of firms to go public. Adopting a modelling strategy first suggested by Hannan (1986) the impact of competition is expressed as the square of the population density of the reference population. Thus, just as population ecologists predict an inverse U shape relating population density to organization foundings, the same general relationship might be expected to relate population density and the propensity or ability of firms to go public. Following Hannan, the following functional form is adopted to model competition:

$$C_t = c_t \exp(\theta N_t^2), \qquad \text{Equation 5-2}$$

where C_t is the level of competition at time t. If the inverse-U reaction to density applies, we would expect to see the sign of θ to be negative. If the non-monotonic reaction to density does not apply (signalled by insignificant coefficients on the quadratic term or an inflection point that is well outside the observed range of the data) the nature of the enterprise would suggest that rising population would lead to a decreased ability to go public. The alternative of finding only a positive impact of rising population on the rate at which firms go public would suggest a notion that legitimacy (as expressed by population density) might have an unbounded positive impact on a firm's financing capabilities. This idea does not seem particularly credible. Given the preceding discussion, the following hypothesis is advanced based on the expectation of a non-monotonic, inverse-U reaction to density:

H5-2: $\theta < 0$

As has already been suggested, however, these first two hypotheses are somewhat tentative and the problems of choosing among incompatible models of responses to population or subpopulation density will be addressed later in this chapter. In this later discussion, informal criteria will are advanced for choosing among models where different conceptions of density are employed.

INDUSTRY AGE AND PERIOD EFFECTS

The fate of the biotechnology sector has been affected by so many critical events that it is difficult to select the definitive set of legal, institutional, technical and financial changes that define the meaningful sub-periods of its history. One might easily choose the founding of Genentech (April 7, 1976),

the Supreme Court's decision on *Diamond v. Chakrabarty* (June 16, 1980) the stock market crash of October 1987 and Roche's acquisition of 60% of Genentech in September 1990 (the month the FTC approved the deal). A variety of other equally defensible specifications of periods are possible though. One could choose the date of the Asilomar conference (February 24-27, 1975), the date of Genentech's IPO (October 14, 1980), the acquisition of Genetic Systems (March 17, 1986), Genentech's launch of Activase (the first drug marketed by a biotechnology firm itself, approved by the FDA November 13, 1987) and the entry of Amgen into the Fortune 500 in January of 1992 as being the defining moments in biotechnology and hence the proper chronological boundaries for the life stages of the industry. Given these difficulties, no subjective designations of historical periods will be reported here.

Instead, in order to allow for unobserved historical shifts, some models are estimated where each year from 1981 onward is assigned a dummy variable. The period from the inception of the industry and the end of 1981 will be counted as a single period (yearly dummies cannot be used prior to 1980 since only 1979 would have an event occurring during the sub-period).

CONTAGION, REPUTATION, AND INFERRED RESOURCE AVAILABILITY

The attention the Genentech IPO generated for biotechnology suggests that this event and others like it may have served as examples for others to follow suit. The idea that going public might be a contagious process is supported by many popular accounts of the biotechnology industry. There are also other factors that support an expectation that IPOs will be clustered. In the IPO market at large, first order serial correlation of monthly

volume of IPOs is in the order of .88 (Ibbotson, Sindelar and Ritter, 1988, p. 39). Hence, if the pattern of activity for the population of biotechnology firms mirrors that of the market as a whole, we would expect quarters of high biotechnology IPO activity to be followed by periods of high activity. Since the preparation period for an IPO is usually in the order of four to six months, if a contagion process is at work, counts of biotechnology IPOs for the preceding two quarters are likely to be positively associated with the rate at which firms go public.

LEGITIMACY BASED ON RECENT EVENTS INSTEAD OF CUMULATIVE PROCESSES

A finding that the rate at which biotechnology firms go public is related to the number of recent offerings is subject to a number of possible interpretations. It is possible that adjacent time periods are influenced by similar economic conditions that affect the ability of a firm to go public. It is also possible, however, that the concept of legitimacy might be reformulated to apply to this situation. This latter suggestion is that, in the context of the financial markets, the degree to which a company is deemed to be a worthwhile candidate for going public is determined more by what has occurred recently in the industry rather than by the cumulative effect of the industry's history.

Population ecologists have typically taken legitimacy to be a cumulative construct of "taken-for-grantedness." In the context of biotechnology, casual empiricism suggests that the degree to which biotechnology (or at least biotechnology as an investment) has been accepted and valued has been much more volatile than a conceptualization of "legitimacy as generated by

population density" would suggest. Since the advent of biotechnology firms, enthusiasm for their prospects has alternated with deep pessimism. At various times conventional wisdom has called for industry "shakeouts" that would see many firms fail (for the most part these predictions have not been realized), or for radical transformation of the industry by sudden waves of acquisitions (acquisitions and mergers have played a prominent part in the industry but the fundamental structure of the industry has not yet been transformed by this activity). In the midst of these prognostications, however, firms continued to be founded and firms continued to go public. Despite relatively constant population growth, the number (and value) of IPOs has continued to fluctuate wildly as is evidenced by Figures 5-4 and 5-5. While the number of IPOs tends to be higher in times when overall IPO activity is highest (compare figures 5-5 and 5-6), a regression of volume of biotechnology IPOs on the number of non-biotechnology IPOs for the period 1979 through the end of 1992 gives an R^2 of only .33.

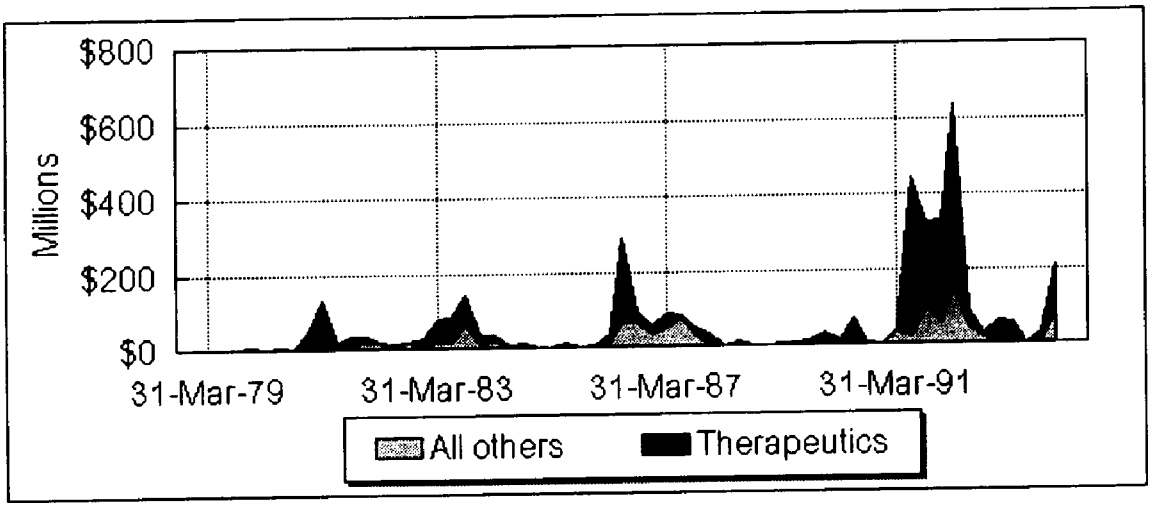

Figure 5-4: Funds (gross proceeds) raised by non-subsidiary biotechnology firms in IPOs (by quarter) from 1979 through the end of 1993

The volatility of the number of biotechnology IPOs pictured in figure 5-5 reinforces the suspicion that there is a "feast or famine" attitude that governs public assessments of industry prospects. Variation in the number of firms formed each quarter also supports this opinion. Finally, if the prices of biotechnology shares are a gauge of opinion, study of a biotechnology stock index constructed by Lerner (1994) indicates that opinion does fluctuate

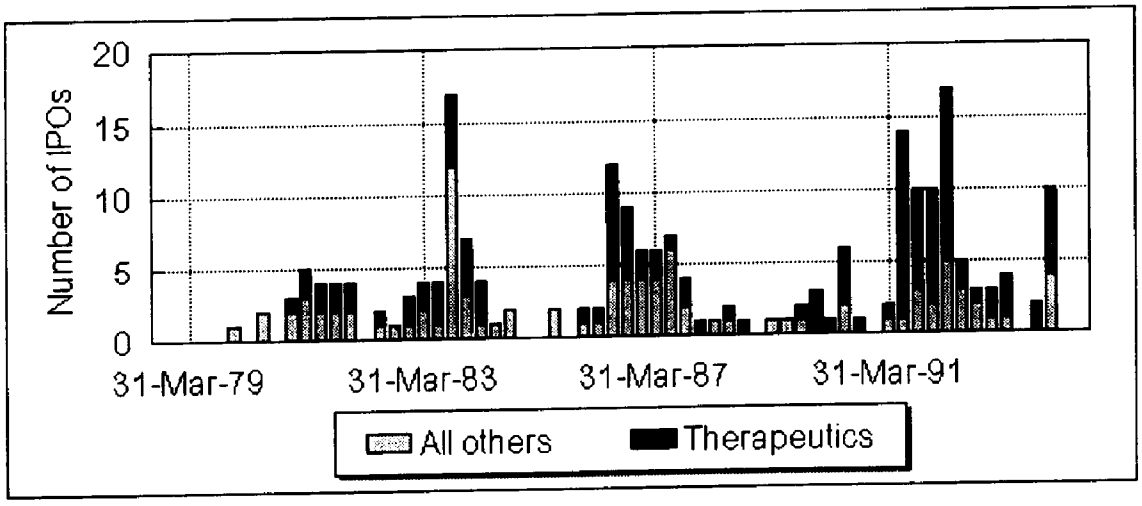

Figure 5-5: Number of IPOs by non-subsidiary biotechnology firms by quarter from 1979 through the end of 1993

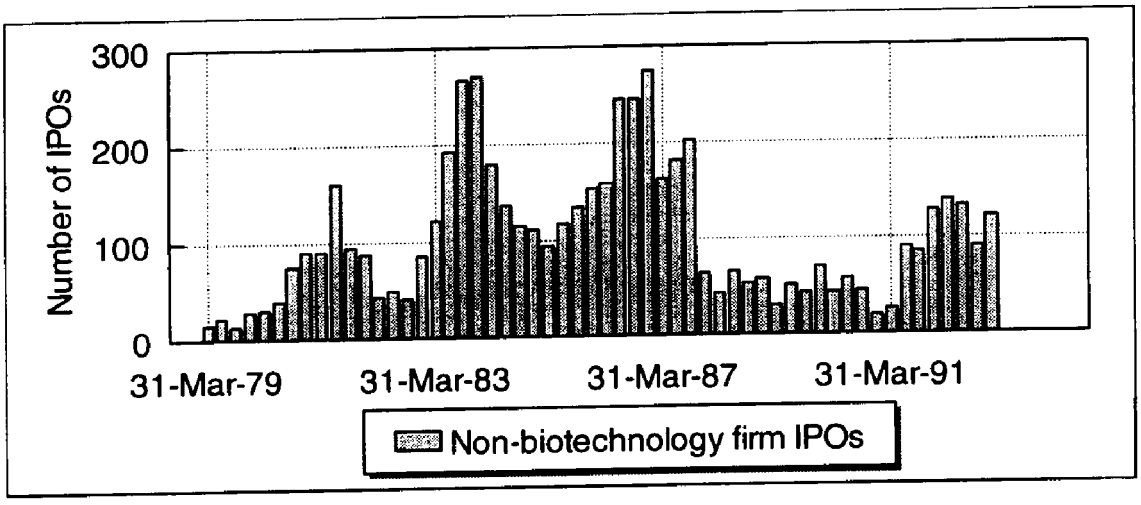

Figure 5-6: Volume of non-biotechnology firm IPOs by quarter from the beginning of 1979 through the end of 1992

rapidly. Regulatory setbacks affecting firms such as Centocor, Xoma, U.S. Bioscience and Synergen are widely credited (Burrill 1992, p. 21; Rothenberg 1994, p. 763) with having had severe impacts for the reputation and prices not only of the firms directly involved but also for biotechnology firms in general.

Whether or not the number of recent IPOs captures the impact of a rapidly changing acceptance of the industry (and the idea of public financing), a contagion process, or is simply an indication that unmeasured influences on IPOs operate across adjacent time periods, I hypothesize that the higher the number of biotechnology IPOs in the preceding two quarters[54] the higher the rate of biotechnology IPOs in the calendar quarter being observed. More formally, I make the following two hypotheses:

H5-3: $\beta_{(\text{IPO count lagged 1 quarter})} > 0$

H5-4: $\beta_{(\text{IPO count lagged 2 quarters})} > 0$

COUNTS OF FIRM BIRTHS, ACQUISITIONS AND DEATHS AS CONTROL VARIABLES.

For reasons analogous to those introduced for inclusion of counts of IPOs as determinants of IPO rates, controls for the lagged values of industry births, acquisitions and deaths are included in models. With the exception of births, the impacts of these phenomena are difficult to predict. In the case of births, both the timing of the events and signals that such events send are

[54] Over the period from 1979 to the end of 1993 first order serial correlation of counts of biotechnology IPOs was .448 (calculated using SAS PROC AUTOREG) and for the full period from 1971 through the end of 1993 was .579.

clear. Firms are founded when knowledgeable participants in the industry believe that the conditions favor the growth and survival of biotechnology firms. Because of the technological demands of the industry, it is difficult for rank outsiders to enter. Of course the technical grounding of most founders is not always accompanied by the necessary business acumen to make their endeavors succeed. Stated formally, I make the following hypothesis:

H5-5: $\beta_{\text{(Count of biotechnology firm births lagged 1 quarter)}} > 0$

In the case of firm failures, the signal the event generates is clearly negative, but, because the process leading to legal dissolution can be lengthy, the signal does not necessarily provide any information about the environment at the time at which it officially occurs. Further, the number of failures of private and public biotechnology firms is relatively small (120 over the 23 year period or about 1.3 per quarter). Stated more formally, the hypothesis related to the impact of firm failures is:

H5-6: $\beta_{\text{(Count of biotechcnology firm failures lagged 1 quarter)}} < 0$

In the case of acquisitions, both the timing of the event and the meaning of the signal are muddy, and, as I consequence, I advance no hypothesis as to the impact these events have on IPO rates. While some firms are acquired at the peak of their success (e.g., Genetic Systems) others clearly are acquired as a consequence of their failures or their cash crises (e.g., IPRI, Transgenic Systems or TSI, and Cetus). Secondly, even though the date at which acquisitions take place is usually clear, the fact that negotiations might have been lengthy may damage the applicability of any signal an acquisition might sends about the environment being favorable or

unfavorable. Conditions affecting the industry could easily shift between the time negotiations began and the time the deal is consummated. Lastly, although there were about 89 acquisitions (30 of public firms and 59 of private firms) over the 23 year period, these events were far less cyclical than were IPOs. Aside from a general increase in activity over time no readily identifiable pattern can be discerned from a visual inspection of the data. Figures 5-7 and 5-8 provide an idea of the way the different vital events are distributed over time.

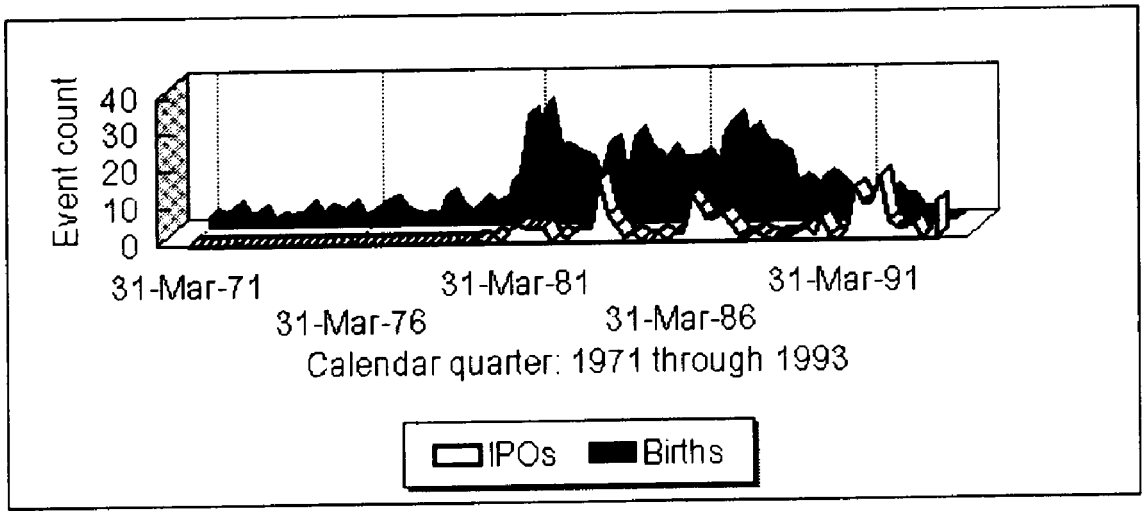

Figure 5-7: Non-subsidiary biotechnology firm births and IPOs

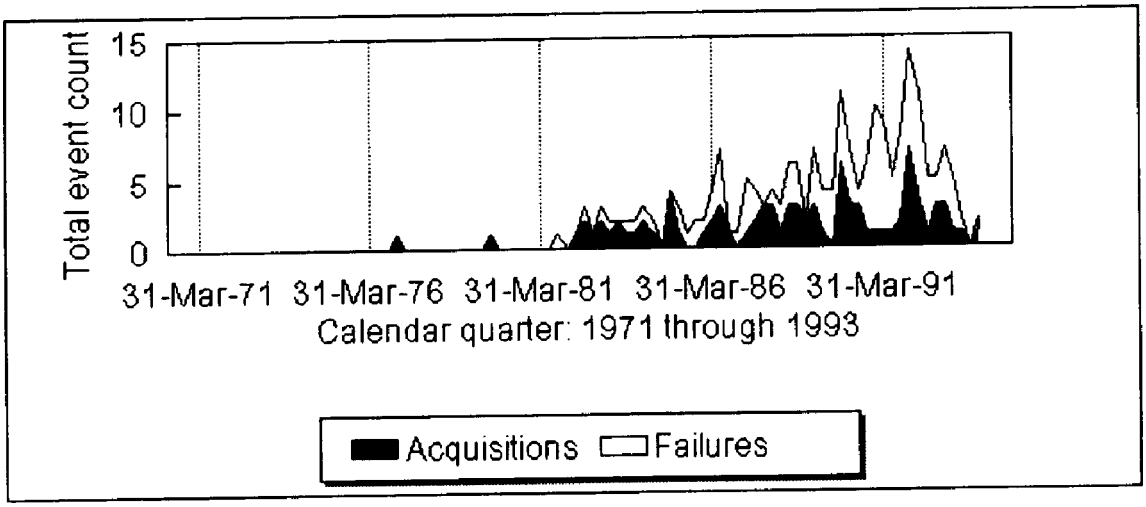

Figure 5-8: Counts of biotechnology acquisitions and failures over time

STOCK MARKET LEVELS AND MOVEMENTS

A number of reasons can be advanced for positing a relationship between the rate at which firms go public and the level of the stock market. Foremost among these is that the higher the price at which stocks are trading and the higher the associated stock market value of individual firms, the more likely it is that the expected selling price of the firm will exceed reservation prices that current owners and managers might have attached to the firms. If insiders evaluate the alternative of public financing with such a reservation valuation in mind, and they act decisively in going ahead with an IPO, such an action would tend to occur in a rising stock market. Given that most biotechnology firms initially listed on the NASDAQ exchange, the level of the NASDAQ Composite index is used as a reasonable measure of condition of the stock market[55] as it relates to biotechnology issues. The considerations outlined above lead to the following two hypotheses:

H5-7: $\beta_{\text{(Close of the NASDAQ composite previous quarter)}} > 0$

H5-8: $\beta_{\text{(Change of the NASDAQ composite last quarter over preceding quarter)}} > 0$

Lerner (1994) found that firms backed by venture capital resort to public equity markets for money when public valuations are high, and rely on private sources of money (venture capital and private offerings of other kinds) when stock market valuations are low. Lerner's findings are consistent with the

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[55] While using an index particular to the biotechnology sector might be preferred, such indexes do not coincide with the period being studied and their construction in the early years of public biotechnology stock trading involve the use of various proxies for actual biotechnology stocks (e.g., Lerner, 1994).

hypothesized impacts public markets have on firm choices as expressed in hypotheses 5-7 and 5-8.

EFFECTS OF FIRM AGING

In almost all contexts, firms have been found to change in profound ways as they age. Debate over the impact aging has on firms has been prominent in studies of the impact aging has on failure rates. Hannan and Freeman (1989, p. 245) go so far as to claim that it "is extremely difficult—if not impossible—to obtain useful estimates of ecological processes if aging is not taken into account." In their discussions of the impact aging has on failure rates Hannan and Freeman (1989) and Hannan and Carroll (1992) emphasize the idea that new organizations have a "liability of newness" whereby new organizations are more fragile than older firms. Borrowing from Stinchcombe (1965, pp. 148-150), these authors argue that the early experience of organizations is especially critical in establishing their ability to survive. Hannan and Freeman summarize the argument thus:

> New organizations are vulnerable because their participants are strangers. Efficient organization requires trust among members; and trust takes time to build. New organizations are also vulnerable because they have to create organizational roles and routines. Inventing and refining roles and routines take time and effort precisely when organizational resources are stretched to the limit. (Hannan and Freeman 1989, p. 245)

They continue by extending this same kind of analysis to the question of building relationships with other actors in their environment.

The process of proceeding towards a public offering bears some resemblance to a firm's early struggles to survive. First, a firm obviously will not be able to go public if it has already failed. Second, the requirements of

public reporting are such that they require a certain organization and sophistication (financial, public relations, and legal). Third, a history of operations, reliability and an indication that research is proceeding according to plan is usually essential for gaining the trust of investors. With the exception of the very earliest days of a company's life, however, there is no period in which it is logically impossible for a firm to go public. Figure 5-9 gives a picture of the age distribution of firms at the time they went public.

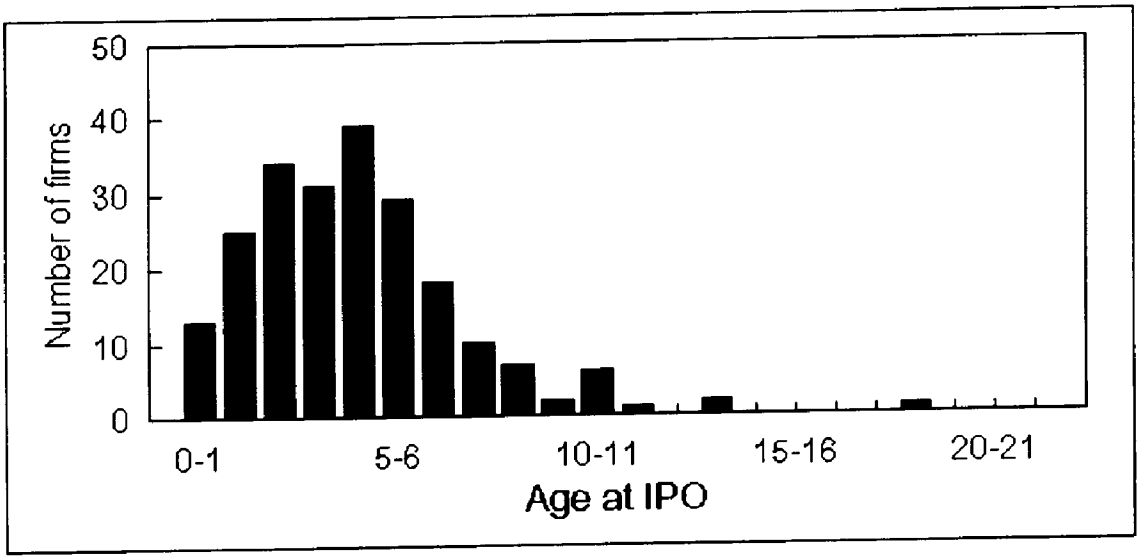

Figure 5-9 Age of biotechnology firms at the time they went public.

A case such as the Blech brothers taking Nova Pharmaceutical Corporation public (when it was about one year old) before it even had a laboratory proves that lack of physical assets is not an insurmountable obstacle to going public. The examples of Quest Biotechnology and Ribi Immunochem Research going public at 152 and 138 days old respectively, prove that raw youth, by itself, didn't bar new firms from accessing the public equity markets. In all, thirteen firms in the database went public before they had reached one year of age. Oddly, in some respects, the attributes of some of the very youngest firms to go public actually support the contention

that doing so is made simpler by age. Of the three examples mentioned above, all three had some element of organization that is usually associated with older firms. Nova had the advantage of being organized by the Blechs whose every energy at that point (see Teitelman for some of the details of their operations) seemed to be directed at founding firms and bringing them public. Ribi was able to buy "a laboratory facility and equipment from two of its principal officers" (Ribi-Immunochem 1982 Annual Report, p. 3) to tide it through until it constructed new quarters. Quest had been founded with the explicit mission of acquiring the rights to a technology that had formerly been licenced to both Polycell (Quest 1987 Annual Report: p. 5) and Quadroma (*McGraw-Hill's Biotechnology Newswatch*, 1983, 1984) whose histories can in some sense be seen as extensions of Quest's own.

At the other end of the age spectrum, there are reasons for suspecting that as firms age they eventually reach a stage in their life cycles where going public might be less likely or less necessary. For the most part, one can assume that the older a firm gets without having gone public the more likely it is that it has established a business which generates positive cashflow and profits. If this is also the case with biotechnology firms (and it seems particularly so with firms that provide goods and services to other firms and least likely with therapeutics firms), then there is no pressing need to surrender ownership to others. In the case of a profitable business, the only reason that one might want to surrender ownership would be if additional capital were required or if there were portfolio balancing or other personal reasons for going public. The fact that many of the private firms remaining in the population have already past the age where most firms go public is illustrated in figure 5-10.

Figure 5-10: Age distribution of non-public firms at the end of 1993

In an interview with the editors of Ernst & Young's *Biotech 90* (Burrill, 1989) Dr. Sigi Ziering of Diagnostics Products described some of the motivations and considerations surrrounding his company's decision to go public in 1982 (which, at the time, was just over ten years old and was profitable):

> We wanted to establish a public vehicle, in part because of estate-planning considerations among some of our early investors. But there are many negatives in a public company. You pay a price in terms of fulfilling reporting obligations, justifying to analysts not only what you have done but what you're going to do, and how you're going to do it, and why you're going to do it.
>
> On the positive side, however, being a public company imposes a certain structured discipline by forcing you to verbalize a corporate strategy, which is often absent in small privately held, seat-of-the-pants companies. Thus the external need to communicate a clear strategy has made us a more competitive and aggressive company. (p. 227)

Other companies that went public at more advanced ages also often have idiosyncratic stories behind the decision. Agridyne Technologies (whose earlier names included Native Plants and NPI) was founded in 1973 but only

went public in 1992. In this case, a venture capital fund had invested in the company in early 1989 when the firm was in financial difficulties and public equity was not available. The passage of three years between the venture investment and going public was broadly consistent with the time frame that such funds experience in securing an "exit" from investments in biotechnology startups.

One final example of a firm that went public at a more advanced age was Seragen Inc. which was founded in 1979 and went public in 1992. In many respects Seragen is among the most interesting outliers in the history of biotechnology. Founded by a Boston University scientist, Seragen was the subject of considerable controversy when it was revealed that a significant portion of the university's endowment fund ($85 Million) had been invested in the company (Flint and Kennedy, 1993; Rosenberg, 1993). At one point, the company was even an issue in politics as Silber, Boston University's president, ran for Massachusetts governor (1990). The novelty of having a university make repeated investments in a risky technology startup with no products and a poor reputation with financial analysts[56] likely reduced the influence of pressures that were felt by the industry as a whole.

In the literature it is often observed that unobserved heterogeneity within the population can lead to the "detection" of spurious effects. Blossfeld, Hamerle and Mayer (1989, pp. 91-95) provide several examples where a variety of false conclusions about age dependence can arise. In the case we

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[56] The novelty of this situation was not that university funds were being invested in biotechnology (many universities do so quite successfully) but that the single investment was coming close to becoming the portfolio. The other singular aspect of this case was that for a protracted period Boston University was the only source of funds and for a time held the majority of the shares in the company.

are dealing with many of the means often employed for detecting unobserved heterogeneity don't apply because some of the main effects to be investigated vary with time. The basic approach taken to guarding against the discovery of spurious age dependence will be to categorize firms as completely as possible along the dimensions of research activities, incorporation choices and conditions at the time of their birth. Since there is every indication that considerable differences exist between therapeutics firms and other biotechnology firms chapter 6 is devoted to estimating separate models for firms dealing in therapeutics and those that are not.

Later in this chapter exploratory methods will be employed to arrive at a representation of how the impact of firm aging on IPO rates can be captured. The considerations raised above suggest that we might expect to find that firm aging might have a non-monotonic impact on IPO rates whereby rates initially rise, reach a maximum, and then begin to decline. Since arriving at an acceptable representation of age dependence is seen to be an essential precursor to the whole modelling enterprise and since this eventual representation is arrived at through exploratory methods, expectations regarding the pattern of age dependence are not presented as formal hypotheses.

THE EFFECTS OF A FIRM'S CHOICE OF RESEARCH AND PRODUCT FOCUS

Many features of individual companies influence their needs for financing, their propensities to seek needed funds in the public equity markets and their abilities to secure the confidence of investors required for raising money at reasonable prices. One factor that helps shape all three of these firm

attributes is the firm's choice of target product market. As has been discussed in earlier chapters, firms working on human therapeutics are particularly likely to need extensive and protracted funding. This is so both because of the amount of funding and because of the extended period of investment. Even therapeutics firms with generous venture capital funding are likely to have to go public relatively early. Finally, possibly because of the very big rewards for success, investors have proven to be particularly interested in funding this type of research.

Even the degree of oversight to which the therapeutics sector is subjected can serve as a mechanism for investors to gauge the quality and progress of firms. A therapeutics firm that is progressing through a definable sequence of mandated clinical trials is able to convey a sense of achievement and success even in the absence of earnings. Given these observations it is expected that therapeutics firms might display a higher rate of going public than firms of other kinds. Because of similar factors[57] in the diagnostics and agricultural fields these firms may also be expected to require public financing sooner and more certainly than other firms. Drug delivery firms and toxic waste treatment firms might also display elevated rates of going public but, because of their relative rarity, for the purposes of modelling they were counted along with all the remaining firms. While dummy variables

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[57] For many years the sensitivity of the public to field testing of plants was a major barrier to getting agricultural products to market. Calgene's FLAVR SAVR tomato could also have been introduced to supermarket shelves much earlier were it not for regulatory barriers and pressure from consumer groups. In the end Calgene got two FDA stamps of approval, the first in 1992 to move toward large-scale production and the second on May 18, 1994 that declared that FLAVR SAVR tomatoes were "as safe as their traditionally developed counterparts" (FDA, 1994). In the case of diagnostics the path to approval is much less onerous and contentious but efficacy and production standards are monitored.

for product market focus are included as critical control variables, hypotheses that firms active in the three main product areas targeted by biotechnology go public at rates greater than those not active in these core areas is also of moderate theoretical interest. The hypotheses associated with product market focus are as follows:

H5-9: $\beta_{(\text{Therapeutics firm dummy variable})} > 0$

H5-10: $\beta_{(\text{Diagnostics firm dummy variable})} > 0$

H5-11: $\beta_{(\text{Agricultural firm dummy variable})} > 0$

EFFECTS OF A FIRM'S INCORPORATION CHOICES

In chapter 4 the question of whether or not a firm chose to incorporate or reincorporate in Delaware was related to questions of a firm's attempts to limit transaction costs of operating as a public company. Figure 5-11 displays the subset of IPO firms which reincorporated in Delaware either before or after their IPOs. As is readily apparent, the most common period in which these reincorporations occur is immediately before going public. Given this pattern of behavior, reincorporation prior to going public can usually be interpreted as being a stage in executing the plan to go public and not a subtle signal that the financing strategies of the firm are in the process of changing. If reincorporation in Delaware is a common precursor to going public, then, by extension, we can hypothesize that firms which incorporated in Delaware at the time of their formation are more likely to be pursuing a financing strategy

from the outset calls for an accelerated passage to going public. Two hypotheses arise out of this discussion of incorporation choices, they are:

H5-12: $\beta_{\text{(Dummy variable for firm origically incorporated in Delaware)}} > 0$

H5-13: $\beta_{\text{(Dummy variable for firm reincorporated in Delaware)}} > 0$

While confirmatory evidence of hypothesis 5-13 would be mundane and of little theoretical interest, this is not the case for hypothesis 5-12. Support of hypothesis 5-12 would suggest that incorporation choices arise out of real differences in corporate strategies that are in place at the time of the firm's birth. Further, it would indicate that these differences are enduring characteristics of the firms involved.

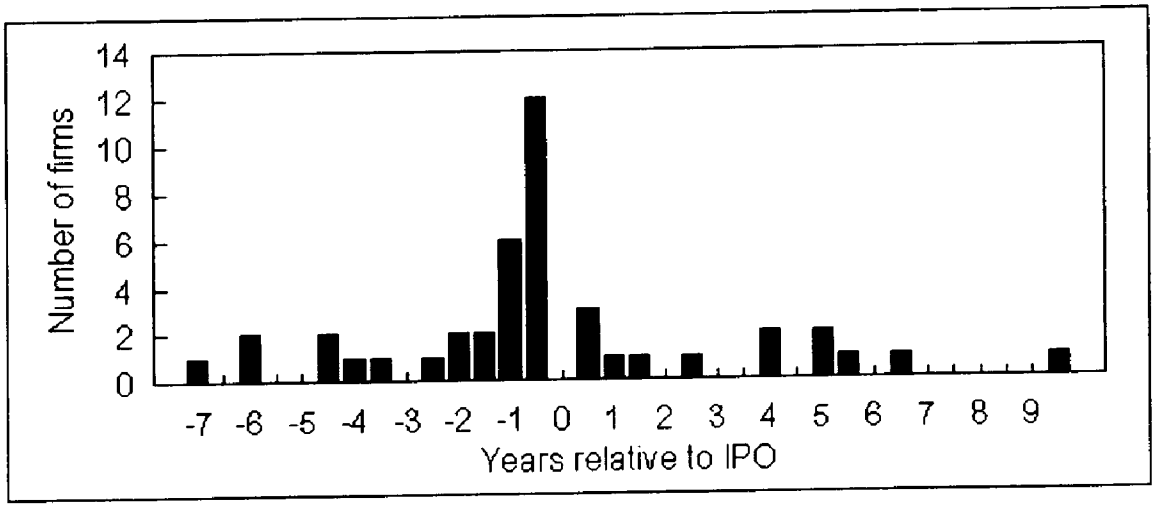

Figure 5-11: Timing of reincorporations in Delaware relative to time of IPO

CONDITIONS AT THE TIME OF A FIRM'S BIRTH

The last category of variables about which hypotheses are made are variables that describe salient features of the environment at the time the firm was founded. The three candidate measures of these environmental conditions

are: the number of IPOs in the quarter preceding the formation of the firm; the population density at the time the firm is founded; and the level of the NASDAQ Composite index at the close of the quarter preceding the firm's birth. In the first and the last instances the prediction is that higher levels will lead to higher propensities to go public. In the case of population density at birth the direction of the effect is not predicted for reasons that will be described below.

FIRMS FOUNDED IN TIMES OF HIGH IPO ACTIVITY

The relationship posited between the timing of IPOs and the births of firms that themselves are more inclined to go public is twofold: imitation and the release of valuable resources into the constituent environment. The imitation argument is simple. Successful IPOs are often noticed for two reasons: they can make people rich and they can amplify the capabilities of the creative individuals who are the firm's most valuable assets. Biologists and biochemists have often held considerable power within academic domains, the rise of the biotechnology firm allowed them to start exercising that power within a broader domain. When Genentech went public the fact that Herbert Boyer had suddenly become a multimillionaire was probably not lost on his colleagues. At the same time, a firm that acquires a pool of research money is able to pursue costly research that would be difficult to fund except in a commercial setting.

While the timing might be coincidental, one of the most telling conversions to the cause of commercializing biotechnology was Paul Berg, one of the earliest researchers into rDNA, a Stanford professor and a Nobel laureate. In 1977 Berg, in commenting on Herbert Boyer's connection with

Genentech (Petit, 1977), had disdained any form of commercial involvement in biotechnology. In an interview Berg stated that commercial involvement "is just not to my taste. This isn't to criticize Herb particularly, but I just can't see it." Berg claimed even to avoid "accepting consultant work with pharmaceutical firms that could use his advice" (Petit, 1977). On December 8, 1980, less than two months after Herb Boyer benefitted from the Genentech IPO, Berg joined the race to commercialize biotechnology by founding DNAX Research Institute, a company that was later acquired by Schering-Plough for $29 million (Kenney, 1986, p. 100). While there is no proving that it was really money that drove the rush to found biotechnology firms or that these firms were expressly founded with a view to going public themselves, it is hard to ignore the possibility that both greed and the heady prospect of corporate funding for large research projects played a role in inducing academics to provide the intellect and the credibility that biotechnology startups required.

The second reason for believing that firms with a higher propensity to go public might be formed in periods of high IPO activity is that investors, venture capital funds and others who have had money committed to biotechnology startups might want to reinvest the money that they have realized in the IPO.[58] This assessment is supported by opinions expressed by industry insiders at a 1992 conference:

> Start-ups will have an easier time finding funding now than in previous years due in part to 1991's large numbers of initial public offerings, said financiers at the 10th annual life sciences

[58] Underwriters frequently impose trading bans on pre-IPO investors for a period after the IPO. Nevertheless, these periods are of limited duration and investors might start committing funds in anticipation of their shares in the newly public firm becoming liquid.

> conference conducted by Hambrecht & Quist, Inc. (H&Q), here. As more firms reach the public market — H & Q's rough estimate is that there are 160 public companies but the figure changes daily — opportunities for new ventures will continue to increase. (*Biotechnology Newswatch,* January 20, 1992: p. 1)

Lastly, the example of company employees who have benefitted from stock ownership may also make it easier for nascent corporations to attract quality employees if potential employees believe that the firm is destined for going public. This belief might be easier to instill in recruits in periods of high IPO activity. In his book *Going Public: MIPS Computer and the Entrepreneurial Dream,* Michael S. Malone describes the atmosphere that the hope of going public can create at technology startups:

> It is estimated that in the instant MIPS went public twenty employees made more than $1 million. Perhaps two hundred more saw their net worth increase by $100,000 to $200,000.
>
> On Going Public Day the individual employees are rewarded for sacrificing years of their lives, for spurning higher-paying jobs elsewhere, and for taking a risk on an enterprise with little chance of survival, much less a payoff. Executives are rewarded for taking a flyer on a deal that might sink their reputations. Venture capitalists are rewarded for betting millions on a few pieces of paper and a handful of inexperienced founder. (Malone 1991, p. 232)

In summary, the conditions surrounding a company formed in an atmosphere where IPOs are occurring is likely to be a different kind of company, with different kinds of employees, with different kinds of investors and different kinds of expectations and plans. If this is so, then the very differences in initial plans for the company will likely start to create the need to go public. Dr. Sigi Ziering of Diagnostics Products described many of the companies founded in the early 1980s as having a "go-for-broke financial structure, with the attendant requirement of frequent financing" (Burrill 1989,

p. 226). Once certain strategies are embarked upon and certain target markets selected, the only way that a young biotechnology firm will be able to stay independent until it starts making money is to go public. While not conclusive, Figures 5-12 and 5-13 provide some indications that firms that

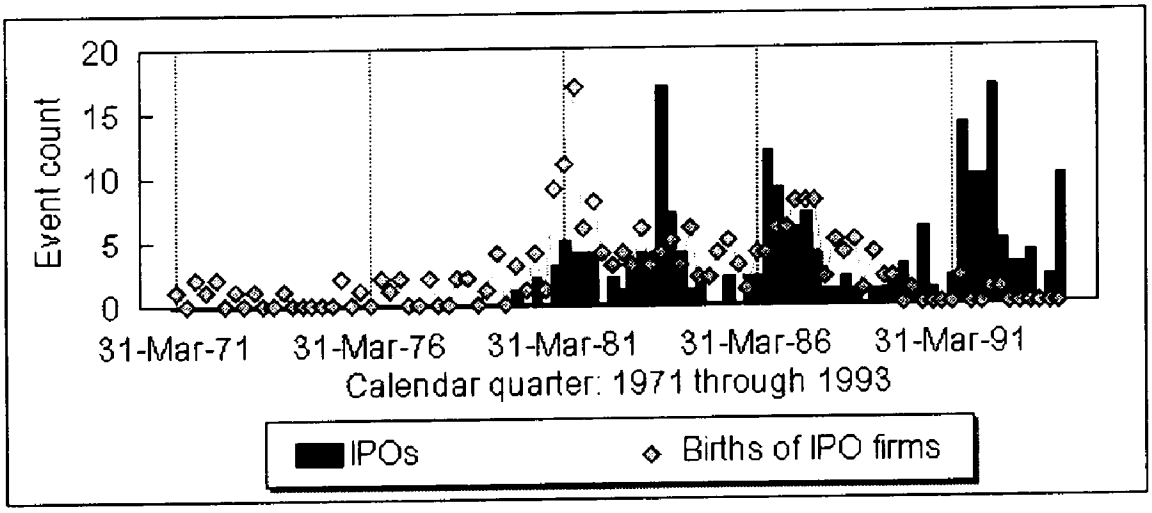

Figure 5-12: Juxtaposition of births of firms which were public by the end of 1993 and the timing of IPOs

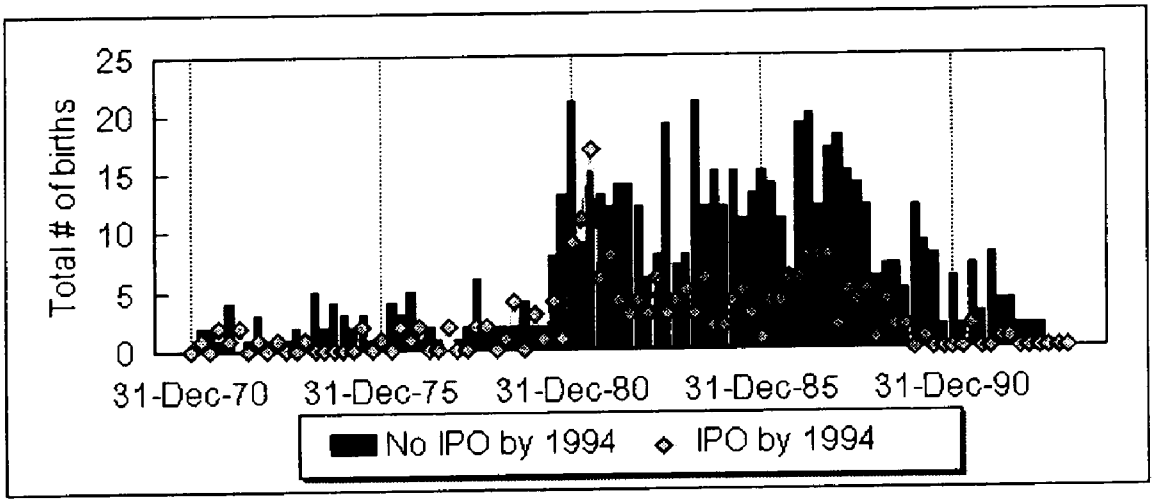

Figure 5-13: Birth patterns for independent firms according to whether they had gone public by the end of 1993

eventually resort to IPOs might be founded at greater rates during periods of high IPO activity. There is also suggestive evidence that the pattern of firm creation for firms that later resort to going public may be different from those

that do not do so (of course these firms still possess the option to do so in the future). All of the considerations advanced above suggest the following hypothesis:

H5-14: $\beta_{\text{(Count of biotechnology IPOs in quarter preceding the firm's birth)}} > 0$

POPULATION DENSITY AT BIRTH

Carroll and Hannan (1989) suggest that population density at time of founding has an enduring impact on the fragility of the organization and its susceptibility to failure. They offer a dual rationale to support this argument. First, they hold that crowding at the time of an organization's birth may force a firm to adopt a strategy that forces it to the less desirable edges of the resource space. Second, they speculate that resource scarcity early in a firm's existence may impair its ability to develop systems and stockpile resources that will be needed later. In a like manner, one would suppose that, as the population of biotechnology firms has grown, the sources of ready financing, earnings available from peripheral activities, and any easy earnings that might be available early in the existence of a firm might have already been appropriated by firms already active in the industry. This reasoning leads to the hypothesis that firms founded when the population is dense may have a lasting need to finance their novel research from direct equity infusions. The rationale for this assertion is that in a more crowded field the only attractive opportunities may be higher risks projects which have not yet been appropriated by existing firms. Even if many start-ups secure venture capital investments, the fact that the preferred "exit" strategy for venture capitalists is an IPO supports the general form of the argument. If we

were to accept the argument advanced above we would make the following hypothesis:

H5-15a: $\beta_{\text{(Population density at end of quarter preceding the firm's birth)}} > 0$

Unfortunately for the purposes of simplicity, another argument can be advanced which leads to a directly contradictory hypothesis. It may be that as population density rises the opportunity arises for firms to make a living by developing symbiotic relationships with already existing firms. Firms created under these conditions might be less likely to embark on high-risk, high-payoff research and be more likely to solicit contracts that offered promise of immediate profits and cashflow. If firms founded in periods of high population density were predominantly of this type, the association between population density at birth and the rate of going public would probably be negative. This argument suggests the following contradictory hypothesis:

H5-15b: $\beta_{\text{(Population density at end of quarter preceding the firm's birth)}} < 0$

LEVEL OF THE STOCK MARKET AT THE TIME OF BIRTH

The last measure of conditions at the time of the firm's birth that will be included in models is a measure of the level of the stock market (NASDAQ composite) at the time of the firm's birth. The rationale for this last inclusion is similar to the argument advanced that a firm founded at a time of high IPO activity might be founded with strategies that presupposed the ability to go public. Analogously, when the stock market levels are high, even if IPO activity is not, founders might be more willing to believe that public equity

would be available for the firm in the future. This suspicion is summarized in the following hypothesis:

H5-16: $\beta_{\text{(NASDAQ close at end of quarter preceding the firm's birth)}} > 0$

RESULTS

The first results that we will examine are models of age dependence in the IPO rates of biotechnology firms. Two diagrams follow. The first, Figure 5-14, is a depiction of hazard rates calculated with the life table procedures in SAS PROC LIFETEST (SAS Institute 1989). The second, Figure 5-15, is a graph of hazard rates computed on the basis of two simple models reported in Tables 5-1 (model 1) and 5-2 (model 3) and calculated using SAS PROC LIFEREG[59] (SAS Institute 1989) according to the procedures outlined in chapter 3. Model 1 (represented by the jagged line in figure 5-15) estimates

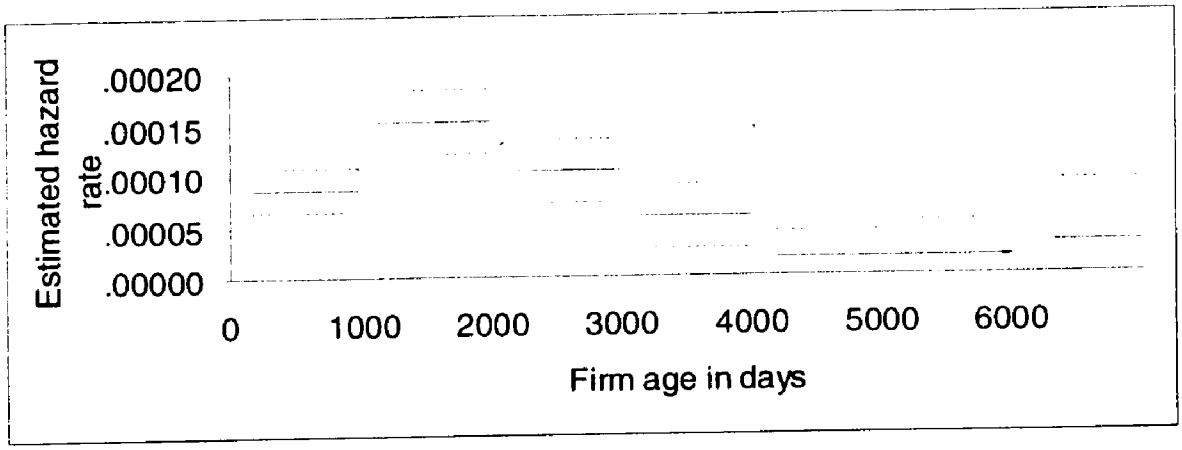

Figure 5-14: Life table estimates of variation of IPO hazard rates over time (interval width=1000 days, 95% confidence interval shown as dashed lines)

[59] As I discuss later in this chapter, models estimated using Cox's partial likelihood produce virtually identical results. Because of considerable differences in computing time required by the two procedures, bootstrap estimates presented in chapter 7 were calculated exclusively with PROC LIFEREG. In order to maintain consistency, all the basic models reported in this chapter are also calculated with PROC LIFEREG.

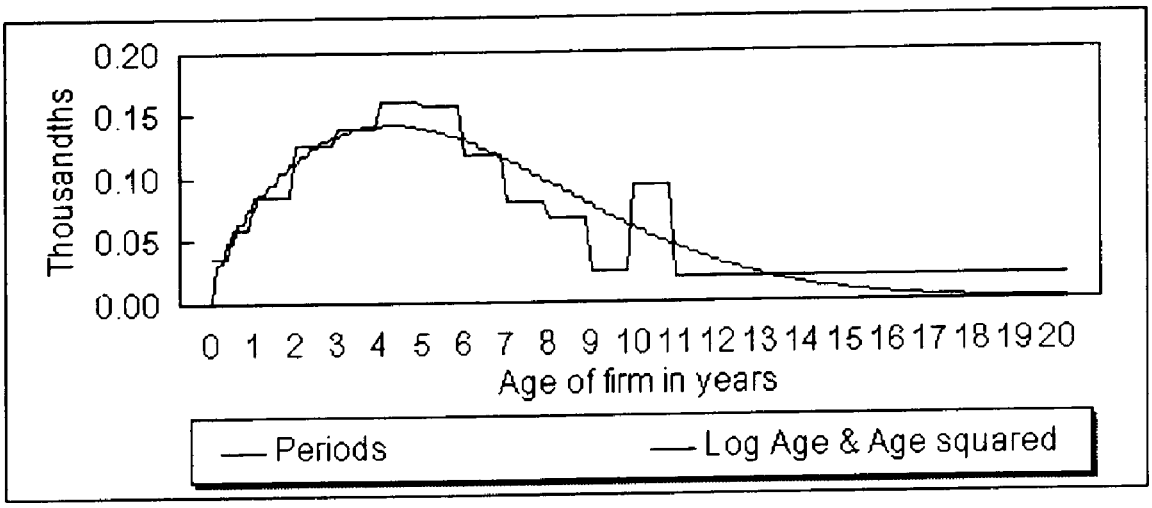

Figure 5-15: Effects of aging on IPO rates of biotechnology firms estimated via a piece-wise exponential model and a model with parametric assumptions

failures rates based on a piece-wise exponential model whereby 11 dummy variables are included to represent different ages of the sample firms. The baseline rate is for the excluded age class of firms older than 11 years. Model 3 (represented by the smooth curve in figure 5-15) is a simple model of time in which the log of the firm's age (measured in days) and the square of the firm's age (divided by a scaling factor of 10,000 to make cited coefficients of the same general order of magnitude) are used to capture the impact of aging on the firm's propensity to go public. In all cases the impact of aging appears to conform to expectations that the rate will first rise rapidly and then decline.[60]

[60] The slight deviations from the smooth curve that we see at 9 and 10 years old are a consequence of both a decline in the effective sample size (246 firms at the beginning of the ninth year and 191 at the beginning of the tenth year), and a fall in the number of events. In fact, there were two IPOs of 9-year-old firms and 6 of 10-year-old firms. Three of the IPOs that involved 10-year-old firms were for firms that were within 38 days of their tenth birthday (10 years and 25 days, 10 years and 37 days, and 10 years and 38 days). A slight change in the age classification would make the apparent anomalies disappear. Careful examination of the IPOs of firms older than nine years old failed to uncover any systematic pattern other than that many of the cases occurred in the early 1980s and the early 1990s. One plausible explanation of this pattern is that both these periods followed periods of very light IPO activity during which firms may have been inclined to delay going public well beyond the point at which they might otherwise have done so.

Table 5-1: Model of IPO rates based only on age classes

	Model 1		
Log-likelihood	-1407.52		
Variables	Coef.		S.E.
Intercept	-10.89	****	.50
< 6 months	.63		.71
6 months to 1 year	1.15	*	.60
1 to 2 years	1.51	***	.54
2 to 3 years	1.91	****	.53
3 to 4 years	2.01	****	.54
4 to 5 years	2.15	****	.52
5 to 6 years	2.13	****	.53
6 to 7 years	1.84	****	.55
7 to 8 years	1.46	**	.59
8 to 9 years	1.28	**	.63
9 to 10 years	.25		.87
10 to 11 years	1.60	**	.65

NOTE: All models are based on 24,924 quarterly observations of firms and 218 IPO events. All models except models one, two and three lose three observations because no lagged values for the NASDAQ were available for the first quarter of 1971. Acquisitions right-censored 59 observations, and failures right-censored an additional 111 observations.

* p < .1, ** p< .05, *** p< .01, **** p < .001

Table 5-2: Models of IPO rates controlling for age and estimating variation of rates by period

	Model 2		Model 3	
Log-likelihood	-1343.37		-1413.33	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-14.853 ****	1.050	-13.260 ****	.928
Log(Age)	.691 ****	.145	.640 ****	.138
$(Age)^2/10,000$	-.0015 ****	.0003	-.0013 ****	.0002
81	2.326 ****	.476		
82	.931	.578		
83	2.405 ****	.445		
84	.739	.556		
85	-.005	.646		
86	1.876 ****	.449		
87	1.325 ***	.472		
88	-.290	.646		
89	.200	.557		
90	.324	.541		
91	1.909 ****	.443		
92	1.849 ****	.453		
93	1.427 ***	.484		

* p < .1, ** p< .05, *** p< .01, **** p < .001

In all cases the maximum rate of going public is in the neighborhood of 5 years old. In general the simplified model of aging whereby age is represented by its log and its square represents an adequate approximation of the apparent response as captured by the piece-wise exponential model. Since the two models are not nested, however, using a simple likelihood ratio test based on the difference in model log-likelihoods is not possible.[61] In all periods a 95% confidence interval on the period based model 1 overlaps the simplified curve constructed from model 3. While the simpler parametric representation of the effect of aging is used in the balance of the models reported in this chapter, running the same models with age represented by dummy variables rather than the Log(Age) and Age Squared specification produced substantially the same estimates for both the coefficients of theoretical interest (standard errors and significance levels were very similar as well).

It must be admitted, however, that it is quite likely that as firms grow older any approximation measure of the IPO rate becomes less and less adequate. The very sparse information on the behavior of older firms makes it very difficult to make informed judgments of the rate at which older firms actually will go public. Nevertheless, for the most part the findings of a rising then declining rate of going public as the firm ages are well supported in this population. Models that were estimated using data that excluded firms older than nine years old were virtually indistinguishable from those reported here. The only appreciable differences between models estimated with all the data

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[61] Alternative means of comparing non-nested models are possible (Judge et al. 1988 p. 851; McAleer and Pesaran 1986), but their application would require making a number of additional assumptions that would be difficult to evaluate in the context of this study.

and those where older firms were excluded were that in the latter models the estimated IPO rate declines more rapidly as the firm ages beyond the point where the rate attains a maximum.

Figure 5-16 and Table 5-2 show the variation of overall hazards of going public when firm age is controlled for (using the log-quadratic specification outlined above) and where 14 different time periods are represented by 13 dummy variables. The period prior to 1981 is used as the baseline period for comparison. Comparison of Model 2 with Model 3 (which just includes covariates of log(Age) and Age squared shows that the periods substantially improve the model of IPO rates.[62] As figure 5-16 shows, the

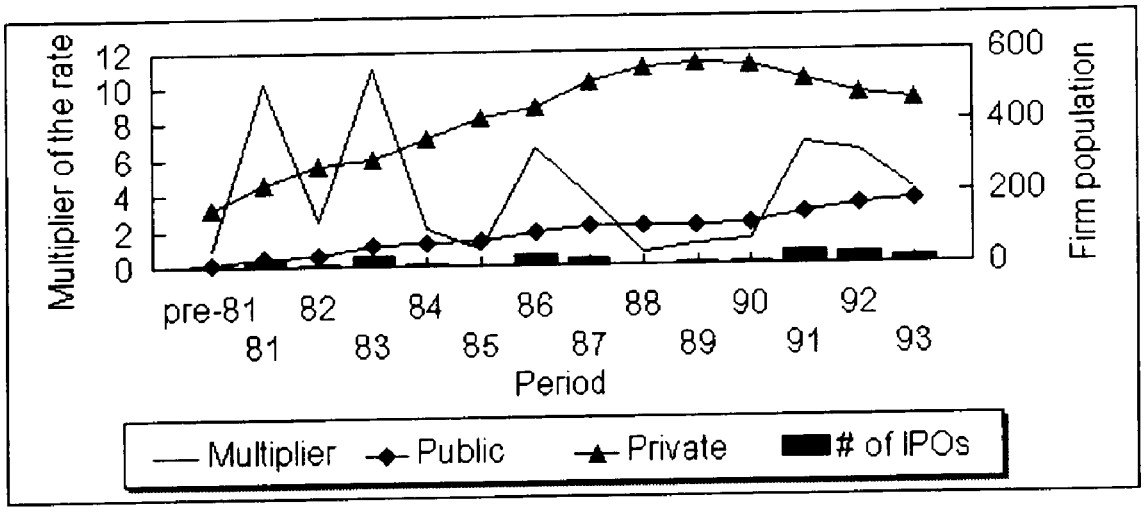

Figure 5-16: Representation of period variation in IPO rates using a piece-wise exponential model controlling for firm age

variation in the multiplier of the hazard rate by period is considerable.[63] Striking in this representation is, that controlling only for firm age, the highest

[62] Since model 3 is nested in model 2, we can use a likelihood ratio test based on minus two times the difference of the log-likelihoods. Using this criterion, the addition of the 13 period dummies is evaluated by a chi-square value of 139.9 with 13 degrees of freedom. This is significant by any traditional standard.

[63] The multiplier of the rate is a representation of the impact variation of an indivicual covariate (or subset of covariates) have on the IPO rates. In a multiplicative model such as

IPO rate was in the early 1980s. This visual impression matches intuitions based on the fact that number of IPOs was almost as high at this early period as it was in the peak period of 1991 even though the population was much smaller in the early 1980s. The juxtaposition of population densities against this simple model of IPO rates also suggests that some caution in interpreting the impact of population density on IPO rates might be in order. Two factors lie behind this caution. First, maximum private firm density happens to coincide the lowest IPO rates of the post-crash period of the late 1980s. Second, the peak IPO rates of the early 1980s are extreme enough that models including quadratic specifications of population may tend to be supported simply because such specifications can sometimes be highly influenced by extreme observations.

RESULTS OF MODELS COMMON TO ALL SPECIFICATIONS OF POPULATION DENSITY

Findings related to most of the hypothesized relationships are clear and unambiguous. Models represented in tables 5-2 through 5-10 all find maximum rates of going public when firms are between 4.7 years old and 5.5 years old.[64] In other models the visual representations of the reactions of IPO

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that employed here, the overall rate is Exp(β'X) where both X and β are vectors. In such a model the impact of an individual covariate is arrived by exponentiating the value of the covariate multiplied by its coefficient. In the case of a dummy variable the multiplier of the rate is simply the exponentiated value of the coefficient, thus, in figure 5-16 the multiplier of the rate for the period dummy for 1981 is simply Exp(2.326) or 10.24.

[64] When the coefficient of Log(Age) is positive and the coefficient of the square of Age divided by 10,000 is negative, simple calculus shows that the maximum multiplier effect is reached when the square root is taken of the ratio of the coefficient of Log(Age)*10,000 and minus two times the coefficient of the square of age.

Table 5-3: Total density models with quadratic specification, with and without controls

	Model 4		Model 5	
Age maximum	5.5		5.5	
Population maximum	154		129.8	
Log-likelihood	-1238.7		-1231.0	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-17.93 ****	1.06	-21.71 ****	1.73
Log(Age)	.93 ****	.14	.98 ****	.14
$(Age)^2/10,000$	-.0011 ****	.0002	-.0012 ****	.0003
NASDAQ	.0027 ***	.0010	.0021	.0018
ΔNASDAQ	.012 ****	.002	.014 ****	.002
IPO lagged 1 Qtr.	.081 ****	.017	.085 ****	.017
IPO lagged 2 Qtrs.	.032 *	.019	.033 *	.019
Therapeutics	1.477 ****	.201	1.455 ****	.201
Diagnostics	.647 ***	.228	.645 ***	.228
Agriculture	.846 ***	.302	.829 ***	.302
Delaware born	1.331 ****	.155	1.319 ****	.155
Delaware reincorporation	1.732 ****	.216	1.770 ****	.215
IPO at birth	.040 **	.019	.042 **	.020
Births last Qtr.	.022 *	.011	.024	.016
Total density	.002	.002	.002	.004
$(Density)^2/1,000$	-.008 ***	.003	-.009 **	.004
CPI			.026	.023
Prime rate			.095 **	.048

* p < .1, ** p< .05, *** p< .01, **** p < .001

Table 5-4: Total density models with controls, with and without quadratic specification

	Model 6		Model 7	
Age maximum	5.3		5.5	
Population maximum			130	
Log-likelihood	-1234.2		-1231.0	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-21.06 ****	1.55	-21.71 ****	1.73
Log(Age)	.96 ****	.14	.98 ****	.14
$(Age)^2/10,000$	-.0013 ****	.0003	-.0012 ****	.0003
NASDAQ	.0004	.0016	.0021	.0018
ΔNASDAQ	.013 ****	.002	.014 ****	.002
IPO lagged 1 Qtr.	.087 ****	.017	.085 ****	.017
IPO lagged 2 Qtrs.	.027	.019	.033 *	.019
Therapeutics	1.450 ****	.201	1.455 ****	.201
Diagnostics	.643 ***	.228	.645 ***	.228
Agriculture	.835 ***	.303	.829 ***	.302
Delaware born	1.300 ****	.154	1.319 ****	.155
Delaware reincorporation	1.767 ****	.215	1.770 ****	.215
IPO at birth	.040 **	.020	.042 **	.020
Births last Qtr.	.046 ****	.012	.0240	.016
Total density	-.006 ****	.002	.002	.004
$(Density)^2/1,000$			-.009 **	.004
CPI	.047 **	.020	.026	.023
Prime rate	.040	.040	.095 **	.048

* p < .1, ** p< .05, *** p< .01, **** p < .001

Table 5-5: Models with controls, quadratic specification of total density and with and without four consistently insignificant variables

	Model 8		Model 9	
Age maximum	4.7		5.5	
Population maximum	22		130	
Log-likelihood	-1230.1		-1231.04	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-21.42 ****	1.81	-21.71 ****	1.73
Log(firm age)	.884 ****	.164	.9834 ****	.144
$(Age)^2/10,000$	-.0015 ****	.0004	-.0012 ****	.0003
NASDAQ	.002	.002	.002	.002
ΔNASDAQ	.014 ****	.003	.014 ****	.002
# IPOs lagged 1 Qtr.	.089 ****	.021	.085 ****	.017
# IPOs lagged 2 Qtrs.	.035 *	.020	.033 *	.019
Therapeutics	1.462 ****	.202	1.455 ****	.201
Diagnostics	.646 ***	.228	.645 ***	.228
Agriculture	.830 ***	.302	.829 ***	.302
Delaware born	1.342 ****	.156	1.319 ****	.155
Delaware reincorporation	1.788 ****	.216	1.770 ****	.215
IPOs at birth	.047 **	.023	.042 **	.020
Last Qtr. births	.024	.016	.024	.016
Total density	.0003	.004	.002	.004
$(Density)^2/1,000$	-.006	.004	-.009 **	.004
Population at birth	-.001	.002		
NASDAQ at birth	-.001	.002		
Failures last Qtr.	-.025	.055		
Acquisitions last Qtr.	.005	.048		
CPI last Qtr.	.039	.025	.026	.023
Prime rate last Qtr.	.085 *	.048	.095 **	.048

* $p < .1$, ** $p < .05$, *** $p < .01$, **** $p < .001$

Table 5-6: Models with controls, quadratic specification of total density, with and without four consistently insignificant variables, and with 13 period dummies

	Model 10		Model 11	
Age inflection point	4.8		5.5	
Population inflection point	311		342	
Log-likelihood	-1208.4		-1209.5	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-22.13 ****	3.86	-21.78 ****	3.55
Log(firm age)	.877 ****	.164	.961 ****	.144
$(Age)^2/10,000$	-.0014 ****	.0004	-.0012 ****	.0003
NASDAQ	.011 ***	.004	.010 ***	.004
ΔNASDAQ	.003	.003	.005	.003
# IPOs lagged 1 Qtr.	.002	.027	.008	.022
# IPOs lagged 2 Qtrs.	.003	.025	.011	.024
Therapeutics	1.459 ****	.202	1.453 ****	.201
Diagnostics	.646 ***	.228	.645 ***	.228
Agriculture	.821 ***	.302	.818 ***	.302
Delaware born	1.336 ****	.156	1.316 ****	.155
Delaware reincorporation	1.760 ****	.2160	1.747 ****	.216
IPOs at birth	.048 **	.023	.044 **	.020
Last Qtr. births	.032	.022	.035	.022
Total density	.028	.019	.030 *	.018
$(Density)^2/1000$	-.045 **	.020	-.044 **	.020
Population at birth	-.001	.002		
NASDAQ at birth	-.001	.002		
Failures last Qtr.	-.002	.067		
Acquisitions last Qtr.	.085	.079		
CPI last Qtr.	.008	.071	-.0175	.064
Prime rate last Qtr.	.036	.125	.0807	.114
13 period dummies included	YES		YES	

* $p < .1$, ** $p < .05$, *** $p < .01$, **** $p < .001$

Table 5-7: Models adding public and private firm density measures with and without financial controls

	Model 12		Model 13	
Age inflection point	5.6		5.5	
Log-likelihood	-1220.6		-1211.0	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-19.57 ****	1.09	-25.88 ****	2.01
Log(Age)	.941 ****	.142	.96 ****	.145
$(Age)^2/10,000$	-.001 ****	.0002	-.001 ****	.0002
NASDAQ	.014 ****	.002	.010 ****	.002
ΔNASDAQ	.006 **	.002	.004 *	.002
# IPOs lagged 1 Qtr.	.072 ****	.017	.068 ****	.017
# of IPOs lagged 2 Qtrs.	.080 ****	.020	.066 ****	.020
Therapeutics	1.468 ****	.201	1.445 ****	.201
Diagnostics	.642 ***	.228	.645 ***	.228
Agriculture	.8284 ***	.302	.818 ***	.302
Delaware born	1.326 ****	.155	1.310 ****	.155
Delaware reincorporation	1.720 ****	.215	1.746 ****	.215
IPOs at birth	.044 **	.020	.046 **	.020
Births last Qtr.	.012	.011	.043 ***	.014
Private firm density	.0029 **	.0013	-.002	.002
Public firm density	-.057 ****	.008	-.070 ****	.010
CPI			.096 ****	.025
Prime rate			-.061	.043

* p < .1, ** p< .05, *** p< .01, **** p < .001

Table 5-8: Models adding public and private firm density measures

	Model 14		Model 15	
Age maximum	5.5		5.5	
Private population inflection			None	
Log-likelihood	-1211.5		-1211.0	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-25.30 ****	1.91	-26.01 ****	2.10
Log(Age)	.955 ****	.144	.966 ****	.146
$(Age)^2/10,000$	-.001 ****	.0002	-.0012 ****	.0002
NASDAQ	.011 ****	.002	.010 ****	.002
ΔNASDAQ	.004 *	.002	.004 *	.002
# IPOs lagged 1 Qtr.	.069 ****	.017	.068 ****	.017
# of IPOs lagged 2 Qtrs.	.072 ****	.019	.066 ****	.020
Therapeutics	1.446 ****	.201	1.445 ****	.201
Diagnostics	.647 ***	.228	.645 ***	.228
Agriculture	.826 ***	.302	.817 ***	.302
Delaware born	1.312 ****	.155	1.311 ****	.155
Delaware reincorporation	1.737 ****	.215	1.747 ****	.215
IPOs at birth	.044 **	.020	.045 **	.020
Births last Qtr.	.036 ***	.012	.041 **	.017
Private firm density			-.0004	.005
Public firm density	-.073 ****	.009	-.069 ****	.010
$(Private)^2/1,000$			-.002	.006
CPI	.083 ****	.020	.094 ****	.026
Prime rate	-.045	.040	-.053	.053

* $p < .1$, ** $p < .05$, *** $p < .01$, **** $p < .001$

Table 5-9: Models with private and public densities with controls or period dummies

	Model 16		Model 17	
Age inflection point	5.5		4.8	
Log-likelihood	-1202.2		-1201.2	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-28.87 ****	4.50	-27.500 ****	4.577
Log(age)	.958 ****	.143	.880 ****	.162
$(Age)^2/10,000$	-.0012 ****	.0003	-.0014 ****	.0003
NASDAQ	.014 ****	.004	.014 ****	.004
ΔNASDAQ	-.003	.004	-.001	.004
# IPOs lagged 1 Qtr.	.038	.026	.055 *	.031
# IPOs lagged 2 Qtrs.	.049 *	.026	.060 **	.030
Therapeutics	1.452 ****	.201	1.457 ****	.202
Diagnostics	.643 ***	.228	.643 ***	.228
Agriculture	.821 ***	.302	.822 ***	.302
Delaware born	1.312 ****	.155	1.329 ****	.156
Delaware reincorporation	1.734 ****	.215	1.748 ****	.216
IPOs at birth	.046 **	.020	.048 **	.023
Births previous Qtr.	.014	.022	.007	.023
Private density	-.002	.008	.003	.009
Public density	-.098 ****	.023	-.101 ****	.023
Population at birth			-.001	.002
NASDAQ at birth			-.001	.002
Failure previous Qtr.			-.062	.069
Acquisitions last Qtr.			-.048	.088
CPI	.137 **	.062	.118 *	.068
Prime rate	-.085	.120	-.049	.128
13 period dummies included	YES		YES	

* p < .1, ** p< .05, *** p< .01, **** p < .001

Table 5-10: Models with quadratic specifications of private and public densities

	Model 18		Model 19	
Age, model maximum	5.5		5.5	
Private, inflection point	949			
Public, model maximum	None		None	
Log-likelihood	-1209.8		-1210.1	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-26.81 ****	2.18	-26.906 ****	2.259
Log(Age)	.957 ****	.145	.967 ****	.145
$(Age)^2/10,000$	-.0012 ****	.0002	-.001 ****	.0002
NASDAQ	.011 ****	.002	.011 ****	.002
ΔNASDAQ	.0040	.0025	.0044 *	.0025
# IPOs lagged 1 Qtr.	.058 ***	.018	.061 ****	.018
# IPOs lagged 2 Qtrs.	.063 ***	.019	.064 ***	.020
Therapeutics	1.446 ****	.201	1.447 ****	.201
Diagnostics	.647 ***	.228	.647 ***	.228
Agriculture	.820 ***	.302	.818 ***	.302
Delaware born	1.313 ****	.155	1.316 ****	.155
Delaware reincorporation	1.74 ****	.215	1.745 ****	.215
IPOs at birth	.045 **	.020	.045 **	.020
Births last Qtr.	.044 ***	.017	.039 **	.015
Private density	-.012	.009	-.005 *	.003
Public density	-.037	.023	-.046 **	.020
$(Private)^2/1,000$	.006	.008		
$(Public)^2/1,000$	-.173	.111	-.117	.085
CPI	.117 ****	.030	.105 ****	.026
Prime rate	-.049	.05	-.032	.049

* p < .1, ** p< .05, *** p< .01, **** p < .001

rates to aging are all very similar to those depicted above. In all models, the coefficients of both log of age and age squared are highly significant. With almost as little variation, the product orientations of the firms are found to be significant at either the .001 or the .005 levels (two-sided). Compared to the baseline category that included all firms other than agricultural firms, human therapeutics firms and diagnostics firms, all three categories showed elevated rates of going public. IPO rates of therapeutic firms were between about 4.2 and 4.4 times higher[65] agricultural firms about 2.2 to 2.3 times higher and diagnostic firms about 1.9 times higher than the rates for the miscellaneous population of other firms in the industry. One thing is clear, the impression that therapeutic firms can and do go public faster and more easily than other firms is supported by these results.

In all models, the propensity of firms to go public was enhanced by the level of IPOs in the quarter preceding their birth. The coefficient of this variable ranges upwards of .04 (generally significant at the .05 level) and translates into a multiplier of 1.04 for each additional IPO in the period prior to the firms birth or about 1.22 for each 5 additional firms that went public in the period prior to birth. Thus firms born in a quarter after one in which 15 IPOs occur will tend to go public at a rate 1.5 times higher than firms that were born after a quarter with only 5 IPOs.

Expectations about the signal incorporation choice generates were very strongly supported in all models at the .001 level and better. Firms that reincorporated in Delaware subsequently had IPO rates over 5.47 times

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[65] The maximum for the coefficient of the dummy variable "Therapeutics" is 1.477 in model 4 leading to a multiplier of exp(1.477)=4.38. The minimum for this coefficient is 1.445 in model 12 of table 5-5, which translates into a multiplier compared to non-therapeutic firms of exp(1.445) or 4.24.

higher than firms incorporated in their home states. Much more telling, however, was the fact that the original incorporation choices send enduring signals about the financing propensities of the firm. In all the models shown here, the IPO rates of firms originally incorporated in Delaware were more than 3.6 times higher than the baseline rates estimated for firms incorporated in their home states. This finding is a clear indication that, right from the start, firms probably have different strategies that impel them towards different patterns of financing. Much of the decision to go public may very well be opportunistic, these findings indicate that these decisions are also outcomes of enduring firm differences.

In all models except where dummy variables for all 13 periods were included (models 10, 11, 16, and 17) the coefficients for the impact of the counts of IPOs lagged one quarter were in the predicted direction and highly significant. Even in the cases where period effects were included the coefficients were of the predicted sign. In the models where period effects were not included the size of the coefficients ranged from a low of .058 (model 18) to a high of .089 (model 8). These values can be interpreted as the IPO rate rising between 5.8 percent to 9.3 percent for each additional IPO that occurred in the previous quarter. Hence a period preceded by a quarter with 10 IPOs would have an IPO rate of between 32 percent and 56 percent higher than a period preceded by only 5 IPOs.

The same general observations can be made about the impact of counts of IPOs lagged two quarters. It should be noted that in this case these coefficients were not always significant even in models where period effects were not included. In the models without period dummies, the values of the coefficients ranged from a low of .027 (model 6 where it does not achieve

significance) to a high of .080 (model 12). If these estimates can be relied upon, the impact of each additional IPO two quarters before the period in question would raise the IPO rate by between 2.7 percent to 8.3 percent.

The calculated effects of the level of the stock market and the impact of rising market over the previous two calendar quarters were also in keeping with predictions and expectations. In all models, a high level of the NASDAQ composite was positively associated with rates of going public. The coefficients were significant in all models except models 5, 6, 7, 8, and 9 (models 5,7, and 9 are actually the same model reproduced in different tables for ease of comparison). All the models in which the coefficients of the level of the NASDAQ were insignificant also include values of the total population or the total population squared which are models I later suggest should be abandoned in favor of models where private and public populations are counted separately. Even in models where total density is included, when period effects are also included the level of the stock market assumes significance. When significant, the values of the coefficients varied between .0027 (model 4) up to .014 (models 12, 16, and 17). Based on these estimates, each 10 point increase in the level of the NASDAQ composite index led to a rise in the IPO rate of between 2.7 percent to 20.3 percent.

The impact of changes in the closing value of the NASDAQ composite over the previous two calendar quarters was somewhat less clear. In two instances where period effects are included (models 16 and 17) the sign is negative (but not significant) indicating a rising market depresses IPO activity. In two further cases where period effects are included (models 10 and 11) the coefficient is positive but not significant. Model 18 is the only model not including period effects where the coefficient is insignificant. Even in this

instance the coefficient is positive. Given that the period effects should capture much of the temporal variation in the rate, non-significant coefficients in these cases is not overly surprising. In the case of model 18 it is likely that the inclusion of two non-significant quadratic effects also might lead to an inflation of the variance for the coefficient of the change in the NASDAQ.

Lagged measures of births were at least marginally significant in eight of the sixteen models reported (or eight of the 14 distinct models reported since models 5, 7, and 9 are identical), and the value of the coefficient was always positive. In cases where the coefficients were significant the values ranged between .022 (model 4) and .046 (model 6), which translate to rises in the IPO rate of between 2.2 percent and 4.7 percent for each additional birth in the previous calendar quarter. All of the cases where the coefficient is insignificant either include quadratic effects (which I argue later may be misspecified), exclude financial controls, or include the 13 period effects.

The results for lagged measures of acquisitions and failures were not significant in any of the regressions in which measures of IPO activity, births and stock market values were also present. The coefficients for the level of the stock market at the time of the firm's birth and population at birth were likewise never significant when other measures such as the level of IPOs at the time of the firm's birth were included. Models 8, 10, and 17 include all four of these variables. Comparisons to models in which these variables are collectively removed reveal that in no case does their inclusion lower the log-likelihood sufficiently to merit inclusion of a even a single one of the variables much less all four of them. A variety of other models not reported here could also have been cited that support the same observation.

The statistical significance of the two financial controls included in models, namely the level of the CPI and the level of the prime rate, vary among models. In the fourteen models in which these two variables are included, CPI appears as positive and significant in eight of them. In all but one of the remaining models the coefficient is positive but in none of these models does the coefficient achieve significance. The fact that coefficient values are in the expected direction (a general upward trend in the rate of going public) and are highly significant in the favored models both argue for retention of this variable as a control variable. Whether or not it is included does not alter the qualitative conclusions drawn about the variables of theoretical interest. In general if one deflates the level of the NASDAQ and the change in the NASDAQ by CPI the qualitative conclusions about these two variables remains the same, but subsequent entry of the CPI still tends to be significant. One reason for this finding could be that, since health care costs have been a significant driver of overall inflation, a rise of CPI has tended to signal growth in the target markets of many biotechnology firms.

Both the values and significance levels of the control variable for the level of the prime rate vary substantially. In models where total density measures are included, the values of the coefficient of prime rate are always positive and often significant (four out of seven cases). In models where private and public densities are included the coefficient is always negative and never significant in the seven cases where it appears. While one would expect investors to be less willing to invest in IPOs when the return from interest bearing instruments is high, perhaps in some instance high interest rates might induce equity mutual fund managers to seek higher risk investments in order to "beat the competition" offered by debt instruments. In

any event, inclusion or exclusion of this variable doesn't tend to alter qualitative results about the variables of more direct interest so this control variable is included in the bulk of the models reported here.

CHOOSING AMONG MODELS

One conventional tool for comparing competing models is to conduct likelihood ratio tests among nested models. The purpose of such tests is essentially to determine the extent to which adding variables adds statistically significant explanatory power of the model. Models presented in tables 5-3 to 5-6 include many models which are nested in one another. Models 4 and 6 are nested in model 5 (also reported as models 7 and 9). Model 4 versus 5 produces a chi square of 15.4 with two degrees of freedom which shows model 5 is a very significant improvement over model 4 (significance in excess of .001). Comparing models 6 and 7 (or equivalently 6 and either 5 or 9) yields a chi square of 6.4 with one degree of freedom which, with a p-value of .0114, is significant at .05. Model 5, in turn, is nested in models 8 and 10 and 10 is nested in model 11. The only tests of these nestings that are significant are comparisons of model 5 with models 10 and 11 (both of which include period effects). These comparisons produce likelihood ratio tests with chi squares of 43.08 with 13 degrees of freedom (model 5 versus model 10), and 45.28 with 17 degrees of freedom (model 5 versus model 11). Both these tests are significant at the .001 level. In the second category of models reported in tables 5-7 through 5-10, models 12 and 14 are nested in model 13. Model 13 in turn is nested in model 16 (which in turn is nested in model 17), and 13 is also nested in model 19 (which in turn is nested in model 18). Using model 13 as the focus, the only likelihood ratio test which is significant

is model 12 versus model 13. Adding financial controls to model 12 produces an improvement in fit that is significant at the .001 level.[66]

The real challenge in evaluating these results, however, lies in comparing the two contending categories of models which are not nested in one another. Two basic modelling approaches are presented in the tables. The real challenge in evaluating these results lies in determining which of the contending measures of population densities make sense in light of the estimated models. Two basic modelling approaches are represented in the tables. In Tables 5-3 through 5-6 population is taken to be a unitary one where all biotechnology firms are counted equally whether they are private or public. Within this class of models the question posed is whether the IPO rate first rises at low densities (signalled by a positive coefficient for total population) and then falls at higher densities (signalled by a negative coefficient for the square of the population density. In the second kind of model (represented in tables 5-7 through 5-10) the unitary conception of biotechnology population is relaxed so that public and private populations are counted separately. As with the cases where only one population count is employed, inclusion of quadratic measures allows for the possibility of rates initially rising with rising populations (signalling growing legitimacy) and then falling at higher levels of population (signalling growing competition for funds and other resources).

In both sets of models two informal criteria are employed to judge the quality of the models:

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[66] The only model not reported here that would represent a simpler model than model 14 without sacrificing statistical significance would be a model where prime rate was also excluded. Since this model is for all practical purposes identical to model 14 it is not included among the tables.

1. Are the coefficients, especially for the quadratic terms, significant?
2. If the signs on the untransformed density and the squared density are opposite in sign, does the maximum rate (or if in the opposite direction to that predicted, minimum) occur within the range of the observed range of population density?[67]

In the case of models based on total population density the second of these conditions is always obeyed. The transition from rising rates due to increased population to falling rates with further increases always occurs within the actual range of the historical population. Even so, the inflection point ranges from a low of changing at a population of 22 in model 8, to a high of 342 in model 11. In only one of seven cases where both terms are included, however, are the coefficients on both terms significant (model 11). In cases where the quadratic term was excluded (one of which is reported in model 6) the impact of population on IPO rates is negative and significant.

It is important to note that model 7 which includes both density and density squared is nested in model 11 which also includes the 13 period dummies. Comparison of models 11 and 7 shows that in this case the chi-squared value for the 13 period dummies is -2*[-1231.0-(-1209.5)] or 43 which, as a chi-square with 13 degrees of freedom, is significant at any

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[67] If a minimum (within the range of the observed data) is encountered this would require re-examination of the theory I have advanced. Inflection points outside the range of the data may just indicate the existence of curvature in the reaction of the rate to change in population, and as such (especially if both coefficients are significant) cannot be rejected outright. Nevertheless, since the form of the argument advanced earlier involves making inferences about the change in direction of change in the rate from positive to negative, an inflection point outside the range of the observed data would definitely preclude making these relatively strong inferences about legitimacy and competition.

traditional level. In this case the inclusion of the ad-hoc period specifications significantly improves the model.

In the models where private and public populations are counted separately, whenever a quadratic term for one of the population counts is included (models 15, 18 and 19) the inflection points based on the calculated models tend to be outside the range of the observed population counts (model 18 private density), or the values of both the first order and quadratic terms are of the same sign (in model 15 private density and in models 18 and 19 public density first order and quadratic terms are all negative). In the only cases where U-shaped reactions to density are estimated to be present (private densities in model 18) the U opens upwards, the minimum occurs outside the range of the historical population and the coefficients are not significant. In sum, the evidence suggests that inclusion of quadratic specifications of either public or private density is not supported by the data.

In the models based on separate measures of public and private density, once we decide to abandon expectations of finding U-shaped reactions to density the picture becomes very simple. If we focus on models 13 and 16 we see that model 13 is nested in model 16. In addition to the density measures of public and private firms, model 16 also includes the 13 dummy variable for the years between 1981 and 1993. In this case the chi-squared assessment of the significance of the 13 period variables is 17.6 with 13 degrees of freedom. This is not significant at the .1 level. In this case, addition of period effects to the models that include both private and public densities has not significantly improved the overall model. Moreover, the reported effects of the population variables are all negative, indicating that the primary impact of increased population is increased competition for the

right to go public. If we rely on the model without period effects (model 13) we find that the impact of public firm density is negative and significant. In this same model, private firm density is also negative (although much less so than for public density) but is also not significant. Based on the value of -.07 for the coefficient of public density we would expect the rate at which firms go public to drop by about seven percent for each additional firm in the public population.

While a formal comparison of the two types of models (a unitary conception of total population or a conception that distinguishes between private and public firms) would be difficult given that they are not nested, some factors definitely point in the direction of preferring the latter type of model. The first of these factors is that the models with public and private density measures appear to capture more of the period variation in IPO rates. The second is that in model 13 (the simplest of the full public/private models that includes control variables) as opposed to model 7 (the simplest of the total population with quadratic models that also includes control variables), more of the remaining variables in the model also appear as significant and with the expected signs.

Relating back to the discussions that began this chapter, the models where population is regarded as a single, unsegregated mass offer support for the adoption of legitimacy/competition model of variation in IPO rates of biotechnology firms. On the other hand, if we look to the models where the population is divided into two distinguishable types, public and private, the rise of population is seen to give rise to increased competition and that is all. In both kinds of model, however, the idea that firm choices (and the degree to which the environment is hostile or friendly) vary in accord with constantly

revised assessments of population viability based on recent actions of member firms is strongly supported. A "legitimated" environment for raising money in public offerings is one where lots of firms are doing so, where the economic conditions are favorable, and where the firm has strategies and features that are most conducive to going public and are most valued by the marketplace.

OTHER ESTIMATION METHODS AND TREATMENT OF COMPETING RISKS

Two final issues must be addressed before leaving the analysis of IPO rates for the full population of biotechnology firms behind. The first issue is whether using a piece-wise exponential model as opposed to a Cox model with spell-splitting can be defended. The second is whether treating the competing risks of acquisition and failure as censoring mechanisms is a reasonable one. The choice between Cox models and piece-wise exponential models is simple. Since there is effectively no difference in the results generated using the two methods, I report piece-wise exponential models largely because their estimation requires less computer time. Table 5-11 presents Cox proportional hazard estimates for the same models as those presented as models 13 and 7 in tables 5-7 and 5-4 respectively. To all intents and purposes, the results are identical both in terms of coefficient values and their standard errors. Even the overall chi-square for the full model is within fractions of a percent of that which obtains when a likelihood ratio test is constructed for the overall models for the piece-wise exponential analogues versus a null model alternative.

Table 5-11: IPO models estimated using Cox's proportional hazards techniques

	Model 20		Model 21	
chi-square for model	451.47		411.37	
Model degrees of freedom	17		17	
Variables	Coef.	S.E.	Coef.	S.E.
Log(Age)	.961 ****	.145	.982 ****	.144
$(Age)^2/10,000$	-.0012 ****	.0002	-.0012 ****	.0003
NASDAQ	.010 ****	.002	.0021	.0018
ΔNASDAQ	.004 *	.002	.014 ****	.002
# IPOs lagged 1 Qtr.	.068 ****	.017	.085 ****	.017
# IPOs lagged 2 Qtrs.	.066 ****	.020	.033 *	.019
Therapeutics	1.445 ****	.201	1.456 ****	.201
Diagnostics	.645 ***	.228	.645 ***	.228
Agriculture	.818 ***	.302	.829 ***	.302
Delaware born	1.311 ****	.155	1.320 ****	.155
Delaware reincorporation	1.749 ****	.215	1.773 ****	.216
IPOs at birth	.046 **	.020	.042 **	.020
Births last Qtr.	.043 ***	.015	.024	.016
Private density	-.002	.002		
Public density	-.070 ****	.010		
Total density			.002	.004
$(Density)^2/1,000$			-.009 **	.004
CPI	.097 ****	.025	.026	.023
Prime rate	-.061	.044	.095 **	.048

* p < .1, ** p< .05, *** p< .01, **** p < .001

The case of the using the competing risks as censoring mechanisms is slightly less clear. In the case of models of acquisitions presented in table 5-12 virtually no coefficients appear as significant. While there may be a relationship between IPOs and acquisitions it is not readily discoverable. In the case of failures, there is some suggestive evidence that the two events are subject to the influence of some of the same covariates. It is particularly apparent that the fragility of biotechnology firms in the face of aging is similar to the influence aging has on IPO rates. There are also strong indications that therapeutics firms fail at a much lower rate than other biotechnology firms possibly due to their preferential access to financing. Finally, failures among biotechnology firms (table 5-13) appear to move in concert with variables such as level of the stock market (both contemporaneous and at birth), levels of the Consumer Price Index, and possibly the density of private firms. Since the set of variables affecting IPO rates and failures are not completely disjoint, using acquisitions and failures as censoring mechanisms must be defended on the basis first discussed in chapter 3 of having a sufficiently large sample that this treatment of competing risks is appropriate.

Table 5-12: Models of acquisitions of private firms

	Model 22		Model 23	
Log-likelihood	-474.97		-475.22	
Age, model maximum	6.7		5.8	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-14.011 ****	2.908	-13.273 ****	2.697
Log(Age)	.075	.268	.067	.269
$(Age)^2/10,000$	-.0001	.0003	-.001	.0003
NASDAQ	-.004	.004	-.005	.004
ΔNASDAQ	.007	.005	.008 *	.005
# IPOs lagged 1 Qtr.	-.032	.051	-.023	.050
# IPOs lagged 2 Qtrs.	.107 **	.042	.099 **	.040
Therapeutics	.107	.333	.108	.333
Diagnostics	-.317	.359	-.317	.359
Agriculture	.046	.455	.048	.455
Delaware born	-.499	.419	-.497	.419
Delaware reincorporation	-.123	.729	-.116	.729
IPOs at birth	-.048	.059	-.049	.059
Private density	.003	.003		
Public density	-.011	.017		
Total density			.003	.008
$(Density)^2/1,000$			-.001	.008
Population at birth	.004	.004	.004	.004
NASDAQ at birth	-.003	.003	-.003	.003
Failures previous Qtr.	.142	.094	.145	.093
Acquisitions last Qtr.	-.140	.089	-.133	.098
Births last Qtr.	.004	.024	.001	.030
CPI	.036	.037	.023	.044
Prime rate	-.033	.088	.002	.084

* $p < .1$, ** $p < .05$, *** $p < .01$, **** $p < .001$

NOTE: Both models are based on 24,924 quarterly observations of firms and 59 acquisitions. Both models lose three observations because no lagged values for the NASDAQ were available for the first quarter of 1971. IPOs right-censored 218 observations, and failures right-censored an additional 111 observation.

Table 5-13: Models of failures of private firms

	Model 24		Model 25	
Log-likelihood	-764.69		-764.86	
Age, model maximum	4.0		4.1	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-21.663 ****	3.912	-22.172 ****	5.035
Log(Age)	.503	.333	.519	.339
$(Age)^2/10,000$	-.0012 ***	.0004	-.0012 ***	.0004
NASDAQ	-.006 *	.003	-.007 ***	.003
ΔNASDAQ	.005	.003	.005 *	.003
# IPOs lagged 1 Qtr.	.033	.027	.040	.026
# IPOs lagged 2 Qtrs.	.034	.029	.026	.028
Therapeutics	-1.184 ****	.338	-1.183 ****	.338
Diagnostics	-.074	.223	-.073	.223
Agriculture	.032	.347	.030	.347
Delaware born	.392	.238	.393 *	.238
Delaware reincorporation	-.785	1.010	-.782	1.010
IPOs at birth	.030	.034	.030	.034
Private density	.005 **	.002		
Public density	-.009	.015		
Total density			.010	.011
$(Density)^2/1,000$			-.006	.011
Population at birth	.004	.003	.004	.003
NASDAQ at birth	-.006 **	.002	-.006 **	.002
Failures previous Qtr.	.072	.067	.080	.067
Acquisitions last Qtr.	-.029	.060	-.018	.060
Births last Qtr.	-.015	.028	-.026	.030
CPI	.091 **	.039	.075 **	.037
Prime rate	-.051	.094	.011	.101

* p < .1, ** p< .05, *** p< .01, **** p < .001

NOTE: Both models are based on 24,924 quarterly observations of firms and 111 failures. Both models lose three observations because no lagged values for the NASDAQ were available for the first quarter of 1971. IPOs right-censored 218 observations, and acquisitions an additional 59 observations.

CHAPTER 6. IPO RATES BY FIRM CATEGORY: AN INVESTIGATION OF COMPETITIVE AND SYMBIOTIC FORCES AMONG SUBPOPULATIONS

A central working assumption employed in the previous chapter was that the IPO rates of all biotechnology firms are influenced by a common set of factors. A second assumption made was that all kinds of firms would react in similar fashions to each of these common influences. In fact, the sole way in which the IPO rates of different kinds of firms[68] were allowed to vary by virtue of belonging to one firm category rather than another, was through the inclusion of dummy variables for firm category in all the models. As a consequence of this modelling strategy, if two firms from different categories happened to have been founded at the same time and had made the same incorporation choices, the estimated IPO hazard rates would differ only by a constant multiple. In the more general case where covariates for firms do not coincide, however, this approach still imposed the restriction that a change in any given covariate would cause the same proportional change in the hazard rate for all firms.

A related constraint inherent to the modelling treatment employed in the previous chapter was the assumption that the population within which competition takes place (and within which legitimacy is earned and lost) was taken to be the nebulous agglomeration designated as biotechnology firms. As was pointed out in earlier chapters, because the target markets of the constituent firms vary widely biotechnology is not an industry in the sense that

[68] Firm class or category was operationalized in these models by coding each firm as belonging to one of the following categories: therapeutics, diagnostics, agricultural or miscellaneous activities.

all firms are competing for sales of similar products. While there is evidence that, to some extent, financial markets have adopted the fiction of the biotechnology industry,[69] the degree to which this simplification actually governs the perceptions of investors bears close scrutiny. In the literature dealing with survival analysis, event history analysis and population ecology, the difficulties of assessing the impact of unobserved differences among the units of observation is generally referred to as the problem of unobserved heterogeneity.

One way to assess the validity of the above simplifications is to estimate separate models for each category of firm and to employ separate population density measures for each firm category. Because of the small numbers of firms (and events) in most categories, the degree to which the industry can be divided into subpopulations is limited. The results of the last chapter suggest that, at the minimum, there is reason for treating therapeutics firms as being distinct from all other firms. In a step towards reducing any potential over-simplification, this chapter first introduces distinct population density measures for therapeutics firms and non-therapeutics firms. Second, this chapter allows for therapeutics and non-therapeutics firms to differ in their reactions to covariates..

The division of the biotechnology population into distinct groupings is not a terribly controversial idea, it is obvious that not all biotechnology firms are the same. The easiest group to identify and defend is that of therapeutics firms. As has been suggested in previous chapters, therapeutics firms share

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[69] An example of how this has influenced firm strategies is the opinion offered by Dr. Jonathan MacQuitty, president of Genpharm International, that "when times are good for biotechnology firms generally...I suspect we'll continue to nestle under the biotechnology umbrella because it will improve our cost of capital" (Burrill, 1989, p. 136).

a regulatory environment (the FDA), have similar cost structures (largely as an outcome of shared regulatory oversight), have enthusiastically availed themselves of the opportunity to go public, rely on similar labor pools, rely on similar research technology, and ultimately depend on introducing products into the domestic American market for therapeutic drugs. I would also argue that it is reasonable to assert homogeneity among therapeutics firms because this simple categorization has been widely accepted as being meaningful. In this instance, widespread adoption of a group definition is relevant because we are dealing with a phenomenon which is extremely dependent upon public perceptions. In practical terms there is also a degree to which information about one therapeutics firm generates relevant information on the prospects of other therapeutics firms, either in terms of direct competitive interactions, or in terms of reputational impacts on biotechnology firms in general.

The argument in favor of a single group for all non-therapeutics firms is harder to support. The primary argument in favor of such a simplification is that it appears to correspond to a popular conception of the industry where biotechnology firm classification is dichotomous: therapeutics firms and "other firms." Biotechnology is an industry where therapeutics firms attract most attention from the public, and where the most salient feature of all the other biotechnology firms is summed up in the recognition of what it is not, namely, a therapeutics firm. The main constraint on classification is a practical one, if one categorizes too finely the resultant samples are too small to employ large sample statistical techniques. In fact, however, the results turn out to very similar for models using only diagnostic firms, or groupings that include diagnostic firms and other sub-sets of the non-therapeutics population.

Given the above observations, the thrust of this chapter is to examine the degree to which models for therapeutic and non-therapeutic biotechnology firms differ from those reported for biotechnology firms in general. This chapter also examines the general issue of how subpopulations interactions can be related to their respective population densities. Following up on this discussion, specific evidence is presented of how the subpopulations within the biotechnology industry differ in their responses to the population densities of the two broad categories of biotechnology firms. With the exception of hypotheses 5-1, 5-2, and 5-8, all the hypotheses advanced in chapter 5 also apply here. Because of the exploratory nature of the investigation of subpopulation densities on IPO rates formal hypotheses are not advanced for these variables.

INTERACTIONS AMONG SUBPOPULATIONS

To a degree, the question of how IPO rates react to the growth of subpopulations has already been introduced in the previous chapter. The division of the biotechnology industry into two classes of firms, namely, public and private, was an implicit recognition that populations are themselves composed of logically and practically distinct subpopulations. This public/private dichotomization, however, was made on the basis of a classification based on the event of interest. In the case where the population was divided on the basis of being private or public it was the nature of the event being studied suggested that the number of firms in the two classes would exert different forces on the competitive and legitimating processes. There are other rationales that can be invoked for sub-dividing the populations into subpopulations. Within the population ecology literature, the possibility is

raised that the growth of subpopulations defined by geography (e.g., brewers as analyzed by Hannan and Carroll, p. 151-156); organization (e.g., craft and industrial unions as analyzed by Hannan and Freeman 1989, pp. 102-106, or mutual and stock life insurance companies studied by Hannan and Carroll 1992, pp. 111-115); and product focus (e.g., commercial and savings banks, Hannan and Carroll, pp. 107-111) can create interdependencies among their vital rates. For our purposes here, we will limit our further partitioning to the last of these alternatives: broad division on the basis of product market distinctions.

This further partitioning of the biotechnology population will be used to discover whether the IPO rates of therapeutic firms are affected by the various subpopulation densities (public therapeutics firms, private therapeutics firms, public non-therapeutics firms and private non-therapeutics firms) differently than are the IPO rates of non-therapeutics firms. At this point it should once again be acknowledged that restricting the partitions of the population to only two categories is driven, in part, by the practical limitations imposed by the data. For firm classes other than therapeutics, with the possible exception of diagnostic firms, the number of events per class is so low that single observations materially affect estimated hazard rates. The problem of low sample sizes is especially troublesome at older ages where few firms have chosen to go public. These considerations will cause us to maintain the fiction of a single class of non-therapeutics firms.[70]

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[70] Roger Salquist, Chairman and Chief Executive Officer of the agricultural biotechnology firm Calgene, observed: "When it comes to financing, we're the tail and they're the dog. If the market is down on the health-care biotechnology stocks, no matter how attractive the product opportunities we're working on, we take the hit, too" (Burrill 1989, 135). Thus perhaps the simple bifurcation of the population into therapeutics and non-therapeutics is as complicated a treatment as the situation warrants.

Hannan and Freeman (1989) suggested that the most likely interaction across populations is one in which the size of one population exerts a purely competitive influence on the other. As they put it:

> Therefore, in developing a multi-population model, we specify only competitive effects between populations. It seems likely, as Lotka and Volterra assumed for the biotic case, that the strength of competitive interactions increases monotonically with density. (p. 141)

Hannan and Carroll (1992) amend this simplest case scenario to include all monotonic interactions among population densities. They write:

> A mixed legitimating and competitive interaction occurs when the growth of one population legitimates the other, but the growth of the second worsens the life chances of the first by eroding its resource base. If the cross-effect involves only legitimation, the density of each population will increase the founding rate and lower the mortality of the other. Finally, interdependence may be asymmetric: One relation is present and the other does not exist. (pp. 99-100)

Hannan and Carroll continue by describing conditions under which one might encounter non-monotonic cross-effects among populations. Because the findings of the previous chapter did not support the inclusion of quadratic terms of the public and private subpopulation densities (nor did exploratory modelling of this subset of the data), these potentially non-monotonic model specifications are not repeated here.[71]

In the context of IPO rates there is little to guide us in postulating the form cross-effects among population densities might take. Relying on the

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[71] In the models referred to, the quadratic terms were either insignificant or they showed maxima or minima that were outside the range of the observed population densities. In fact, exploratory models including squared sub-population density terms were run but the results were qualitatively similar to those reported for the models reported in chapter 5.

results from the last chapter, we might expect the various subpopulations to all exert purely competitive pressures on the financing capabilities of the individual firm. On the other hand, evidence that therapeutics firms are substantially different from other firms might cause us to speculate that the density of therapeutics firms exerts different pressures on the two subpopulations. While therapeutics firm density might exert purely competitive pressures on other therapeutics firms seeking to go public, this same effect might not be felt by non-therapeutics firms. If one were to speculate that the bulk of the publicity for biotechnology as a whole is generated by therapeutics firms, then some contrarian investors might seek out non-therapeutics firms in the belief that these firms might represent an undervalued component of the biotechnology sector. The more therapeutics firms succeed, perhaps the more credible the expectation of future successes within agricultural biotechnology might seem. Because there are a wide range of defensible hypotheses about the impact subpopulation densities exercise on IPO rates, no hypotheses will be made. Instead, a post-hoc attempt will be made to interpret actual findings.

MODELLING STRATEGY

To examine the effect lifting the constraints of the previous chapter might have, I employ a four stage modelling strategy. First, I estimate life table, piece-wise exponential and log-quadratic models of age-dependence for the two proposed subpopulations to determine whether the log-quadratic model continues to provide a reasonable approximation of the effect aging has on IPO hazard rates. Second, I estimate models of all firms where the original assumption of proportional hazards is maintained, but subpopulation

densities are included among the covariates. Third, I split the original population into two subpopulations, one comprising all therapeutics firms and the other comprising all non-therapeutics firms. For each of these subpopulations, I estimate a model using total density measures of public and private firms. These results are then compared with those for the most directly comparable model estimated using the full population. Fourth, for each of the two subpopulations, I estimate models which allow for differential reactions to own-population and other-population densities. These last models allow us to assess the degree to which processes of competition and legitimation are localized to a firm's own subpopulation.

RESULTS

In chapter 5 a log-quadratic specification of age-dependence in IPO rates was strongly supported in every model estimated. A pattern of rising then declining hazard rates can, however, be produced by fitting a common model to a population where one sub-grouping has a low hazard and the other sub-grouping has a high hazard. In cases where this form of heterogeneity exists, the hazard estimates are initially dominated by the failure of members of the high-hazard population and then, as time passes, the hazard estimates decline as the sample comes to be dominated by members of the low-hazard subpopulation.

Examination of graphs of life table estimates of hazards for the therapeutics firms (figure 6-1) and non-therapeutics firms (figure 6-2) suggests that the general pattern of rising then falling hazards as the firm ages is exhibited by the subpopulations. The wide age bands (1000 days) make it difficult to discern rapid shifts in IPO rates but even with the

dampened fluctuation in rates that such life table estimates produce, IPO rates in both subpopulations appear to have non-monotonic relationships to aging.

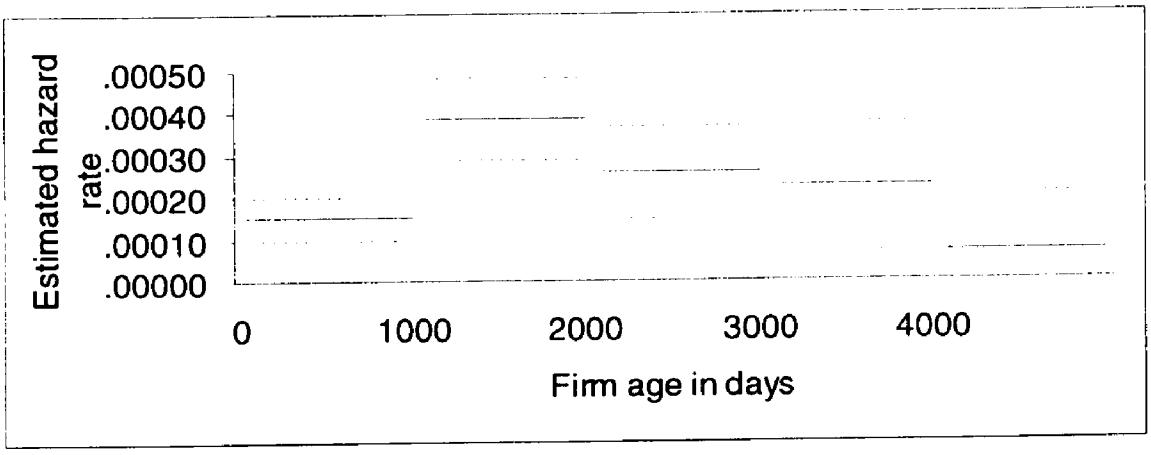

Figure 6-1: Life table estimates of variation of IPO hazard rates for therapeutics firms (interval width=1000 days, 95% confidence interval shown as dashed lines)

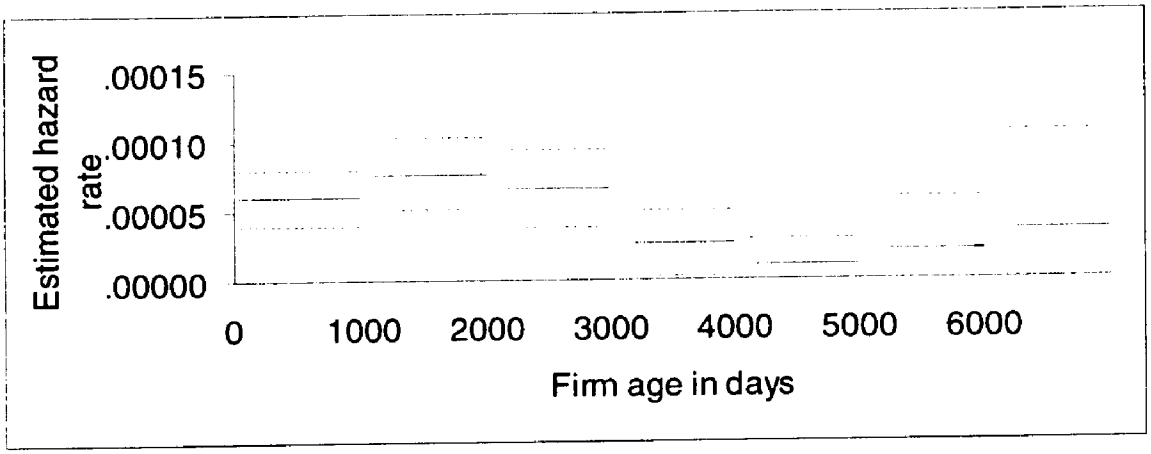

Figure 6-2: Life table estimates of variation of IPO hazard rates for non-therapeutics firms (interval width=1000 days, 95% confidence interval shown as dashed lines)

When I estimate piece-wise exponential models and models with log-quadratic specifications of aging, the results also support the continued use of a log-quadratic approximation of age dependence. Figure 6-3 presents a graph of the two models of age dependence of therapeutics firms reported in

Table 6-1. This picture differs from both the picture of the reaction of IPO rates to aging for the whole population (figure 5-14), and the picture of this reaction for non-therapeutics firms alone as estimated by the models in table 6-2 and represented in Figure 6-4.[72] The primary form of this difference is

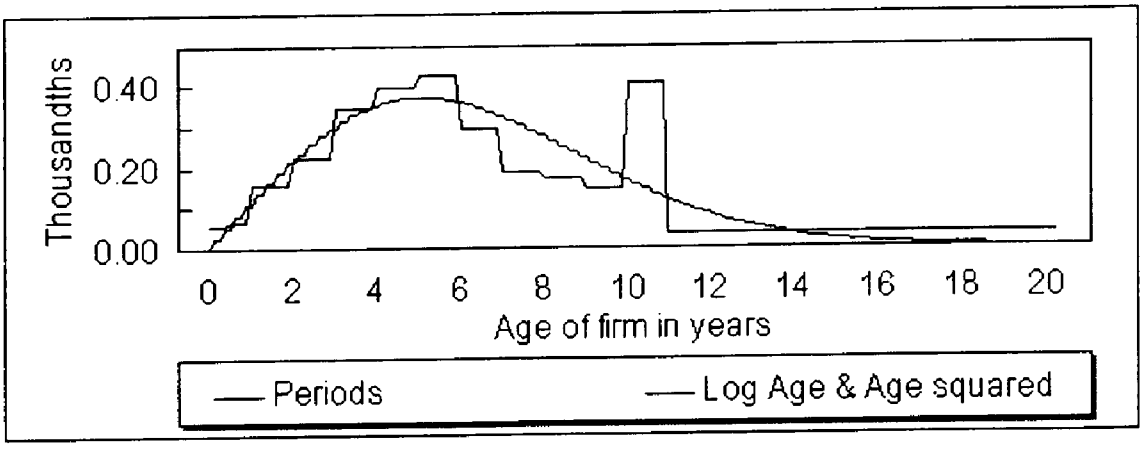

Figure 6-3: Effects of aging on IPO rates of therapeutics firms estimated via a piece-wise exponential model and a model with parametric assumptions

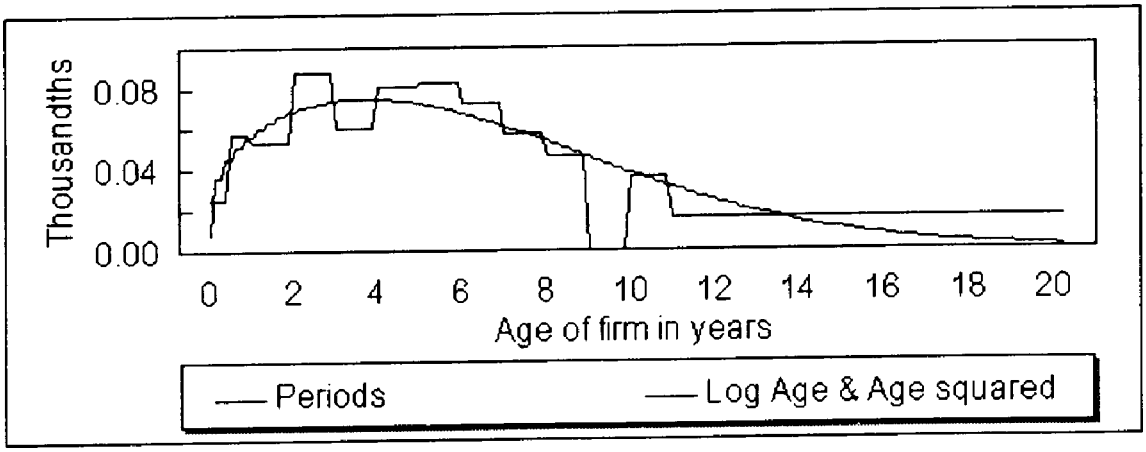

Figure 6-4: Effects of aging on IPO rates of non-therapeutics firms estimated via a piece-wise exponential model and a model with parametric assumptions

[72] As was noted in the commentary on figure 5-15, the apparent deviation of jagged curve associated with the model based on age classes is a function of a falling sample size (in this case 40 firms reach their ninth birthdays without IPOs, acquisitions, failures; and 31 firms continue past their tenth birthdays), and a declining number of events. Two therapeutics firms had IPOs when they were 9 years old and 4 when they were 10 years old. Two of the IPOs of ten-year-old firms were of firms within 38 days of their tenth birthdays.

Table 6-1: Age-dependence models of IPO rates for therapeutics firms

	Model 26		Model 27	
Log-likelihood	-671.56		-673.75	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-10.304 ****	1.000	-15.472 ****	1.504
Log(Age)			1.077 ****	.222
$(Age)^2/10,000$			-.002 ****	.0004
< 6 months	0.528	1.225		
6 months to 1 year	0.647	1.155		
1 to 2 years	1.541	1.035		
2 to 3 years	1.897 *	1.029		
3 to 4 years	2.338 **	1.029		
4 to 5 years	2.477 **	1.018		
5 to 6 years	2.542 **	1.029		
6 to 7 years	2.182 **	1.054		
7 to 8 years	1.729	1.118		
8 to 9 years	1.643	1.155		
9 to 10 years	1.498	1.225		
10 to 11 years	2.500 **	1.118		

* p < .1, ** p< .05, *** p< .01, **** p < .001

Table 6-2: Age-dependence models of IPO rates for non-therapeutics firms

	Model 28		Model 29	
Log-likelihood	-681.52		-687.13	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-11.026 ****	.577	-11.700 ****	1.168
Log(Age)			.327 *	.174
$(Age)^2/10,000$			-.0009 ***	.0003
< 6 months	0.446	.913		
6 months to 1 year	1.252 *	.707		
1 to 2 years	1.193 *	.651		
2 to 3 years	1.683 ***	.626		
3 to 4 years	1.324 *	.677		
4 to 5 years	1.602 **	.626		
5 to 6 years	1.625 **	.645		
6 to 7 years	1.504 **	.667		
7 to 8 years	1.275 *	.707		
8 to 9 years	1.042	.764		
9 to 10 years	-20.481	26,298		
10 to 11 years	.799	.913		

* p < .1, ** p< .05, *** p< .01, **** p < .001

that, at very early ages, the IPO rate of therapeutics firms is lower and rises less quickly than it does for other firms. This contrast may be attributable to the fact that a therapeutics firm can secure a better price for its equity if it first gets to the point where drugs are progressing through clinical trials, and that progressing to this stage cannot be rushed beyond a certain point. By contrast, diagnostics firms and other biotechnology firms may be able to produce credible signals of their prospects for future product success earlier in their existence. Non-therapeutics firms may also have a more opportunistic approach to financing, and some may actually be founded as vehicles for taking quick advantage of "windows of opportunity" in the IPO markets.[73]

While I do not present the results here, further investigation of age dependence in even finer separations of the population of biotechnology firms continue to support the generality of the pattern that, as firms age, IPO rates first rise and then begin a gradual decline. The exception to this general rule is provided by the category of firms that I was unable to categorize by target product market. In this case the IPO rate is low throughout their lifetimes. In this case, however, my very inability to identify the areas of activity of the firms concerned is partially a consequence of the fact that this particular sample of firms failed to go public. Consequently, the difficulties I encountered in categorization and low IPO rates are not entirely independent of one another.

The results of reanalyzing full population IPO rates using four density measures (private therapeutics, public therapeutics, private non-therapeutics and public non-therapeutics) are reported as model 31 in table 6-3.

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[73] The comments made about the hazard rate for 9-year-old, and 10-year-old firms made for the full sample (figure 5-15) and for therapeutics firms (figure 6-3) apply here as well. The sample size is dropping, the rarity of the event is increasing (only five IPOs of firms older than 9), and one of the IPOs occurs 37 days after the firm's tenth birthday.

Table 6-3: Model of IPO rates for full population based on inclusion of density measures of subpopulations of private and public therapeutic and non-therapeutic firms

	Model 30		Model 31	
Age, model maximum	5.5		5.5	
Log-likelihood	-1211.0		-1208.5	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-25.88 ****	2.01	-29.67 ****	3.20
Log(Age)	.96 ****	.145	.9725 ****	.145
$(Age)^2/10,000$	-.001 ****	.0002	-.0012 ****	.0002
NASDAQ	.010 ****	.002	.011 ****	.002
ΔNASDAQ	.004 *	.002	.005 *	.003
# of IPOs lagged 1 Qtr.	.068 ****	.017	.065 ****	.018
# of IPOs lagged 2 Qtrs.	.066 ****	.020	.074 ****	.020
Therapeutics	1.445 ****	.201	1.450 ****	.201
Diagnostics	.645 ***	.228	.646 ***	.228
Agricultural	.818 ***	.302	.815 ***	.302
Delaware born	1.310 ****	.155	1.321 ****	.155
Delaware reincorporation	1.746 ****	.215	1.743 ****	.216
Births last quarter	.046 **	.020	.025	.018
# of IPOs at birth	.043 ***	.014	.044 **	.020
Total private density	-.002	.002		
Total public density	-.070 ****	.010		
Non-therapeutics, private density			.007	.007
Non-therapeutics, public density			-.064 **	.025
Therapeutics, private density			-.026 **	.012
Therapeutics, public density			-.082 ****	.023
CPI	.096 ****	.025	.120 ****	.036
Prime rate	-.061	.043	.034	.066

* $p < .1$, ** $p < .05$, *** $p < .01$, **** $p < .001$

NOTE: Both models are based on 218 events (IPOs), and 24,924 sub-spells (data for 3 firms for one sub-spell were missing).

Qualitative results for all non-density variables are substantially the same as those obtained for model 13 of table 5-7 (which for ease of comparison is reproduced in table 6-3 as model 30). Even for the density measures, the general reaction is similar to those previously found, namely that the density of public firms depresses the ability of private firms to go public. Densities of public firms, both therapeutic and non-therapeutic, exert substantial competitive pressure on the ability of firms to go public. The addition of each additional therapeutics firm to the public population depressed the IPO rates of remaining firms by about 7.9 percent (on a net basis[74] this would be lower). The addition of each non-therapeutics firm depressed the ability of remaining firms to go public by about 6.2 percent. In the case of private densities, an increase in densities of private therapeutics firms also had a significant competitive impact. The coefficient for non-therapeutics firm density is non-significant and positive, perhaps suggesting that an increase of private non-therapeutics firms has a legitimating effect for rates of going public. Given the size of the associated standard error for this positive coefficient, however, no conclusions can really drawn. In summary, adding further discrimination to our measures of density doesn't materially alter the conclusions as long as models are run on the full population of biotechnology firms.

THERAPEUTICS FIRMS ALONE

The second set of models are those that were run using observations of therapeutics firms only. These models are reported in table 6-4. The first

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[74] When a therapeutics firm goes public it increases the public density by one but also decreases the private density by one. In this particular case this leads to a percentage change on the IPO rates of remaining firms of about [1-Exp(.026-.082)]*100 or 5.3 percent.

Table 6-4: Model of IPO rates for therapeutics firms alone using total density

	Model 32	
Log-likelihood	-597.7	
Age, model maximum	5.8	
Variables	Coef.	S.E.
Intercept	-27.84 ****	3.16
Log(Age)	1.240 ****	.241
$(Age)^2/10,000$	-.0014 ****	.0004
NASDAQ	.012 ****	.003
ΔNASDAQ	.007 **	.003
# of IPOs lagged 1 Qtr.	.081 ****	.024
# of IPOs lagged 2 Qtrs.	.069 ***	.026
Delaware born	1.034 ****	.210
Delaware reincorporation	1.264 ****	.311
Births last quarter	.022	.022
# of IPOs at birth	.021	.027
Total private density	.0003	.0023
Total public density	-.084 ****	.014
CPI	.106 ***	.035
Prime rate	-.023	.064

* p < .1, ** p< .05, *** p< .01, **** p < .001

NOTE: All models for the therapeutics sub-population are based on 121 events (IPOs), and 5983 sub-spells (data for one sub-spell for one firm missing).

of these models is basically comparable in structure to the full population model reported as model 30 in table 6-3. The differences for the model results using therapeutics data are, for the most part, minor. In model 32 of table 6-4, the IPO rate reaches a maximum at a slightly higher firm age, the reaction to stock markets and recent IPO activity is more intense (with comparable p-values), and the signal sent by incorporation choices is slightly less intense (although still highly significant) than was the case for the full population model. Slight contrasts exist in reactions to prior quarter births and number of IPOs immediately prior to the firm's own birth, with the coefficients in the therapeutics-only model being smaller and less significant. What is most interesting in this model is that the effect of total private density has virtually disappeared (and is even further from being significant) and the apparent intensity of the competition offered by public firms is higher and is still highly significant. Controls for the CPI level and prime rate differ slightly in the two models but retain the same signs.

The changes that occur when we replace total density measures by measures of subpopulation densities are quite striking. In models 33 and 34 of table 6-5, the replacement of density measures leaves most coefficients unaffected (exceptions are increased sensitivity to recent IPO counts and the reversal in sign of the coefficient of prime rate). What is eye-catching about these models is that own-densities (private therapeutics and public therapeutics) both appear to exert significant competitive pressures on the IPO rates of the remaining firms. The small change in log-likelihood (not sufficient to achieve significance even if only one variable were being added to the model) resulting from the addition of density measures for non-therapeutic firms in model 34 indicates that the rate at which therapeutics

Table 6-5: Models of IPO rates for therapeutics firms alone using subpopulation density measures

	Model 33		Model 34	
Log-likelihood	-595.6		-594.6	
Age, model maximum	5.9		5.8	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-39.32 ****	5.48	-37.74 ****	6.19
Log(Age)	1.223 ****	.236	1.232 ****	.238
$(Age)^2/10,000$	-.0013 ****	.0004	-.0014 ****	.0004
NASDAQ	.015 ****	.003	.015 ****	.003
ΔNASDAQ	.007 **	.003	.006 *	.003
# of IPOs lagged 1 Qtr.	.095 ****	.023	.121 ***	.041
# of IPOs lagged 2 Qtrs.	.101 ****	.027	.102 ****	.026
Delaware born	1.057 ****	.211	1.050 ****	.211
Delaware reincorporation	1.238 ****	.311	1.255 ****	.311
Births last quarter	.025	.023	.073	.053
# of IPOs at birth	.019	.027	.019	.027
Therapeutics, private density	-.036 ****	.009	-.031 *	.019
Therapeutics, public density	-.165 ****	.031	-.175 ****	.037
Non-therapeutics, private density			-.004	.009
Non-therapeutics, public density			.0004	.037
CPI	.216 ****	.057	.218 ****	.064
Prime rate	.103 *	.054	.037	.094

* $p < .1$, ** $p < .05$, *** $p < .01$, **** $p < .001$

NOTE: Both models are based on 121 events (IPOs), and 5983 sub-spells (data for one sub-spell for one firm missing).

firms go public is not significantly affected by the size of the other subpopulations of biotechnology firms. In sum, therapeutics firms seem to experience their primary competition for funds (at least within the biotechnology sector) from the addition of other firms to the therapeutics subpopulations.[75]

NON-THERAPEUTICS FIRMS

The last set of models presented are those models run using just data on non-therapeutics firms. These models are presented in tables 6-6 and 6-7. As with therapeutics firms, the model run using total-density measures (model 34) generates results basically similar to those that obtained for the full set of firms. Not surprisingly, the changes in the model coefficients are mostly opposite to those that occurred in the models of therapeutics firms. IPO rates for non-therapeutic firms are somewhat less affected by the stock market and by recent levels of IPO activity. The signal generated by incorporation choices is stronger than it is for the full population or for therapeutics firms alone. For the population of non-therapeutics firms a firm originally incorporated in Delaware goes public at a rate more than five times higher than for corporations incorporated in their home states. The impact of prior period births and the number of IPOs at the time of the firm's birth (both at least marginally significant in all models in tables 6-6 and 6-7) also accelerate the IPO rate more than is the case for the full population or for therapeutics firms alone. As with the other models, increases in the population of public

[75] Once again because the models with sub-population density measures are not nested in the models with full population density measures, a simple likelihood ratio based on comparison of the log-likelihoods of the models cannot be invoked to support the rejection of one in favor of the other.

Table 6-6: Model of IPO rates for non-therapeutics firms alone using total density measure

	Model 35	
Log-likelihood	-597.9	
Age, model maximum	5.2	
Variables	Coef.	S.E.
Intercept	-23.16 ****	2.63
Log(Age)	.712 ****	.180
$(Age)^2/10,000$	-.0010 ***	.0003
NASDAQ	.010 ***	.003
ΔNASDAQ	-.001	.004
# of IPOs lagged 1 Qtr.	.057 **	.026
# of IPOs lagged 2 Qtrs.	.055 *	.031
Diagnostics	.559 **	.230
Agriculture	.731 **	.310
Delaware born	1.610 ****	.224
Delaware reincorporation	2.252 ****	.301
Births last quarter	.073 ****	.021
# of IPOs at birth	.073 **	.029
Total private density	-.004	.003
Total public density	-.061 ****	.013
CPI	.093 ***	.035
Prime rate	-.114 *	.062

* p < .1, ** p< .05, *** p< .01, **** p < .001

NOTE: All models of the non-therapeutics sub-population are based on 97 events (IPOs), and 18,842 sub-spells (data for one sub-spell missing for two firms).

Table 6-7: Models of IPO rates for non-therapeutics firms alone using subpopulation density measures

	Model 36		Model 37	
Log-likelihood	-597.1		-593.8	
Age, model maximum	5.1		5.2	
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-19.28	2.03 ****	-22.44	3.32 ****
Log(Age)	.674	.178 ****	.697	.181 ****
$(Age)^2/10,000$	-.0010	.0003 ***	-.0010	.0003 ***
NASDAQ	.010	.003 ***	.010	.003 ***
ΔNASDAQ	-.003	.004	-.002	.004
# of IPOs lagged 1 Qtr.	.047	.027 *	.034	.029
# of IPOs lagged 2 Qtrs.	.047	.032	.051	.033
Diagnostics	.558	.230 **	.556	.230 **
Agriculture	.743	.311 **	.720	.310 **
Delaware born	1.600	.224 ****	1.614	.224 ****
Delaware reincorporation	2.256	.301 ****	2.248	.300 ****
Births last quarter	.075	.021 ****	.045	.025 *
# of IPOs at birth	.076	.029 ***	.070	.029 **
Non-therapeutics, private density	.009	.005 *	.023	.010 **
Non-therapeutics, public density	-.140	.028 ****	-.145	.043 ****
Therapeutics, private density			-.037	.015 **
Therapeutics, public density			.006	.034
CPI	.028	.030	.039	.045
Prime rate	-.078	.065	.049	.090

* $p < .1$, ** $p < .05$, *** $p < .01$, **** $p < .001$

NOTE: Both models are based on 97 events (IPOs), and 18,842 sub-spells (data for one sub-spell missing for two firms).

firms decelerates (significant at .001) the IPO rates. In this instance, private density is not significant but does have a positive coefficient indicating the possibility that higher numbers of private firms is actually a good sign for non-therapeutics firms going public.

Two very surprising results appear when total densities are replaced with subpopulation densities. The first of these results (that obtains in both model 36 and model 37 and that is at least marginally significant in both cases) is that density of private non-therapeutics firms has a mildly positive impact on IPO rates. This is contrasted with very substantial deceleration (about 12 percent for each additional firm) in IPO rates attached to increases in the population of public non-therapeutics firms. The second of these results is that, while private densities of therapeutics firms appear to inhibit the ability of non-therapeutics firms to go public, there appears to be very little impact associated with the addition of further public therapeutics firms to the population.

There is a danger of over-interpreting these findings but certain broad conclusions are probably safe to draw. The first conclusion is that, for therapeutics firms, the only populations that are relevant to the decision to go public are the populations of other therapeutics firms.[76] In the case of therapeutics firms, growth in the populations of therapeutics firms simply increases competition. The second conclusion is that non-therapeutics firms are less reactive to movements in the IPO markets (and financial markets at large) and possess a different reference group of which firms constitute

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[76] Because models with full-population densities do not nest, models with measures of sub-population densities this conclusion cannot be evaluated using a simple likelihood ratio test based on the difference in log-likelihoods of the two models..

competition in the race to go public. Non-therapeutics firms apparent lack of responsiveness to market conditions may simply be a consequence of their being crowded out of the most desirable periods of the IPO market by more favored therapeutics firms. Primary issues affecting the financing capabilities of non-therapeutics firms appear to be how many already-public non-therapeutics firms there are, and how many therapeutics firms there are that are waiting to go public. To these two relatively non-controversial conclusions, we might add the slightly more tenuous assertion that increases in the number of other private non-therapeutics firms actually increases the rate at which other firms of the same kind go public.

INTERPRETATION OF FINDINGS

Explanation of these findings is more fraught with danger than is the exercise of simply reporting the empirical regularities that appear in the data. A tentative explanation that I will offer for these results is that a financing pecking order exists among the biotechnology firms. All other things being equal, potential investors in biotechnology might have a first preference for investing in therapeutics firms that are already publicly traded. This investment could either be take the form of buying shares in a new issue of stock (which adds to the stock already available for public trading) or simply buying shares from the existing public float. Two factors would favor this kind of investment. First, a price history for the stock would be available. Second, more extensive information on the company's research progress would likely be available, as would a history of the company's ability to husband its resources and to deal with the pressures of being publicly traded.

Investors might then have a second, slightly lower, preference for investing in therapeutics firm IPOs. This preference for therapeutics firm stocks might be partly rooted in a general belief that it is therapeutics firms that have the most potential to realize "blockbuster" success. In a portfolio of biotechnology stocks the prospect of a single big payoff stock might compensate the investor in part for the high risk of any individual stock.

Below therapeutics IPOs, the third preference of biotechnology investors might be to invest in public non-therapeutics firms. Only in the last instance might investors choose to support the IPO of a non-therapeutics firm. Because many non-therapeutics firms are not automatically excluded from the possibility of making a profit in their early years, the willingness of owners to sell shares in the company is not entirely without signalling value. The desire of a non-therapeutics firm to make an initial public offering is likely to offer more negative information about the firm's prospects than it would for a therapeutics firm.

All of the preceding discussion presumes, however, that there is a finite pool of new money available for investment in biotechnology at any given time. Being last in the line for financing might also explain that the IPO rates of non-therapeutics firms are less determined by the number of recent IPOs and the movement of the stock market. Perhaps non-therapeutics firms cannot afford to be as selective about the time they go public as therapeutics firms can be. Indeed, if one refers back to figure 5-5, non-therapeutics firms appear more likely to go public in the periods between IPO booms than their therapeutics cousins.

The final piece of speculation is attached to explaining why growth in the population of private non-therapeutics firms enhanced the ability of non-

therapeutics firms to mount an IPO. Of the biotechnology firms, non-therapeutics firms are probably able to sell their products and services at an earlier age than are therapeutics firms. No therapeutics biotechnology firm has ever introduced a significant human therapeutics product prior to going public. Non-therapeutics firms on the other hand have usually still been unprofitable at the time of their IPO, but, all the same, have often already introduced at least one core product.

If growth in the population of non-therapeutics firms is a broad measure of the carrying capacity and profitability (or anticipated profitability) of the underlying markets, then a larger population of these firms can be taken to be a positive signal that the individual firm has the potential to generate profits. This same general argument can also be used to explain why prior period birth rates are associated with higher rates of going public. In a nutshell, firms are created when the potential for profits is seen to exist, the potential for profits is regarded positively by IPO investors, so, in high-birth periods non-therapeutics firms are more likely to be able to go public. The fates of therapeutics firms are more closely tied to their ability to compete within the financial markets early in their lives. The fates of non-therapeutics firms are also dependent on financing, but, even early in their corporate histories, the fortunes of these firms are more closely linked to the general economy and to the product markets in which they intend to compete.

While this concludes the investigation and discussion of what factors have influenced the IPO rates of American biotechnology firms, the results strongly suggest that freely borrowing from a variety of theoretical perspectives has contributed to developing models with high explanatory value. The results obtained support a wider application of the kind of thinking

that inspires the organizational literature on population ecology. The results are also broadly consistent with what the financial literature would lead us to expect with regard to comparisons of the IPO rates of different types of companies. The marriage of population ecology with insights drawn from other disciplines can be a happy one, and one which illustrates the broad strategic implications of population level thinking about the processes of competition, legitimation, and symbiosis.

CHAPTER 7. SUMMARY AND CONCLUSIONS

The primary findings of this dissertation are that the financing behavior of biotechnology firms during the study period exhibited a high degree of uniformity and consistency. Further, the degree to which firm failures and acquisitions could be modelled was considerably lower than it was for IPOs. If we were to associate going public with happiness and success; and failure or acquisition (at least many acquisitions) with unhappiness, we might be tempted to attempt to paraphase Tolstoy's claim that "happy families are all alike, every unhappy family is unhappy in its own way." In fact, though, what appears to be the case is that despite the considerable diversity in the passage to going public, event history methods allow for the identification of nature of this diversity as well as its commonalities.

Talking first of the way in which all biotechnology firms appeared to be alike, the primary source of competition for the right to go public appeared to emanate from firms that were already public, not from other private firms that were awaiting the chance to do so. The sole exception to this general rule was that private therapeutics firms appeared to have precedence over non-therapeutics firms in the race to go public. The second general rule that appeared to operate was that the rate at which biotechnology firms went public was non-monotonic with age. At early ages firms exhibit a low IPO rate, the rate achieves a maximum at around five years old and then begins to drop. Third, all firms were more likely to go public when the stock market was high, when many IPOs were occurring (not universally significant) and when biotechnology firms were being born (not always significant).

The models also support the idea that significant differences exist among firms. Firms formed in periods of high IPO activity are more prone to going public, firms originally incorporated in Delaware have a higher IPO rate throughout their lifetimes, and distinct sub-populations of biotechnology firms are defined by target product market. It also was apparent that the densities of different sub-populations had different impacts on the IPO rates of different groups of firms.

In sum, regarding the IPO as a process which takes place in the context of a reference population proved to be a fruitful one. The behavior of firms and of investors is contingent on the activities and demands of a host of organizations, which, on the surface, might appear to operate independently of one another. In this population, competition tended to be the dominant relationship among organizations.

Another striking aspect of the findings of this study is their robustness to both differing estimation techniques and to changes in the data analyzed. When time-varying covariates required splitting the time axis into sub-spells no effective differences were observed between models estimated with piece-wise exponential models versus models estimated using Cox's partial likelihood models. When partial likelihood methods were employed the results proved to be insensitive to what methods were used to deal with tied durations. In terms of sensitivity to changes in the data the results were similarly robust. As part of the process of checking the sensitivity of results to how age-dependence was modelled, I estimated using only firms younger than nine years old. These results (details of which were not included in this dissertation) proved to be very similar to the results obtained for the full dataset. Even more telling is the degree to which the results of study proved

to be robust against perturbations in the sample data as evaluated by the bootstrap analysis reported in the appendix.

Some of the most intriguing suggestions of this study relate to questions that it does not answer. Because I didn't have the data, and because of certain definitional considerations, I did not distinguish venture-financed firms from those without venture financing. It would be interesting to test the degree to which firms incorporated in Delaware and formed in times of high IPO activity were also firms that founded with the benefit of venture capital. Since the rate of venture capital financing is almost certainly much higher among therapeutics firms and there might consequently be little variation among these firms in terms of certain founding characteristics, this could potentially help explain much of the differential predictive value of covariates describing founding conditions with regard to the therapeutics and non-therapeutics populations.

The second major omission of the study was the role alliances and other connections among firms play in the transfer of resources and the alteration of firm capabilities. Highly connected firms might both display a greater abililty to go public due to enhanced reputation or legitimacy and a lesser need to do so due to enhanced access to external financing. This kind of analysis might also prove particularly productive in modelling the determinants of both firm failures and acquisitions.

A different kind of question that arises from this study is to what extent the valuation of IPO firms is subject to modelling and prediction. Because of the diversity of the activities of biotechnology firms and because of the difficulties of predicting the success or failure of research programs one might expect the valuation of firms to be extremely idiosyncratic. In preliminary

investigations not reported here, however, I find that the valuation of biotechnology IPOs is far more regular and predictable than one might expect.

The biotechnology industry presents considerable opportunities for extending our understanding of how social and economic relations among firms and institutions influence the development of both populations of firm and the form of the individual firms from which the populations are formed. Consideration of the public/private ownership dichotomy within this population is critical to understanding the dynamics of this population. On the basis of the results of this study I would also argue that counts of IPOs and the state of the stock market must also be included in future studies that purport to model dynamic processes within the biotechnology industry.

APPENDIX: ASSESSING MODEL SENSITIVITY BY BOOTSTRAPPING

In all models reported in the body of this dissertation, the significance levels of estimated coefficients have been evaluated using the assumption of asymptotic normality. The variances employed in assessing these models have also based on the assumption that employment of the Cramer-Rao lower bound is justified. This practice is in keeping with that employed in most previous studies in the organization literature on population ecology and indeed is the default practice in most social science studies that employ survival analysis. It is well recognized, however, that employing asymptotic variance estimates is not justified when the sample size is too small. Likewise, the more the underlying structure of the data depart from assumptions of the model being employed the less appropriate automatic invocation of large sample properties and using variances based on the Cramer-Rao lower bound becomes. Unfortunately, strict guidelines for what constitutes "large enough" samples are not readily available. The problem of justifying the use of asymptotic variances is even more pronounced in studies where the properties of the data being employed are relatively unstudied.

MOTIVATION FOR USING BOOTSTRAP ANALYSIS

In this study many of the individual properties and the joint properties of the variables employed are unknown. In particular I employ lagged counts of the number of IPOs when it is known that these lags are highly correlated. Other potential problems include high correlations among variables such as the density measures of related populations, and measures of economic variables such as those of stock market, CPI and interest rate levels. In any

regression model identifying problems engendered by outliers, high-influence observations and related problems of unobserved heterogeneity is an important step in data analysis. Unfortunately, while the spell-splitting methodology outlined in chapter 3 is a valuable tool, few diagnostic and data visualization techniques have been specifically designed for use in this context.

Despite the observations made above, certain features of the models estimated in previous chapters give us confidence in the robustness of the results obtained. Firstly, the fact that over a variety of model specifications both the quantitative and qualitative interpretations of the coefficients are stable provides some insulation from worries over the impact model specification has on the conclusions being drawn. Secondly, the fact that the virtually no differences in results are observed when employing Cox's proportional hazards model and those obtained using an exponential model (or other parametric models for that matter) provides reassurance that the study results aren't sensitive to the specific assumptions behind the estimation procedures employed.[77] What remains to be determined, then, is the degree to which these results are sensitive to variation in the data itself. In order to address this question and the questions raised above as to the validity of using asymptotic estimates of variances I employed a data resampling technique referred to as bootstrapping.

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[77] Although I don't report them here, the overall qualitative results using SAS PROC PROBIT and normal, logistic, and Gompertz distributions are also very close to those obtained using survival analysis.

BOOTSTRAP METHODS AND THEIR APPLICATION

In a discussion of bootstrap methods Robert Stine describes the rationale behind the bootstrap as follows:

> Just as maximum likelihood refers to an estimation procedure rather than to any specific estimator, bootstrapping is a methodology for *evaluating* statistics based on an appealing paradigm. This paradigm arises from an analogy in which the observed data assume the role of an underlying population. As a result, bootstrap variances, distributions, and confidence intervals are obtained by drawing samples from the sample. (Stine 1989, p. 243)

In the context of regression models, the implementation of the bootstrap consists of random sampling with replacement from the original data where the resultant sample is the same size as the original dataset. In the usual case encountered in the economics and sociology where the regressors are random rather than fixed,[78] the generation of the dataset used in each stage in the bootstrap is straightforward. With random regressors and an original dataset with N observations, the dataset used in each iteration of the bootstrap is generated by taking N random samples with replacement from the observations. The dataset generated from this sampling procedure is then used to estimate the model of interest and the values of the vector of coefficients is recorded. If we take B to be the size of the bootstrap sample, this process of dataset generation by sampling with replacement and recording of the values of the vector of coefficient estimates is repeated B times. At the end of B iterations of this procedure, we have a matrix of coefficient estimates, where the columns represent B separate estimates of

[78] Stine provides a good discussion of bootstrapping techniques in the cases of both random and fixed regressors.

the true parameter value of a given variable. The values within each column are then averaged, and the variance of the values of are calculated using (B-1) degrees of freedom. The resultant means of the coefficient values together with their variances are the bootstrap estimators of the parameter values. While the mean and variance of the bootstrap can be compared directly to the estimates made using distributional assumptions (in this case calculated using maximum likelihood methods), calculation of bootstrap significance levels and confidence intervals themselves can involve simulation (Stine pp. 352-354; Hall 1986a, 1986b). Here, however, I will confine the discussion to a single model, and I will use the bootstrap as a general test of the robustness of the regressions. Here I attempt to assess model robustness by first comparing bootstrap means and variances with those of the estimates based on the observed data. After having completed this comparison I then provide the basis for a visual comparison of the empirical distribution of the bootstrap coefficients and the theoretical distribution of the coefficients based on the assumption of asymptotic normality and attainment of the Cramer-Rao lower bound.

In the case we are dealing with only one modification of the procedure outlined above is required. All the models we are interested in have been estimated by breaking the history of each firm into an observation for each calendar quarter. If we treated the quarterly sub-spell as the observation to be sampled we would be constructing a bootstrap sample that has no analogue in reality. If we use Stine's analogy of regarding the observed data as the underlying population it is clear that the unit to be randomly sampled is the full life history of an individual firm. This sampling scheme leads to creation of bootstrap samples that vary in terms of the number of sub-spells

but is constant in terms of the number of firms. As is always the case with the bootstrap, the norm is for some firms to be sampled more than once and for other firms not to appear in the bootstrap sample at all.

NUMERICAL RESULTS OF THE BOOTSTRAPPING PROCEDURE

I use model 13, one of the primary models of chapter 5 and first reported as part of Table 5-7, as the basis for the bootstrapping procedure. Model 38 in Table 7-1 reproduces these estimates for ease of comparison. Model 39 in Table 7-1 presents the means and standard errors of the bootstrap sample of coefficients. In keeping with common practice, estimates are based on drawing 500 bootstrap data samples and generating 500 realizations of the coefficient vectors. All bootstrap data samples were of 844 firms. Although I present the mean of the log-likelihoods of the models estimated during the bootstrap process, these are not truly comparable since they are based upon a varying number of quarterly sub-spells.

With the possible exception of the bootstrap standard error for ΔNASDAQ, these are results are notable primarily for the degree to which bootstrap estimates conform to those calculated for the original model. At first glance, then the model appears to be relatively robust against perturbations in the sample data.

VISUAL COMPARISON OF THEORETICAL DISTRIBUTIONS AND BOOTSTRAP RESULTS

The second stage in the assessment of the robustness of model 38 (model 13) is based on a visual comparison of plots of the distributions of the

Table A-1: Comparison of model values based on assumption of asymptotic normality of coefficients and values based on bootstrapping original model

	Model 38		Model 39	
Log-likelihood	-1211.00		-1205.20	64.60
Variables	Coef.	S.E.	Coef.	S.E.
Intercept	-25.88	.96	-26.38	1.88
Log(Age)	.963	.145	.999	.162
$(Age)^2/10,000$	-.0012	.0002	-.0012	.0003
Private firm density	-.002	.002	-.002	.002
Public firm density	-.070	.010	-.071	.009
NASDAQ	.010	.002	.010	.002
ΔNASDAQ	.004	.002	.004	.003
# IPOs lagged 1 Qtr.	.068	.017	.069	.019
# of IPOs lagged 2 Qtrs.	.066	.020	.065	.021
IPOs at birth	.046	.020	.047	.022
Therapeutics	1.445	.201	1.474	.215
Diagnostics	.645	.228	.660	.236
Agriculture	.818	.302	.822	.294
Delaware born	1.310	.155	1.310	.161
Delaware reincorporation	1.746	.215	1.734	.189
Births last Qtr.	.043	.015	.044	.015
CPI	.097	.025	.099	.023
Prime rate	-.061	.044	-.062	.046

coefficients estimated during the bootstrap process and the distribution of the coefficient estimate based on the assumption of normality and the attainment of the Cramer-Rao lower bound. The distributions pictured in figures 7-1 to 7-18 are centered around the coefficient estimates of model 38, and the bins each represent a band with a width of .5 standard normal deviations. The horizontal axes are all centered around the coefficient estimated in model 38 and the vertical axes are relative frequencies (observed or theoretical frequencies within the bin range, divided by 500). Thus each bar represents the percentage of the bootstrap coefficients that fell within that range of values and each diamond represents the expected frequency given the assumption of normality and use of the asymptotic variance. Although all coefficient value ranges are presented in their raw form, the 15 bins represent the following ranges expressed in terms of standard normal deviates:

$(-\infty, -3.25)$, $(-3.25, -2.75)$, $(-2.75, -2.25)$, $(-2.25, -1.75)$,
$(-1.75, -1.25)$, $(-1.25, -.75)$, $(-.75, -.25)$, $(-.25, .25)$, $(.25, .75)$,
$(.75, 1.25)$, $(1.25, 1.75)$, $(1.75, 2.25)$, $(2.25, 2.75)$, $(2.75, 3.25)$
and $(3.25, \infty)$.

While visual inspection of the pictured distributions hardly constitutes a formal verification of the assumptions on which the model is based, at the very least, it does appear that the bootstrap distributions and those based on the assumption of normality and asymptotic variances are very near to one another. Based on the results in Table 7-1 and the inspection of the pictured distributions, I consider the use of the significance levels employed in models reported in previous chapters to be reasonable. While these comparisons are only conducted for one model, given the similarity among model specifications, and given that these models were all estimated using the same

data, employing the asymptotic standard errors in assessing significance in other reported models is also probably justifiable.

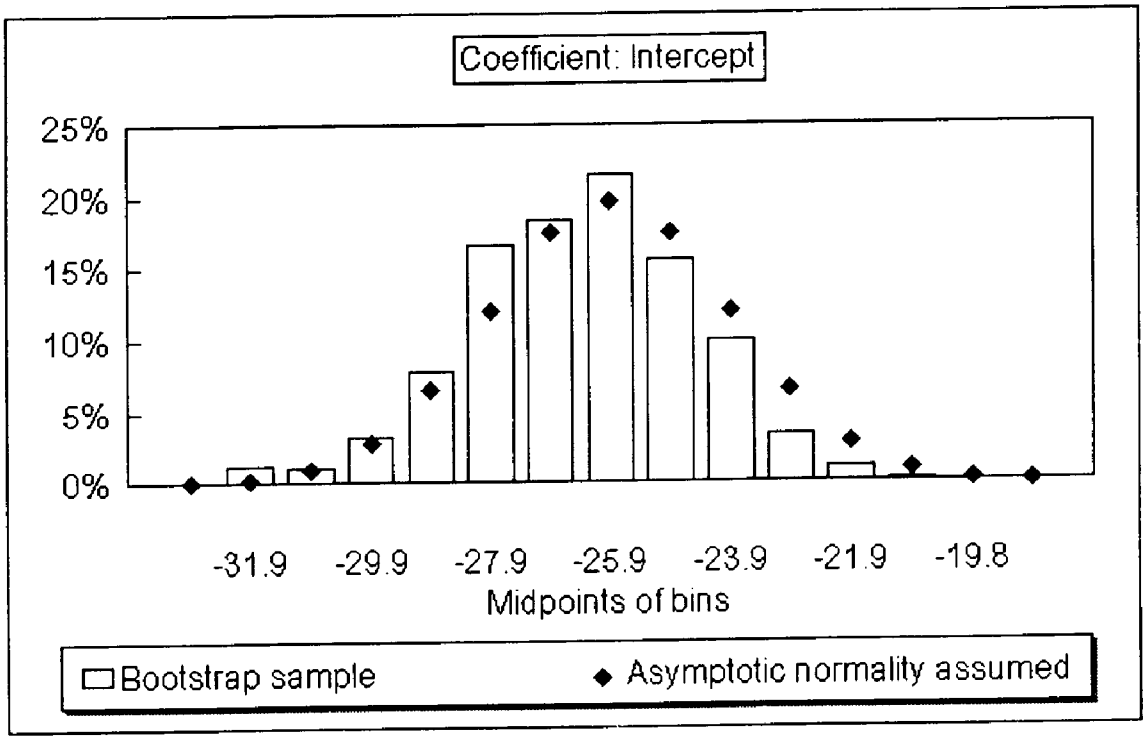

Figure A-1: Comparison of distribution of the estimate of the intercept based on asymptotic variance and the distribution of the bootstrap sample

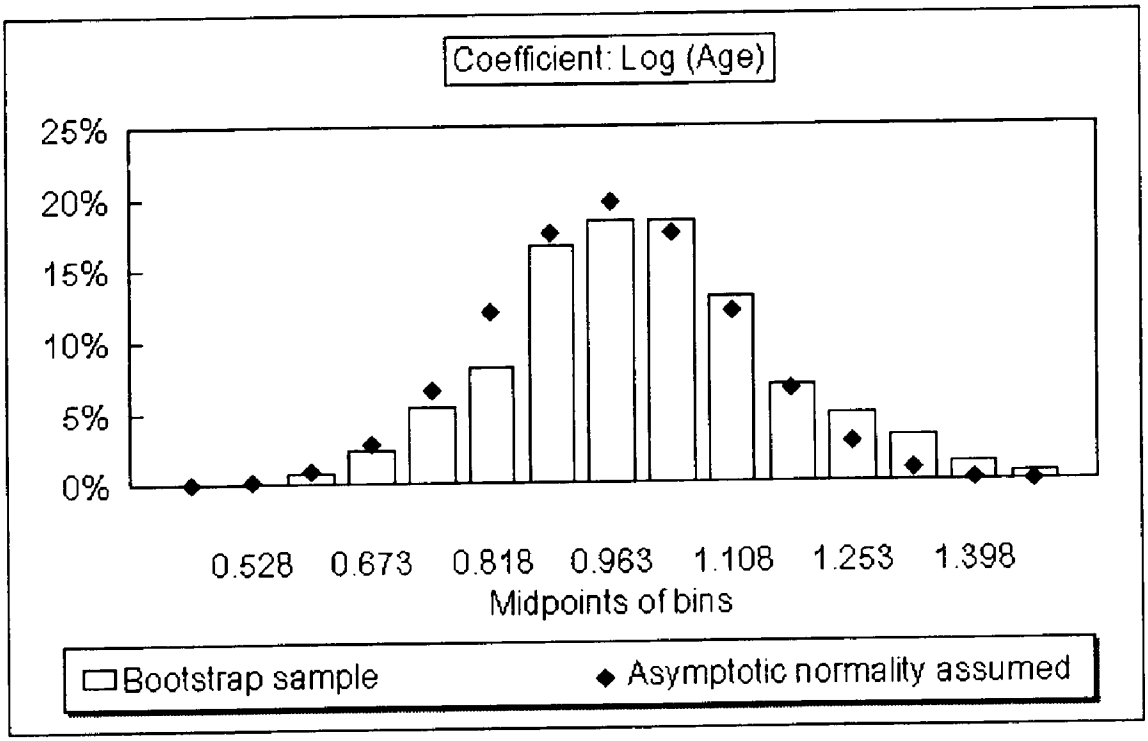

Figure A-2: Distribution of Log(Age)

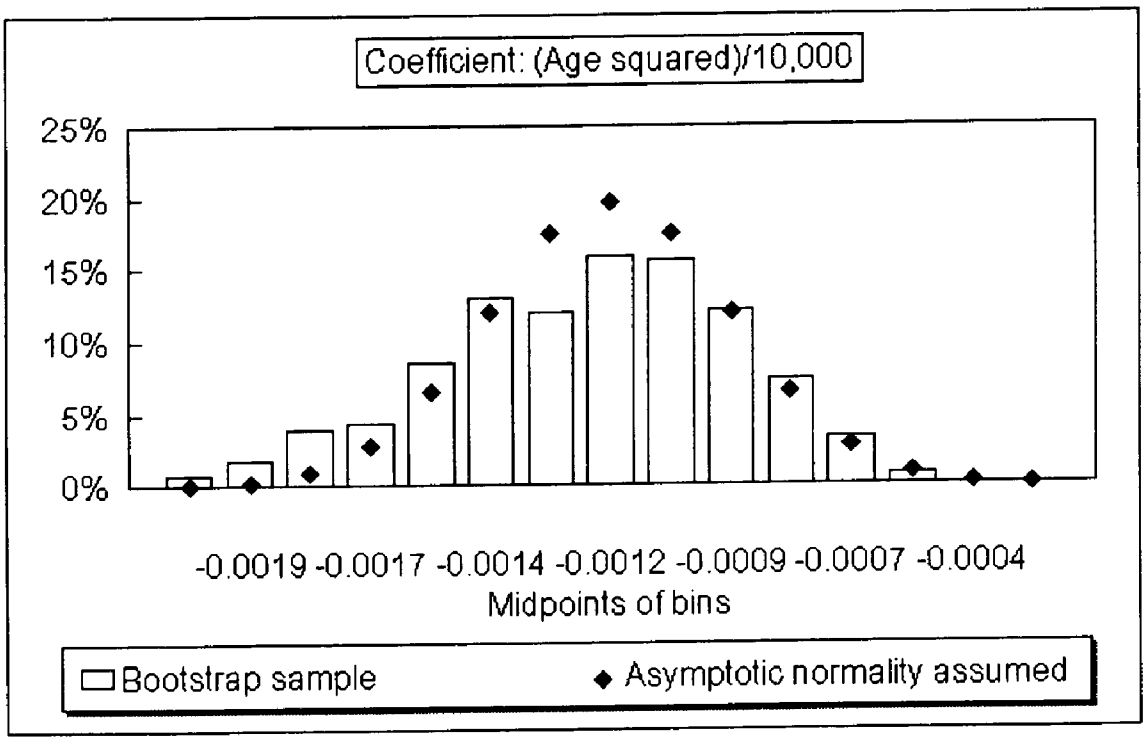

Figure A-3: Distribution of (Age squared)/10,000

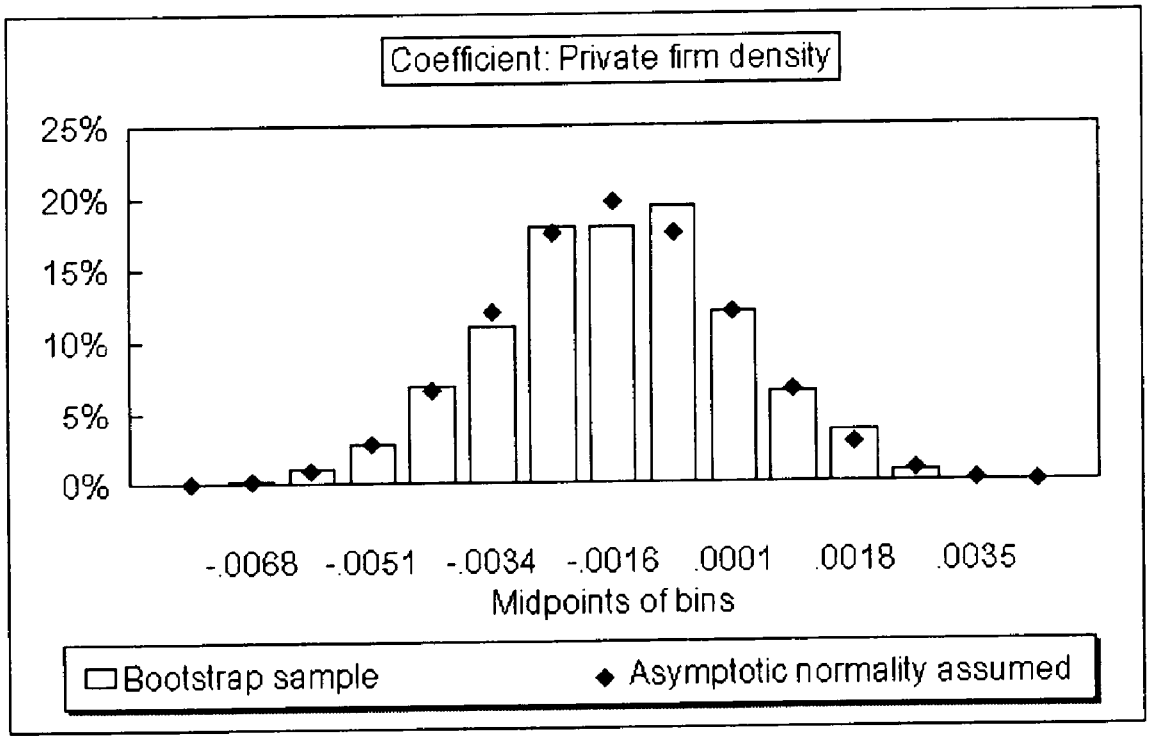

Figure A-4: Distribution of private firm density

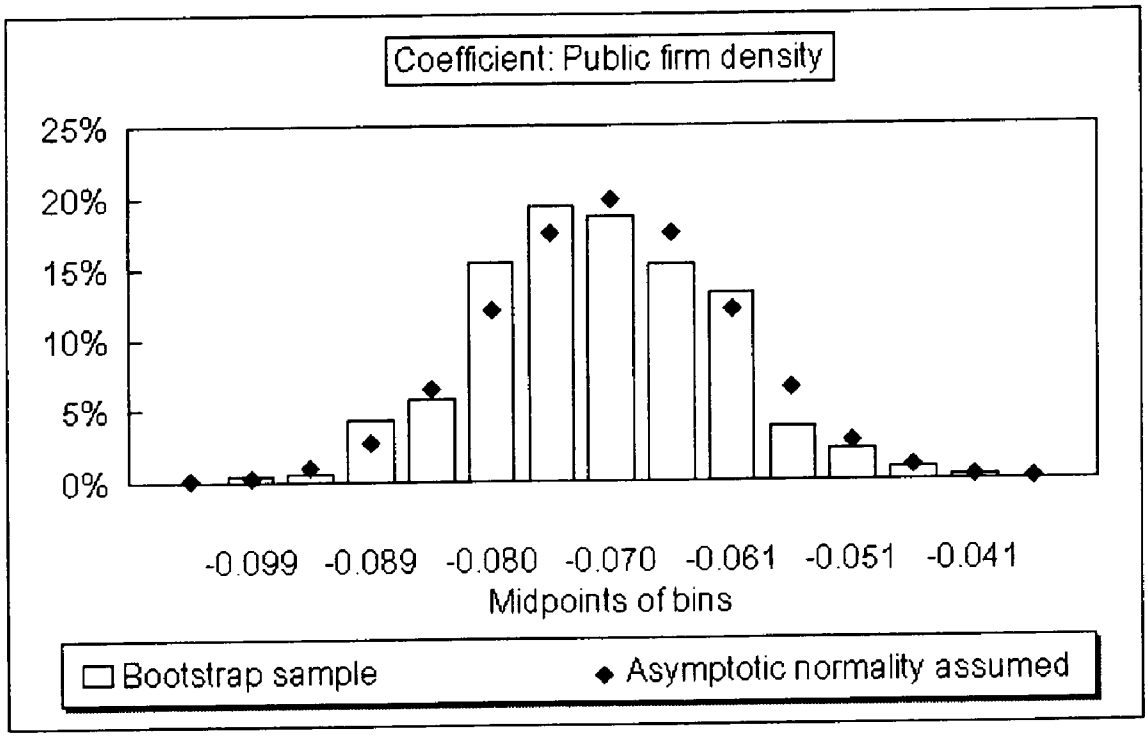

Figure A-5: Distribution of coefficients of public firm density

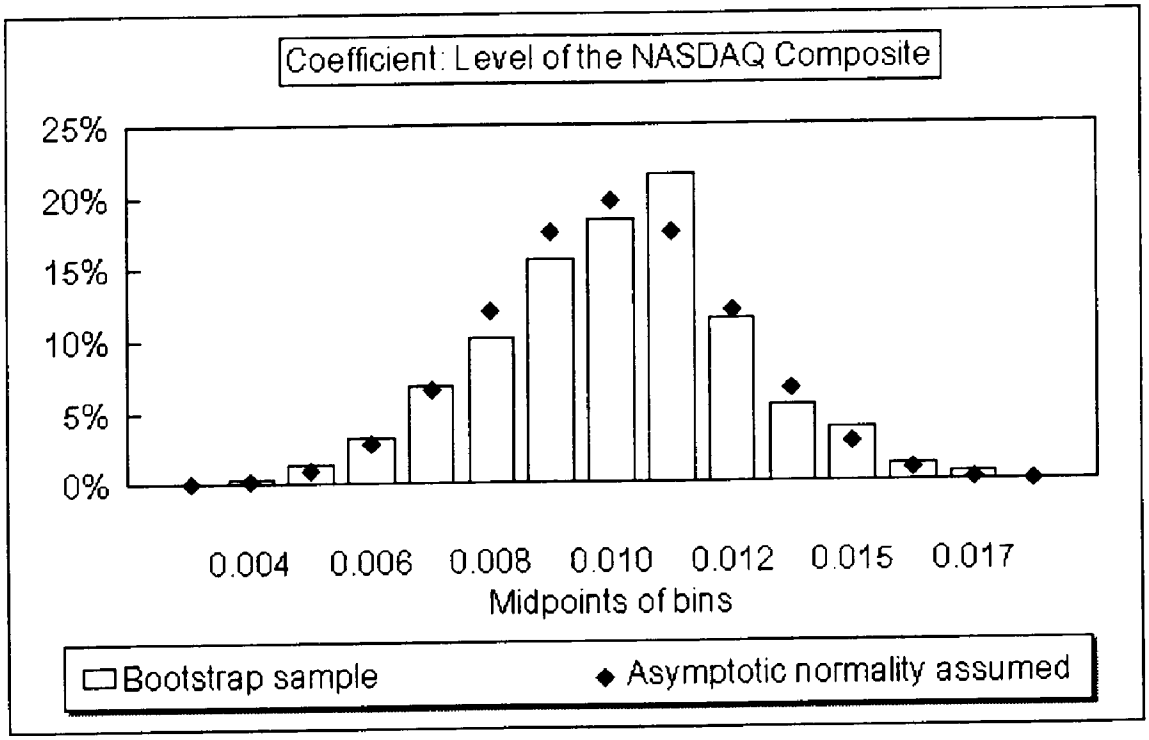

Figure A-6: Distribution of coefficients of the level of the NASDAQ

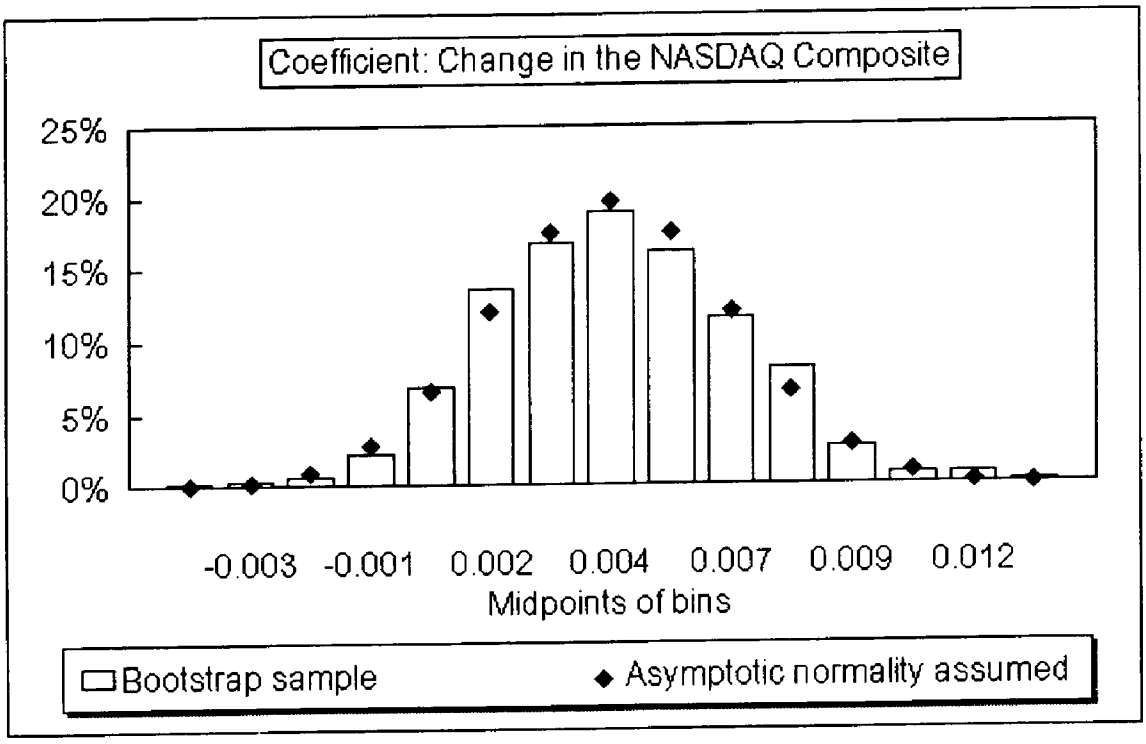

Figure A-7: Distribution of coefficients of the level of the NASDAQ

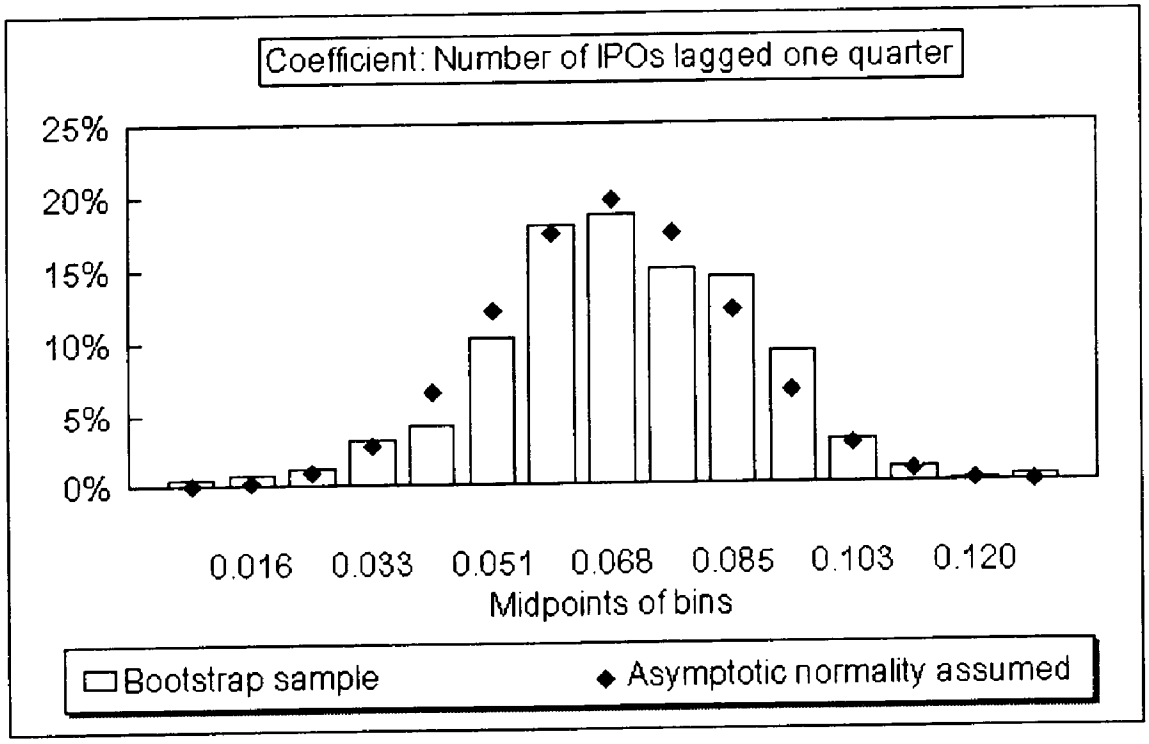

Figure A-8: Distribution of coefficients of IPOs lagged one quarter

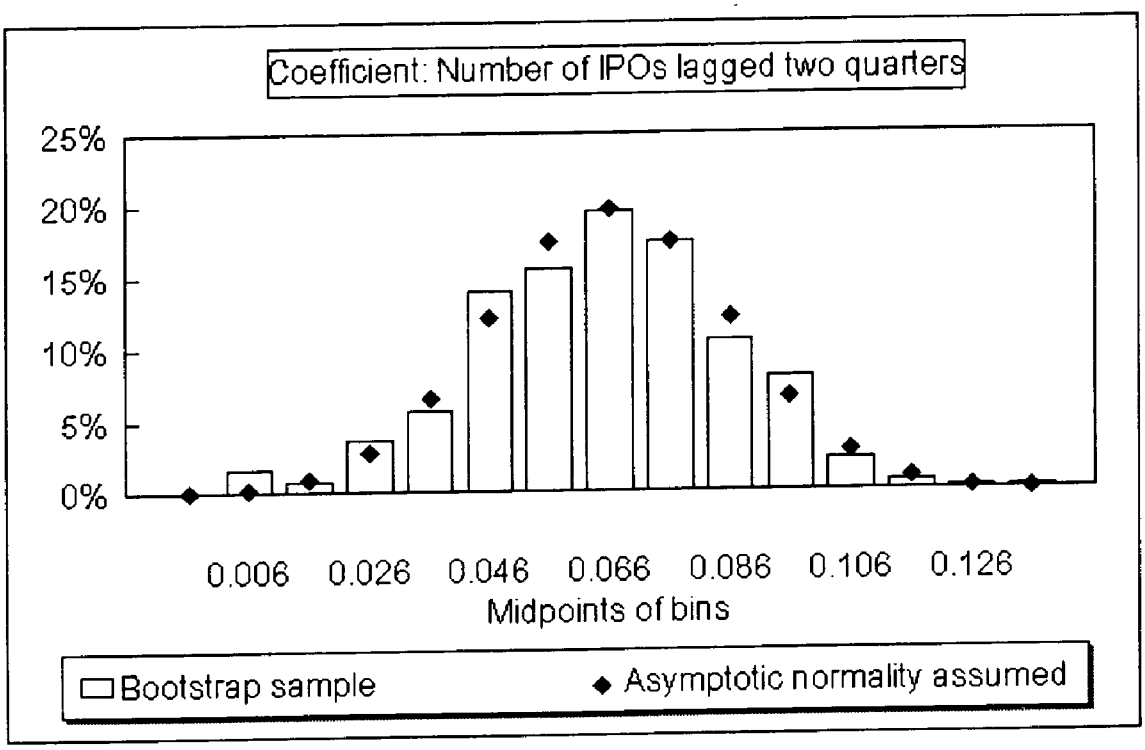

Figure A-9: Distribution of coefficients of IPOs lagged two quarters

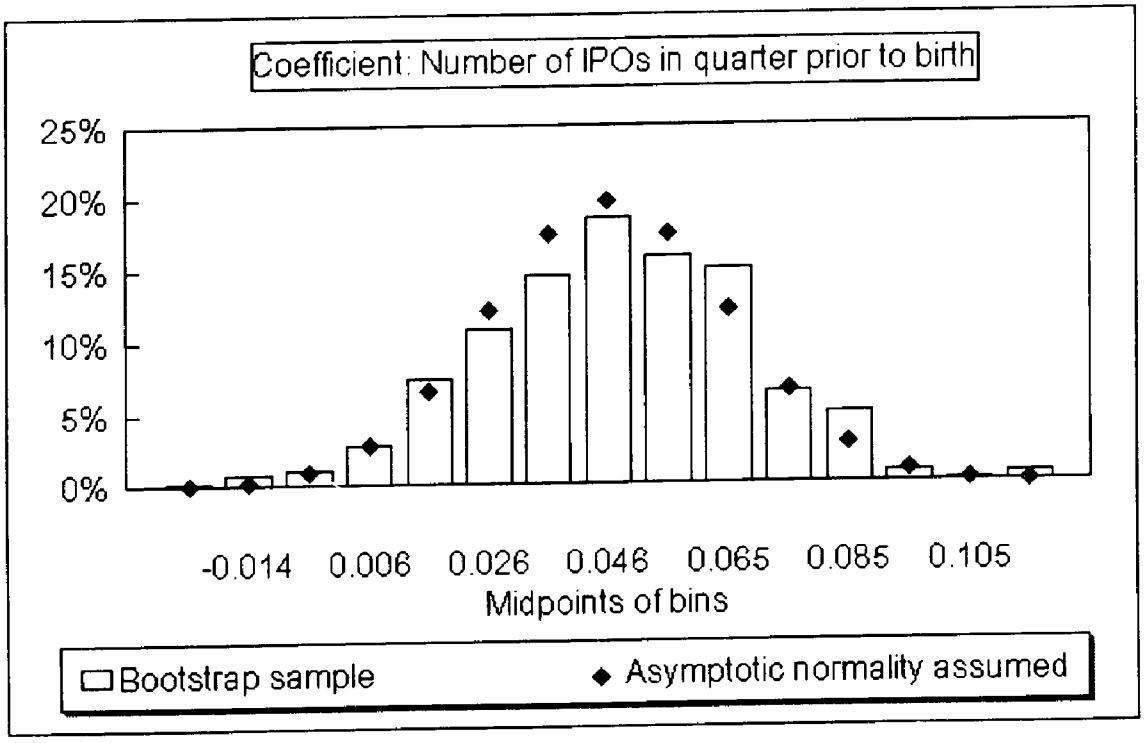

Figure A-10: Distribution of coefficients of number of IPOs prior to birth

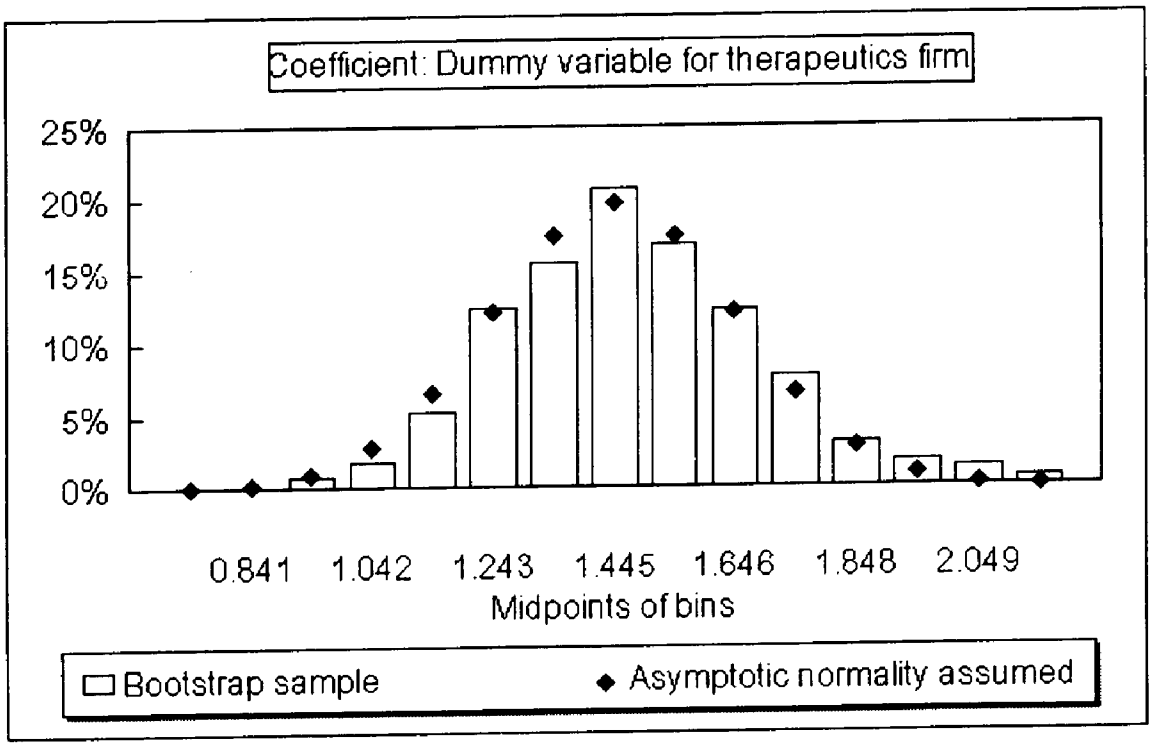

Figure A-11: Distribution of coefficients of dummy for therapeutics firm

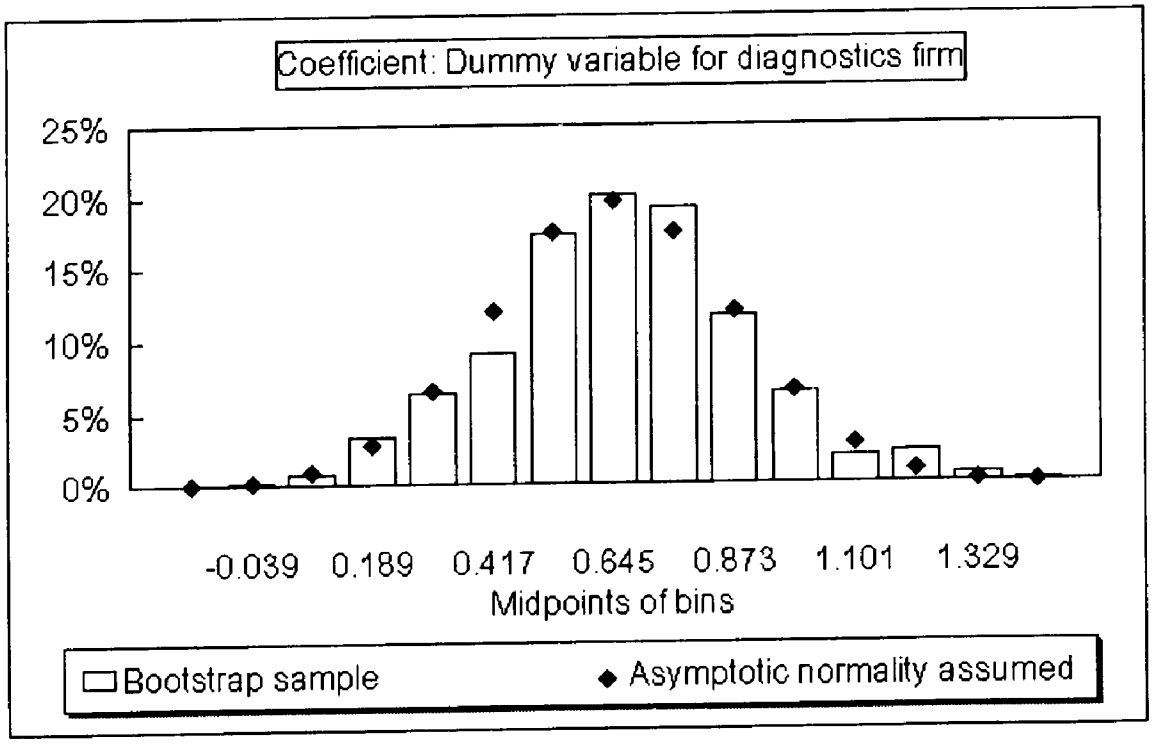

Figure A-12: Distribution of coefficients of the dummy for diagnostics firms.

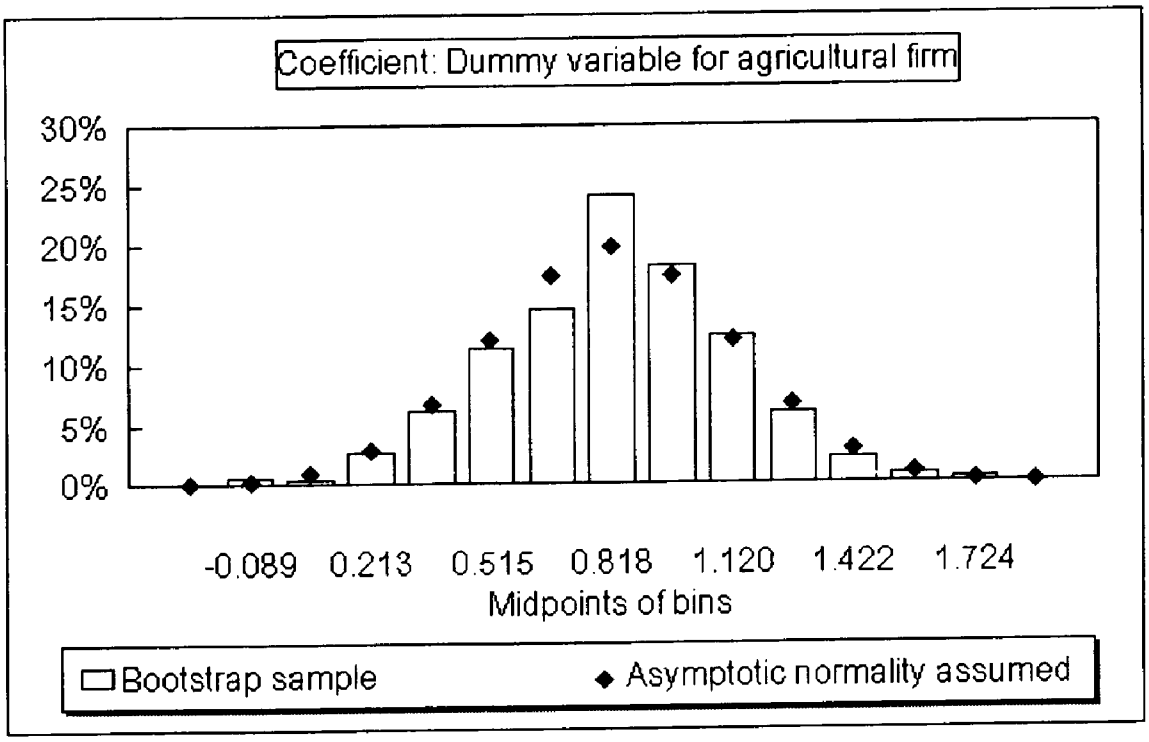

Figure A-13: Distribution of coefficients of the dummy for agricultural firms

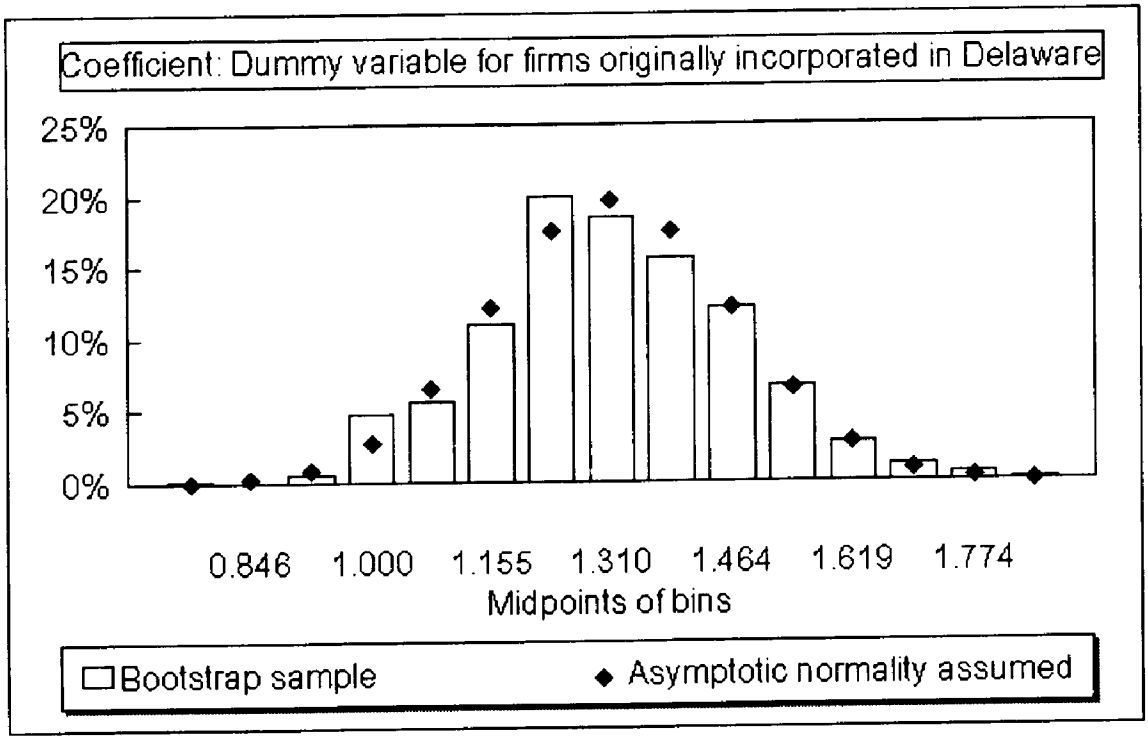

Figure A-14: Distribution of coefficients of dummy for firms incorporated in Delaware

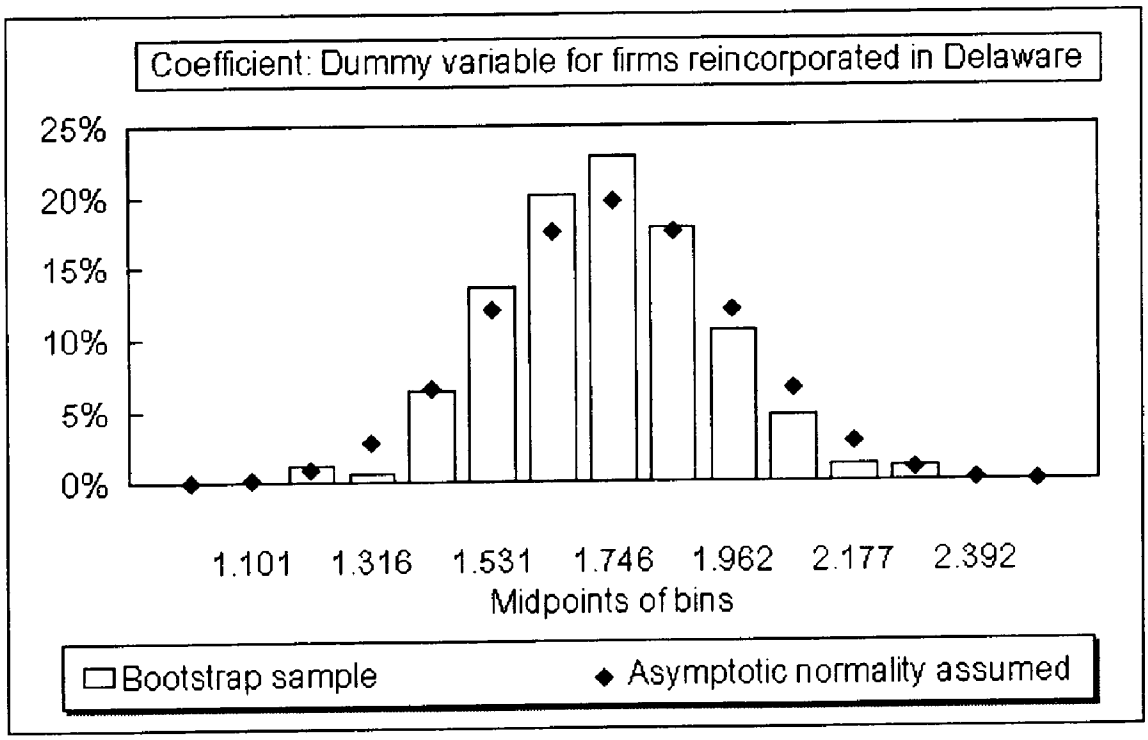

Figure A-15: Distribution of coefficients of the dummy for firms reincorporated in Delaware

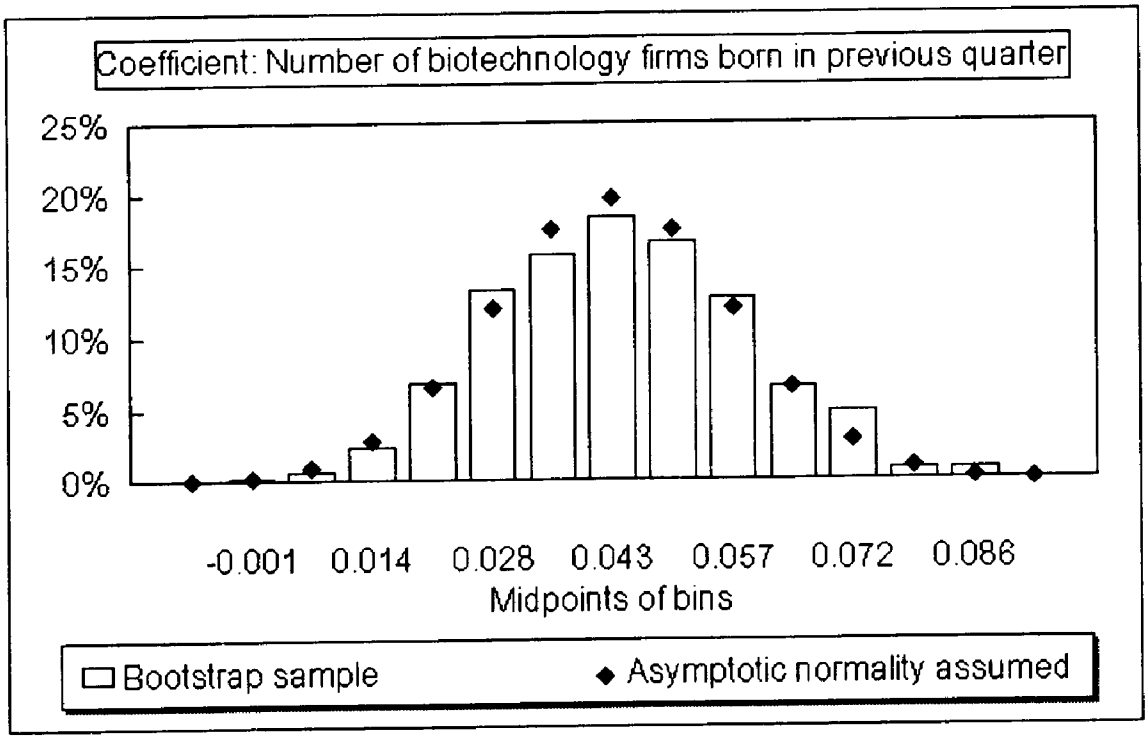

Figure A-16: Distribution of coefficients of the count of prior period biotechnology firm births

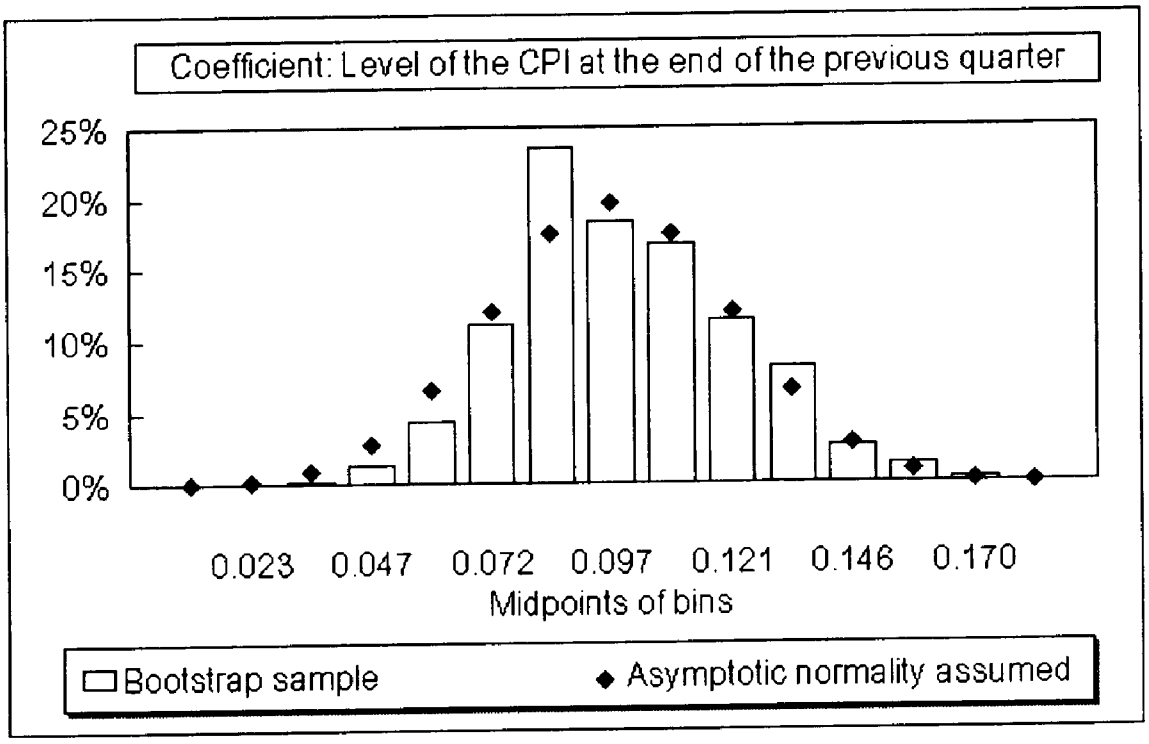

Figure A-17: Distribution of coefficients of the level of the CPI

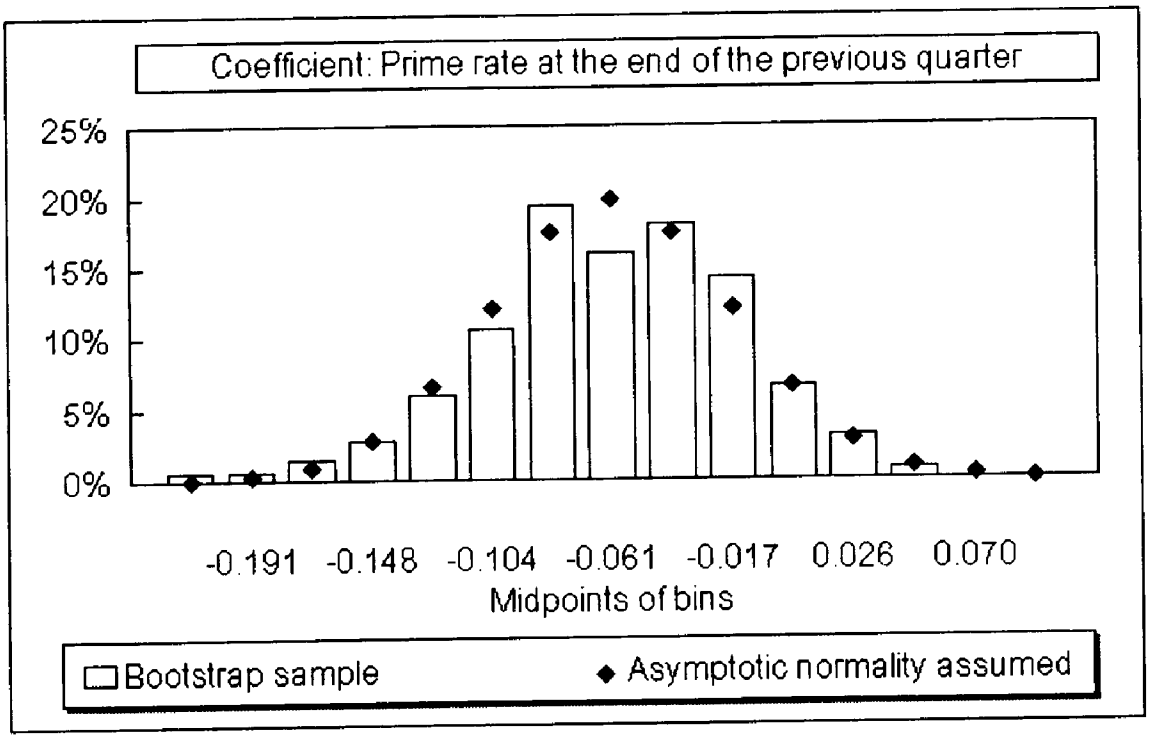

Figure A-18: Distribution of coefficients of the level of the prime rate during the previous quarter

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