Technological Innovation, Venture Formation and Resource Allocation:
The Impact of Economic Downturn on Life Sciences Venture Capital and Start-Ups

By

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Submitted to the Engineering Systems Division
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Abstract

The Massachusetts life sciences supercluster is a source of tremendous innovation. The Commonwealth's academic and industrial institutions produce a consistent stream of cutting-edge scientific research and the region has a well-developed professional and financial infrastructure to support the translation of these ideas into useful products. Venture capital (VC) plays a particularly important role in this ecosystem. VC funding is essential to most life sciences companies due to their high research and development costs and long time to market. The economic downturn of 2008 led to a rapid and significant contraction in the ability of venture capital firms to raise the funding that supports their work. We use this setting to test the impact of a funding shock on life sciences focused venture capital resource allocation. Specifically we looked at the rate and direction of funding choices made by venture capitalists before and after the downturn.

We analyzed data on yearly venture capital fundraising and 22,345 observations of investment dyads between venture capital firms and the portfolio companies which they invested in from the ten year period beginning in the year 2000. Additionally, seventy-six interviews with stakeholders in the Massachusetts life sciences community were conducted to help us understand the actual impact of data trends. This resulted in four major findings: (1) Although all venture capital fundraising was hindered in 2008 and 2009, life sciences focused venture funds were impacted disproportionately lightly in 2008 and disproportionately severely in 2009. (2) There has been a decline in the mean level of venture capital funding that companies are receiving. (3) The rate of new company formation is slowing as the rate of reinvestment in existing companies increases. (4) Innovation is being negatively impacted as fewer new companies translate technology into useful products and existing companies scale back their research and development pipelines.

Thesis Supervisor: Fiona E. Murray
Title: Sarofim Family Career Development Professor of Management of Technological Innovation & Entrepreneurship

Acknowledgments

Anyone who has written an academic thesis can verify that although there is only one author listed on the title, the work is definitely a team effort. Not only does it take a group of people to push the research forward but every graduate student needs a group of friends to share the experience with for the sake of sanity.

First and foremost I gratefully thank my advisor, Professor Fiona Murray. She has my deepest gratitude for taking a gamble in supporting a biomedical engineering student with a professed interest in, and only a vague understanding of, the concept of "innovation." Working with Professor Murray and her colleagues in the MIT Sloan School of Management Technological Innovation, Entrepreneurship, and Strategic Management group has helped me find my passion for the commercialization of science. I have been exposed to more mind opening thought and learned more about what technology policy really means while researching under your tutelage than through any other experience I've had.

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Thanks to my family and friends back home. You're amazing for putting up with my complaints about how different "the north" is from Texas. My heart will always be there even if my person is not. Zemed and Juan: leave Dallas already. Go to Austin. Amos: good job on leaving Dallas. Mom, Dad, Rachel, Deborah, and my Grandparents living and deceased: I love you all, but you already knew that. Cuddles, I miss you. You weren't a good dog but that's probably what made you a great Wolfson.

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1 Introduction

The work underlying this thesis was commissioned by the Massachusetts Life Sciences Collaborative (MLSC). The stated goal of the MLSC is "...to create a cross-sector collaboration that can sustain dialogue among life sciences leaders in academia, industry and government and also over time develop a comprehensive, integrated strategy to grow the life sciences mega-cluster in Massachusetts." The Collaborative is co-chaired by the Presidents of Harvard University (Drew Faust), The Massachusetts Institute of Technology (Susan Hockfield), and The University of Massachusetts System (Jack Wilson), and the Chief Executive Officer of Genzyme (Henri Termeer). These Co-Chairs directed the staff of the MLSC to analyze the impact that the economic downturn of 2008 had on the healthy functioning of the Massachusetts life sciences ecosystem and, in particular, the ability of new startup ventures to form.

To carry out this mandate the MLSC staff enlisted the assistance of PriceWaterhouse Coopers consultancy and the MIT Entrepreneurship Center. These organizations supported the effort by providing (1) quantitative data such as university technology transfer metrics, venture capital fundraising and investing trends, and measures of new company formation and (2) qualitative data regarding the health of new ventures that was obtained by interviewing seventy-six Massachusetts life science community thought leaders. This thesis presents an academic consideration of one question stemming from the larger study that is critical to understanding the impact of economic downturn on new venture formation: **How does venture capital (VC) resource allocation shift in response to an exogenous funding shock and what are the implications of these shifts on new venture creation?**

1.1 The Massachusetts Life Science Supercluster

The Massachusetts life sciences community is comprised of over six hundred biotechnology companies, four-hundred medical device companies and manufacturers, and seventy five pharmaceutical companies (PriceWaterhouse Coopers, 2007). It boasts over one-hundred universities and colleges including some of the world's top ranked medical schools and research institutions (New England Association of Schools and Colleges). Nationwide, Massachusetts is rivaled only by Northern California's Silicon Valley region in overall balance of other indicators of life science vibrancy such as venture capital investment, patents generated, PhDs granted, and alliances between large companies and early stage

research based companies (Cortright & Mayer, 2002). In 2009, Massachusetts received almost $3.5 billion in research funding from the U.S. National Institutes of Health (NIH) and the Commonwealth consistently receives ten to eleven percent of the NIH national research budget, making it the highest funded state on a per capita basis (U.S. National Institutes of Health Budget Research Portfolio Online Reporting Tool, 2009).

This "supercluster" is an enviable source of economic growth for the state. The 1997 Economic Census counted 26,368 people employed in manufacturing positions for medical devices and pharmaceuticals, and another 9,311 employed by biotechnology research establishments (U.S. Department of Commerce, 2000). Employees of these industries tend to be paid higher wages than workers in other industry sectors which helps explain why every dollars generated in life science output generates positive spillovers to other areas in the Massachusetts state economy (Clayton-Matthew, 2001, Ernst & Young Economics Consulting and Quantitative Analysis Group, 2000). Over ten percent of exports from Massachusetts come from life sciences related industries and these industries are thought to have had a positive mitigating effect on the state's economy during the recession of 2001 (Clayton-Matthew & Loveland, 2004). The need for healthcare solutions and the manufacturing of those solutions has outpaced growth in other industrial sectors and an aging population poises this trend to continue.

The supercluster's success has bred sustained excellence. Successful technology commercialization requires a talented pool of researcher-scientists, entrepreneurs, investors, medical clinicians, and industry veterans. In a simplified model of the venture creation process, researchers develop cutting edge technology, entrepreneurs innovate those technologies into market ready forms, and then the entrepreneurial companies are either acquired by larger companies, grow into larger companies themselves or fail (Best, 2006). The whole process is facilitated by a highly educated workforce (also a product of good universities), investors who can help entrepreneurs with money and advice, and supportive government policy. The true interactions are quite a bit more complex than this simplified model as there are feedback effects between the marketplace, universities, companies, and all of the professionals required by the ecosystem (United Kingdom Consulate for Science and Innovation, 2010). The Massachusetts cluster has been further supported by quasi-public organizations that help fund life sciences companies and train students (Battelle Technology Partnership Practice, 2008), university programs focused on translating technology from academia into the market, and by supporting a close-knit community of deeply experienced professionals (PriceWaterhouse Coopers, 2008).

However, the early stage life sciences ventures that are the lifeblood of the Massachusetts supercluster are characterized by high research and development costs, technological uncertainty, and regulatory burden. These factors lead young life sciences companies to have a long time horizon before they are able to generate revenue, a longer time before they are profitable, and even longer before a company that makes it to profitability is able to pay off its initial investments. Although these are the companies that allow academic and industrial innovators to move their ideas from concept to product to market this process is fraught with risk that most sources of funding are unwilling to undertake and capital requirements that most founders cannot finance themselves.

1.2 The Venture Capital System

Venture capital plays a vital role in funding this early stage gap. The individuals who manage venture capital investments, known as venture capitalists, provide large amounts of money to early stage companies in exchange for partial ownership stakes (equity shares). Venture capital investments allow these expensive high risk projects time to develop their products. Good VCs also have well developed social networks and deep expertise in running the types of companies they invest in so they serve as valuable sources of guidance to the management teams of their portfolio companies. Thus, having venture capital backing not only maximizes a life science startup firm's chances of success, sometimes venture backing is essential to it.

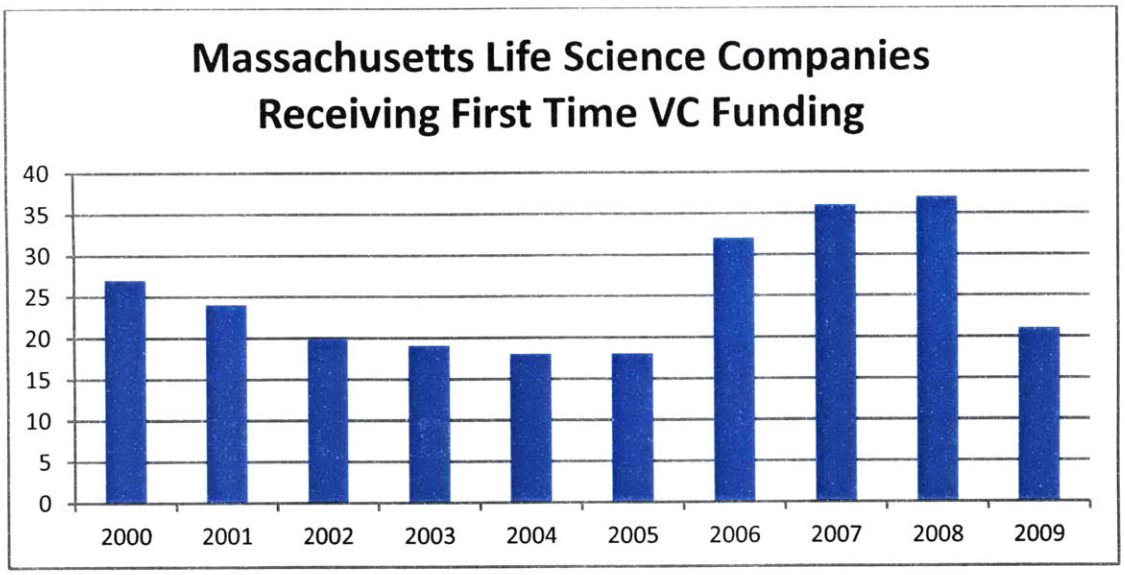

Figure 1: Number of Massachusetts Life Science Companies Receiving First Time VC

As Figure 1 shows, VCs have invested in creating over two-hundred-fifty life science companies in Massachusetts alone over the past ten years. These companies have received over $10.5 billion in combined VC investment over this time period. The last decade has seen thirty VC backed life science companies go public via an IPO and another fifty-seven get acquired by other entities. Many of the companies have failed or have no growth prospects but the ones that have been successful have created many jobs, and provided returns to their investors that could then be used to make new investments in other companies.

The majority of the money invested by VCs is not their own. Within a venture capital firm the VCs themselves are known as general partners (GPs) and they make and manage investments. Most of the funding however comes from limited partners (LPs) who invest in a VC fund in the hope that the fund generates a sizable profit that will be shared with them. LPs can be wealthy individuals investing their personal fortune or fund managers who invest institutional money from endowments, pensions, or other types of collective funds. The greater the level of LP investment in venture capital is, the greater the number of companies that VCs can in turn fund is.

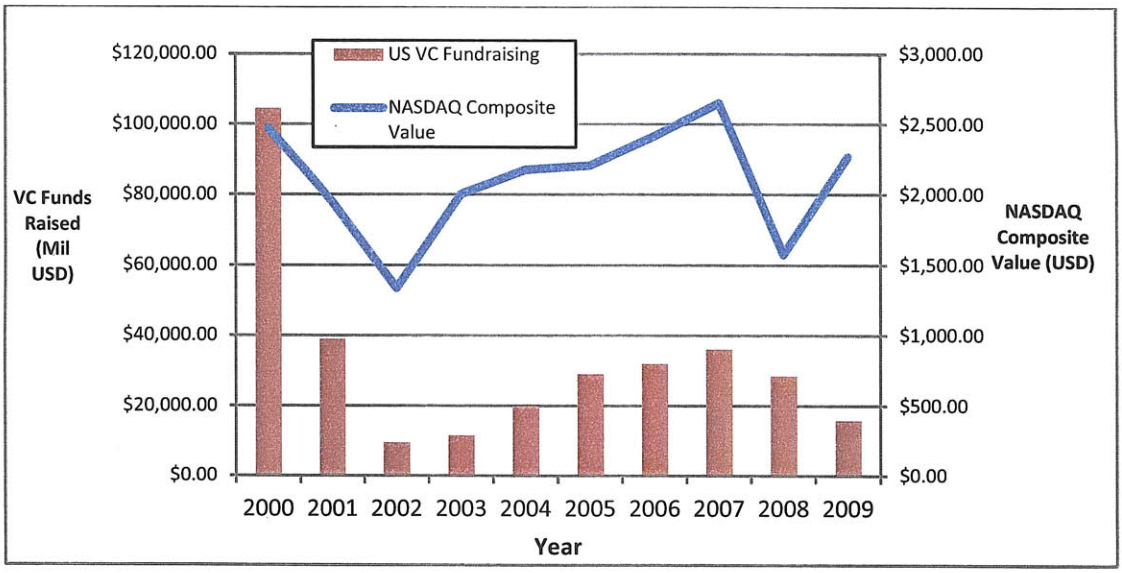

Figure 2: NASDAQ Composite Value and US VC Funds Raised

Figure 2 highlight the trend between stock market performance and VC fundraising. It is clear that there is a relationship between market performance and the amount of money that venture capital firms are able to raise. Because an investment in venture capital is one choice among many that fund managers can select for how to invest the resources at their disposal, the following claims help explain why the correlation between market cycle and VC fundraising exists:

1. *Availability of Capital* - Depressed public markets are representative of low points in economic cycles. During such points investors have less money to invest. Even if VC received the same proportion of investment as normal, the overall amount would be smaller. Conversely, periods of market exuberance are characterized by easily available capital. With more money to invest overall, VC firms find that they too have fuller coffers.

2. *Availability of Optimism* – Only a small fraction of VC backed companies ever generate a substantial return on investment. The risks to these companies are high and investors need to believe that VCs will defy the odds stacked against their companies. This requires a certain degree of optimism that is generally lacking in times of downturn and more prevalent in times of plenty.

3. *Availability of Options* – As was stated above, venture capital investment is one option among many. When markets are priced excessively high many investors believe common stock to be overpriced and so will seek investment in a more diverse portfolio including venture capital. When markets are

down the reverse holds true: common stock looks like a more appealing investment when compared with venture capital.

4. *Availability of Exits* – Venture capital investments produce a return when portfolio companies are either sold or go public via an IPO. In either of these cases the investors are ultimately able to convert their shares into cash and distribute proceeds to LPs and GPs. When markets are good then venture capital portfolio companies are more likely to achieve these liquidity events and investors will find themselves with money to reinvest and the optimism needed to do so. When companies cannot achieve high valuations for IPOs and large companies do not have the resources to finance acquisitions the liquidity events are rare. During these times existing VC investments have difficulty providing their investors with returns. In turn those investors are less likely to make further investment.

5. *Availability of Liquidity* – LPs have their own demands that require cash. Fund managers have investors of their own that clamor for money and individual investors have individual debts. These demands are particularly pressing during downturns as creditors make calls for their outstanding debt and are more relaxed during times of abundance. Venture capital is a relatively illiquid investment compared to others. VC backed companies take several years to position themselves for an exit and, as point (4) explained, exits are more likely under robust economic conditions. It is also difficult for LPs to recall their investments from VC firms because those investments are wrapped up in portfolio companies. When LPs face lower demand for cash then they are more likely to invest in VC knowing that they won't see a return for a fairly long time. When demand for cash is high, though, investors prefer to put the cash they do have into more liquid assets.

1.3 The Economic Downturn of 2008

On September 15, 2008, Lehman Brothers investment bank filed for Chapter 11 bankruptcy. It was brought down by its heavy debt burden and overexposure to arcane mortgage backed securities that relied on ever increasing real-estate values (The Economist, 2009). This event marks a key turning point in recent global history. After the collapse of Lehman, already shaky stock markets fell into an all-out tailspin. The Dow Jones Industrial Index and the NASDAQ Technology Composite Index both lost 40% of their value over the next six months (Google Finance). United States unemployment proceeded to more than double from less than 5% in 2007 to greater than 10% by the end of 2009 (United States Bureau of Labor Statistics, 2010). Fears abounded that major U.S. banks were experiencing cash flow insolvency

and despite government interventions their willingness to lend was greatly abated (The Economist, 2009).

As lending dried up and public markets constricted, venture capital felt a strong impact too. Venture capital funds raised less money in 2009 than they had since 2003: only $13 billion was invested in venture capital in 2009 compared with more than double that amount only the year before (Moore, 2010). Fewer venture capital firms were able to raise money and those that did raise new funds did so in greatly reduced amounts (Weisman, 2009).

As went venture capital, so too went startup activity. The amount of money invested by venture capitalists in firms fell by 31% between 2008 and 2009 and the median deal size declined since 2008 (Dow Jones, 2010). Since it is very difficult for entrepreneurs to find substitutes for the level of investment that venture capitalists provide (Shane, 2009) young companies had to become more capital efficient by making careful choices regarding the products they chose to develop and the applications for those products (Gambon, 2009). The capital constraints faced by small life sciences companies created a "buyer's market" that favored large companies. Rather than purchasing entire startups at high valuations, industry incumbents developed advantageous deals with smaller companies such as directly funding the smaller firm's research in exchange for future licensing options to any technology developed. In short, the large companies were better able to mitigate their risk without sacrificing potential gains (Clarke, 2009).

The relationship between economic downturn, the life sciences venture capital industry, and life sciences startup companies is what underlies this thesis. First, this work explores how life sciences venture capital resource allocation responded to a period of economic downturn. Specifically it analyzes the rate and direction of venture capital funding of life sciences entrepreneurial ventures in three geographic areas: Massachusetts, California, and the rest of the United States. Next, it considers the impact of this changing resource allocation on the formation and operation of venture backed life science firms in Massachusetts. This insight is derived from interviews with entrepreneurs, technology transfer professionals, venture capitalists, and industry leaders in the region. The next chapter of this work explores what previous academic literature has established regarding venture capital resource allocation and its response to economic conditions. Chapter 3 details the data that were analyzed for this project and the methods by which that analysis was done. Chapters 4 and 5 present the results of that analysis. Chapter 6 offers recommendations for addressing future challenges to economic downturn and Chapter 7 concludes.

2 Literature Review

Venture capital firms are a major source of support for innovative companies. Venture capital dollars have been shown to be more effective than corporate R&D funding at generating and defending patents (Kortum & Lerner, 2000). VC backed companies get their products and services to market faster than non-VC backed firms (Hellmann & Puri, 2000) because the venture capitalist investors have a financial incentive to make their portfolio companies attractive and have them sold for a profit. A manifestation of this is that VC backed firms are more likely to realize early revenue streams from selling, licensing or partnering their technologies with other firms (Hsu D. H., 2006) and that their performance is more sensitive to market conditions than that of non-VC backed firms (Hsu D. H., 2000).

2.1 What Venture Capital Firms Do

A good VC firm adds value to its portfolio companies not only by investing in them but also through activities like helping them build a management team, establish corporate policies and strategies, and giving their companies access to their expansive interpersonal (and inter-firm) networks (Hellman & Puri, 2002 and Sapienza, Manigart, & Vermeir, 1996). The extensive due diligence that VCs perform on companies prior to investing, and the insider information they have on a company once having invested in it have a strong signaling effect. For portfolio companies to receive capital from new VC investors in later funding rounds the original investors should show their continued confidence in the company by reinvesting as well (Myers & Majluf, 1984). Trusted VCs that have a track record of success and are good at providing "extra-financial" services have been shown to be more desirable for companies to attract as investors and they are able to acquire greater equity stakes on more favorable terms (Hsu D. H., 2004).

The amount of value that a venture capital firm is able to add to a portfolio company is largely a function of the VC's experience in understanding a particular market sector and portfolio company's business stage. This leads VCs to specialize in specific high potential, high growth industries (Zider, 1998) and in particular stages of company maturity (Sapienza, Amanson, & Manigart, 1994). Because many venture capital firms are very involved in the companies that they invest in and often even have membership on the board of directors, VCs also tend to invest in companies located geographically nearby (Sorenson & Stuart, 2001).

2.2 Venture Capital Firm Decision Making

The work above describes why venture capitalists invest and why entrepreneurs value that investment, but it is also important to understand how venture capitalists make their investment decisions. This question sheds light on the direction that VC backed innovation takes. Importantly, reputation and trust are known to play a large role in venture capital decision making. It is far more common that a VC learns about a deal that will ultimately receive investment through a network of other VCs and confidants rather than through an unsolicited business plan submission (Tyebjee & Bruno, 1984) and a VC is more likely to invest in a non-geographically convenient company if there is another trusted VC co-investing that is near the company (Jaaskelainen, Maula, & Seppa, 2002). Less established VC firms are more likely to co-invest in projects with established firms because they believe that reputable firms will tend to be more successful in the future and a successful co-investment with a strong partner will enhance their own reputation (Lerner, 1994). It has been suggested, though, that this phenomenon of "herding around success" has a negative consequence of VCs over-funding some industries (ex: telecom, computer hardware) to the exclusion of other industries that might have had ripe opportunities (Lerner, 2002).

Although there exists an optimal non-zero number of companies that any given VC should invest in, each additional company invested in has a diminishing marginal return to the investor (Kannianinen & Keuschnigg, 2000). As a VC firm adds companies to its portfolio, each company will receive less of the venture capitalist's time and advice – the factors that have been shown to be critical to company success. This raises the risk of failure for every portfolio company. The VC will have to compensate for this increase in risk to portfolio companies by taking less equity in each one to make up for less service rendered (Gompers & Lerner, 2000). Although funding more companies might be optimal from a social welfare perspective it will not benefit the VC and so the venture capital industry as a whole will fund a non-socially optimal number of companies and VCs will give too little time to each company that is funded (Kannianinen & Keuschnigg, 2004).

The reasons that researchers have found for any particular venture capital firm investing in any particular company are unsurprising. Screening activities assess the quality of the business plan, the quality of the management team, and the market and technology risks to the project (Fried & Hisrich, 1994 and Kaplan & Stromberg, 2000). Companies are more likely to both receive investment and get better valuations if they have a strong patent portfolio (Hsu & Ziedonis, 2007)and if their founders have

had prior success in starting companies, hold doctorate degrees, and have robust social networks of their own (Hsu D. H., 2007).

2.3 Rate of Investment

If venture capital is thought of like a pie that underwrites innovative activity, research has analyzed not only how the pie is distributed, but how big the overall pie to be shared is. The basic economic model of VC investment rate assumes that there is a free market for venture capital. A supply and demand framework is used to determine how much venture capital the market will provide and accept. When capital markets are depressed, there will be less money available to invest in VC and in turn fewer companies will be invested in. This means that only the "best" companies receive funding and ultimately the venture capital investments that are made in downturns will produce high returns for investors and encourage more money to be put into future VC rounds. This increase in the supply of VC will in turn lead to more "average" companies receiving funding. These average companies will not perform as well and will not generate the same level of return to the industry. Downward pressure will then mitigate the desire to invest in VC until equilibrium is reached (Gompers & Lerner , 1996).

This simple model is complicated by the fact that in the short run venture capitalists are in very limited supply and any single venture capitalist has limited time to dedicate to managing companies. There exists a point where the venture capital industry has raised enough money to invest in the maximum number of companies that its VCs have the time to manage. Further investment into venture capital causes each portfolio company to simply receive more money rather than increasing portfolio size. Each investment receiving more money drives up the need for VCs to make higher returns on their investment and forces valuations to increase. This has the curious implication that under bullish market conditions valuations for companies are higher even though innovative productivity is actually lower. Under such conditions, inexperienced VCs will enter the market to try to capture the available rents. The combination of their inexperience and the rise in valuations relative to firm output will cause the market to crash. These effects are found to be particularly pronounced in areas where lots of venture firms are concentrated, such as California and Massachusetts (Gompers & Lerner, 2000).

The above propositions have led researchers to wonder about what situations exist that would induce the venture capital industry to invest in more companies. The answer appears to be that when markets are strong and portfolio companies sell for greater returns then VCs are willing to accept less equity because they expect a greater overall return on investment (Cumming, 2006). This frees them up to

invest in more companies while being satisfied with a smaller portion of each (Keuschnigg, 2004). With less VC time dedicated to each company the portfolio companies will operate less efficiently and become less innovative per dollar invested (Lerner, 2002). Separately, Gompers and Lerner (2001) analyzed the impact of the U.S. Department of Labor's clarification of the "prudent man rule." Their study, which controlled for the availability of "good ideas," found that once pension funds were legally allowed to invest in venture capital funds (and consequently the greater the amount that venture capital funds had to invest), VCs became more competitive in trying to attract top portfolio companies to invest in. The valuations of venture backed companies increased between seven and twenty-one percent. The increase was accompanied by rapid growth in venture capital firms, the volume of investment in new companies, and subsequent boom and bust periods.

2.4 Research Questions

While it is clear that there is a relationship between VC investment and innovation and that market forces have an impact on this relationship, a key question is still unanswered: How does the venture capital industry react to a rapid capital constriction and what is the impact of this reaction on innovation? This thesis supplements this gap in the literature. Innovations in the industrial sectors that make up the life sciences sector (medical devices, molecular development, and non-molecular biotechnology) are grounded in basic scientific advances. The inputs and outputs of the basic science system were not negatively affected by the financial crash of 2008. In fact, if anything they were made more robust. However, the downturn did have a strong impact on the amount of capital that VCs had access to. The economic downturn was an exogenous shock to an industry that had no change in underlying potential for innovation (scientific progression) but a large change in the venture capital psyche. This study takes advantage of this situation in order to explore the changing strategies that VCs employed to survive this tumult and how those strategies affected the companies under their management.

Specifically, we address several questions of rate and direction by evaluating the veracity of six hypotheses. The hypotheses to be tested are as follows:

Questions of rate:

H1. Investment by LPs into life sciences venture capital has declined significantly

H2. The number of life sciences focused companies being invested in by venture capitalists has declined significantly

H3. The amount of money invested into life sciences focused companies that are receiving investment has declined significantly

Questions of direction:

H4. The types of life sciences companies (i.e. molecule development, medical devices, other biotechnology) that venture capitalists are funding is changing in an attempt to lower exposure to "risky" industries

H5. A greater portion of the VC portfolio is being allocated to later stage, less risky companies than higher risk early and seed stage companies

H6. A greater portion of the VC portfolio is being re-invested in existing portfolio companies to help these companies "weather the storm"

3 Research Methodology

3.1 Research Setting

The objective of this thesis is to analyze the impact of economic downturn on venture capital resource allocation and the effect of this allocation on new ventures. In order to achieve this goal we selected an experimental setting bounded in time, industry, and geography.

The industry selected for analysis is broadly referred to as the life sciences. Life sciences companies focus on areas ranging from design and production of medical devices, synthetic or protein based drugs, or a wide variety of non-healthcare related applications of biological organisms. Life sciences was chosen as the industry for analysis because of the importance of venture capital backing to the successful commercialization of life sciences technologies. Because of the complexity of the science underlying these products and the regulatory burden faced by developers of medical devices and drugs, life sciences companies face a long, expensive and risky path to market. For these reasons the long term funding that venture capital provides is ideally suited to life sciences companies and the industry should be uniquely sensitive to changes in venture capital investing.

We analyzed data from the decade beginning in the year 2000 for its position in the evolution of venture capital history. In 1978 the U.S. Department of Labor clarified what is known as the "prudent man rule" which allowed pension funds to invest in venture capital. The next decade saw an order of magnitude increase in venture capital investment (from approximately $354 million in 1978 to over $4 billion in 1988) followed by a leveling off in the early 1990s. Fueled by the so-called "dot com boom" of the mid 1990s, venture capital increased by yet another order of magnitude and in the year 2000 alone, venture capital funds raised over $100 billion. The 2000 decade then proceeded to contain the two most significant crashes in the recent history of venture capital fund raising: the bursting of the dot com bubble in 2000 and then the economic downturn of 2008. After the first crash the venture capital market began to recover before crashing again at the end of the decade. We define years 2000-2001 as downturn years, 2002-2003 as recovery years, 2004-2007 as pre-second downturn years and 2008-2009 as second downturn years.

The United States was selected as our region of study for several reasons. The U.S. is the most developed venture capital market in the world, estimated to account for about half of all global venture capital activity (Deloitte Touche Tohmatsu Consulting, 2009). The United States economy was at the

epicenter of both the great market crashes of the past decade and U.S. financial institutions have strongly felt the impact of these events. The United States also has robust requirements for public reporting of venture capital backed deals and so the quality of data available pertaining to venture capital investments is of the highest quality. Finally, the United States can easily be further segmented into relevant geographic sub-groups. Specifically, California and Massachusetts receive the greatest amount of venture capital activity, particularly in the life sciences.

3.2 Research Design

This thesis utilizes a mix of quantitative and qualitative data. Quantitative analysis was required to establish an initial scope of the rate and direction of venture capital resource allocation, in other words, knowing something about what types of investments venture capitalists are making and what level of funding those companies receive. Qualitative interview based data were used to shed light on the impact of these resource allocation decisions.

To accomplish our goals, we constructed a dataset based on existing venture capital databases. The Thompson-Reuters VentureXpert database aggregates several venture capital data sources including the PricewaterhouseCoopers MoneyTree report, public filings of companies selling shares to venture capitalists, publicly available press releases, and a proprietary industry survey[1]. We extracted a subset of data with which we constructed variables as described below to quantitatively answer our research questions.

These data were analyzed for both changes within key groups of interest over time. Changes that appear to have been influenced by economic downturn were noted and descriptive statistics were calculated. For instance, venture capital investment in early and seed stage life sciences companies was analyzed for changes due to economic downturn in each of our geographic regions of interest. Specifically, the parameters of interest were compared with a difference of means hypothesis test to measure whether

[1] VentureXpert captures detailed information along a wide variety of dimensions regarding private equity deals. These data come from publicly available press releases, a quarterly survey of venture capital and private equity firms, and Form D filings with the United States Securities and Exchange Commission (SEC)[1]. The Form D filing is an SEC form that small companies who are exempt from other regulatory requirements must fill out providing notice that they are selling shares of the company. It is often associated with investment in growing companies from venture capitalist or angel investors (National Venture Capital Association, 2009). Thomson Reuters has stated that they do not expect that their database captures 100% of venture capital deals but that they do update it daily with all sources of publicly available information and their own survey based proprietary information[1] so it is likely the best source of information for these deals that is on the market.

the values obtained in the post-second downturn years (2008 and 2009) had a statistically significant difference from the mean of the pre-second downturn years (2004 – 2007). The form of the tests was as follows:

H_0: $\mu_{\text{pre-second downturn for parameter of interest}}$ = Value of parameter of interest in post-downturn years

H_A: $\mu_{\text{pre-second downturn for parameter of interest}} \neq$ Value of parameter of interest in post-downturn years

For cases where we hypothesized that the parameter of interest has decreased post-second downturn relative to the pre-downturn mean then the alternative hypotheses was that the mean of the pre-downturn years was greater than the post-downturn value. Conversely, when we hypothesized that the parameter of interest has increased over pre-downturn levels than the alternative hypothesis was that the pre-downturn mean was less than the post-downturn value. Both of these cases required that a one-tailed T-test of difference of means be performed. For cases where we hypothesize that there is simply a change in the parameter of interest between pre- and post- second downturn levels, but that we are agnostic with respect to the direction of the change, then a two-tailed T-test was used.

The interviews were then used to explain the impact of these changes as they have been felt by venture capitalists, entrepreneurs, and other life sciences community members.

3.3 Data Utilized

As typically used (Gompers & Lerner, 2000 and Lerner, 1994 among others) and presented, the databases we employed provide information at a very granular level which catalogues each individual deal between a venture capitalist and a company that the VC funds. In order to shed light on our key question, we coded and aggregated these data to understand key factors of interest. To glean more detailed insight, interviews were conducted with key stakeholders in the technology commercialization pipeline. These focused on the stories of how these stakeholders have been affected by venture capital activity pre- and post- 2008 downturn. The following section details the data sources that were used to support the analyses and the methods by which those data sources were utilized.

3.4 Venture Capital Deal Data

Our analysis is structured around a sample of venture-backed firms in the life science in the years 2000 through 2009. We use data from the Thomson Reuters VentureXpert database to construct a dataset over this time period with 22,345 observations. Each observation is a venture capital deal dyad pair

between a VC firm and the portfolio company receiving investment. These observations include information such as the date of the investment and the value of the equity stake taken by the investor. Each observation was assigned a unique identifier number in order to categorize deals that involved the same venture capital firms making investments and companies receiving investments. Prior to analysis, all dollar values were adjusted for inflation by using the United States Department of Labor's Consumer Price Index conversion factors to convert all figures to 2009 dollar value equivalents. Several definitions and boundaries had to be determined when building our dataset – most importantly, the segmentation of life sciences firms.

The term "life sciences" is very broad. It encompasses activity ranging from design of medical devices to modifying living cultures to carry out non-medical purposes. In our analysis we consider three more narrow categories of life sciences that venture capitalists can choose to invest between. Medical device companies were defined as medical aids such as hearing aids or monitoring equipment, medical diagnostics, and devices used for therapeutic purposes like implantable devices. Molecule development consists of traditional pharmaceutical companies and protein therapeutic companies. Other biotechnology is a catchall category for life sciences companies that do not fall into the other two classes. This often applied to companies that use life sciences principles but do not have products applied towards human health or wellness.

Another important area of analysis is stage of company investment. Many venture capital firms specialize in investing in companies at a particular life cycle stage. While there is a wide spectrum of stages that such firms might specialize in (i.e. expansion stage in which companies are growing their product offerings or mezzanine stage in which a fairly large company receives a large investment prior to an IPO), our analysis considers two meta-levels. Seed and early stage companies are characterized as being firms at a very early stage and usually pre-revenue. We consider everything that is not in this seed or early stage category as later stage.

Because this work is concerned with commercialization of technology, one more designation was created to characterize the data. "First time funding" was used to denote a company receiving their first funding event. Because life sciences companies are incredibly capital intensive, most successful ones will require venture capital investment at an early stage in their incorporated lives. First time funding therefore acts as a proxy for the date of formation of a company.

The final segmentation by which we sorted data was geographic location. In order to determine whether different geographic regions were affected differentially, all data was sorted by location. We determined three regions of interest for this project. Massachusetts and California were each included as regions of interest because they are the states with the greatest amount of life sciences commercial activity in the country. California has the greatest overall volume of life sciences funding and companies and Massachusetts has the greatest density per capita. The final region of interest is the United States with the exception of Massachusetts and California. This catchall category is referred to as "the rest of the United States" when presented in the results section of this thesis.

3.5 Venture Capital Funding Data

Understanding the changes in venture capital resource allocation requires an understanding of investment into venture capital funds. In addition to tracking venture capital deals, VentureXpert has data on venture capital fundraising. We utilized this to form a venture capital funding dataset that extended from 2000 through 2009. To understand changes in the rate and direction of investment into venture capital we again segmented this data source along useful dimensions.

We characterized the investment data by target investment area. Most venture capital funds invest in a particular area in which the fund directors have deep expertise. In any given year between half and two thirds of all funding in our database was invested in a portfolio that is classifiable in this way. The remainder of investment into venture capital is in funds that have no known specific focus. The major fund categories employed for our analyses were high-tech focused funds (i.e. computer, telecommunication, semiconductor, and internet companies), energy focused funds (power generation and transmission), life sciences focused funds (medical devices, drug development, and other biotechnology), and funds with a specific focus not captured by these other categories (retail, media, etc...).

We also categorized venture capital fundraising geographically. Locations of venture capital firms receiving investment were organized in the same manner as were the companies receiving venture investment. The three major categories were Massachusetts, California, and the rest of the United States. Again, California and Massachusetts are responsible for the greatest volume of venture capital funding raised and the greatest density of venture capital funding raised per capita, respectively.

3.6 Interviews

Qualitative interviews were performed to help better understand the trends present in the data. While the VentureXpert dataset allowed for various analyses of rate and direction of venture capital resource allocation, it is important to understand the reasons underlying these trends and the impact that the trends have on venture formation and operation. These interviews were conducted with venture capitalists, entrepreneurs, philanthropic foundation directors, technology transfer office directors, community organization directors, and executives from both large and small companies and from across each of the life science domains focused on by this project. A total of seventy-six interviews were performed and they were conducted in two rounds. A list of all subjects interviewed can be found in Appendix A.

The first round of interviews included fifty-two individuals. These interviews were performed utilizing a distributed action model. Fourteen MIT graduate students volunteered to assist with the interview process. Each of these students was provided with a list of questions to ask the individuals to be interviewed. They were then asked to contact some number of potential interviewees, request their permission to be interviewed, and then conduct the interview. Interviews were meant to be fluid in the sense that interviewees were encouraged to give their opinions on the impact of the economic downturn on their business activities. However, the student interviewers were required to at least ask the pre-specified questions. After an interview was completed, the student interviewer wrote an interview summary that included some key quotes and the general responses to their questions. These summaries were then collected by the author of this thesis for later analysis.

The second round of interviews included 24 people. All interviews in this round were conducted by the author. Generally these interviews were more extensive than those in the previous category. Unlike the previous category of interviews, there was no master list of questions, although many of the same questions were used for consistency and relevance.

All interviews were reviewed for key recurring themes. While opinions on events are important, what are more valuable are the facts observed and noted by the interviewed individuals. General insights gained from interviews will be interspersed among the results chapter of this thesis. Interview subjects were told that their responses would be kept confidential and so while quotes are presented the specific names of the subjects have been redacted.

4 Results

This thesis examines two overarching issues that define the impact of economic downturn on venture capital resource allocation. The first is a question of rate of investment. How much did the overall volume of venture capital investment change, if at all, and, if in fact such changes occurred, is life sciences venture capital investment affected in the same way that venture capital as a whole is? The second question is one of direction: Has the composition of the life sciences venture portfolio changed? More specifically, with the tightening of capital availability in public and private markets, how have investment strategies change with regards to investment stage, sub-sector, new versus current investments?

Hypothesis 1: Investment by LPs into life sciences venture capital has declined significantly

As has been previously discussed, there are good reasons to believe that the ability of venture capital firms to raise money is closely tied to the performance of public markets. The introduction to this thesis demonstrated that with the decline of public markets in 2008 venture capital saw a significant decline in its ability to raise funds. First it will be helpful to see if Massachusetts and California followed the same trend as the rest of the country in this decline

Figure 3 indicates that Massachusetts has actually fared relatively better than the rest of the nation. While California's venture capital fundraising fell substantially in 2009 from 2008 (a 64% decline), Massachusetts was able to raise $300 million more in 2009 than the year before for a net gain of about 10%. The rest of the country declined in fund raising but only half as drastically as California.

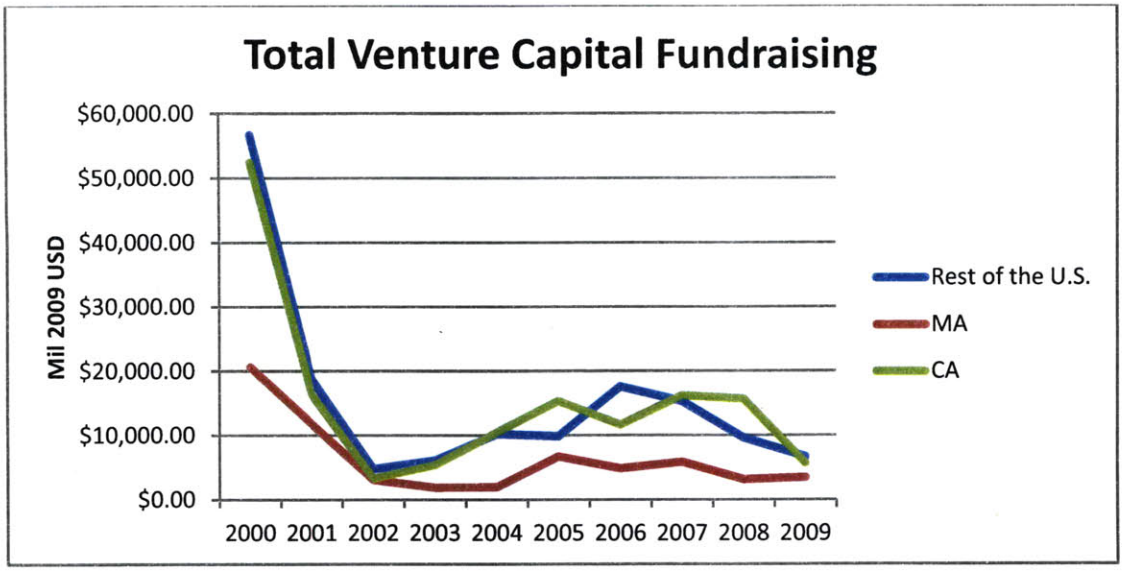

Figure 3: Venture Capital Funds Raised

Table 1 explains these trends statistically. California showed no evidence of having fundraising negatively affected by the downturn until 2009 when there is strong evidence of impact. Massachusetts saw some evidence of negative effect in 2008 but by 2009 the amount raised was again statistically not significant even at the 10% level. The rest of the United States saw a statistically significant impact in both 2008 and 2009.

Table 1: P-values of one sided t-test of mean in pre-downturn years being greater than funds raised in post-downturn years

	2008 Funds Raised	2009 Funds Raised
Massachusetts	0.100*	0.138
California	0.899	0.006***
Rest of the United States	0.077*	0.021**

*: Result significant at 10% level
**: Result significant at 5% level
***: Result significant at 1% level

Although the long term impact on fundraising cannot be exactly known, it is helpful to look at the impact of the bursting of the dot com bubble in 2000. Similarly to the most recent downturn, California and the rest of the United States declined far more quickly than Massachusetts did. 2001 saw Massachusetts raise 43% less money that it had the previous year, whereas the other two groups each had their VC fundraising fall by over two-thirds. California and the rest of the United States bottomed out a year later, in 2002, raising less than 10% of their peak level from two years prior. Massachusetts however, continued to slowly decline and did not hit its bottom until 2003. At this point it had also fallen by 90% from peak levels where it stayed for an additional year.

Massachusetts venture capital did recover from the downturn of 2001 quicker than the other regions, though. While Figure 3 clearly shows that VC fundraising has never approached its 2001 level, eventually all three regions in this analysis were able to return to almost one third of their peak. Massachusetts reached this mark in 2005; a year before the rest of the country did and two years before California did. Massachusetts also sustained this level of fund-raising with far less volatility than did the other regions of interest.

The question remains, though, whether or not life science venture capital maintained its share of a smaller pool of capital and thus was diminished in volume, or if the life sciences maintained its volume and now comprises a larger share of all venture capital funding. Figure 4, Figure 5, and Figure 6 illustrate how fundraising for industry specific venture capital funds has behaved over the past decade.

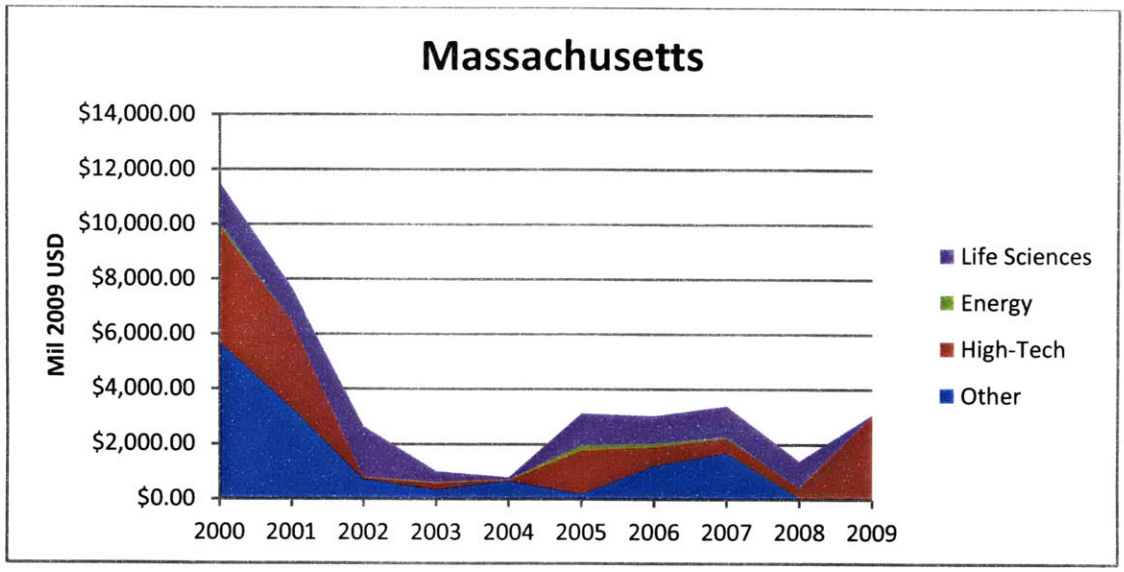

Figure 4: Funding Raised by Industry Focus for Massachusetts

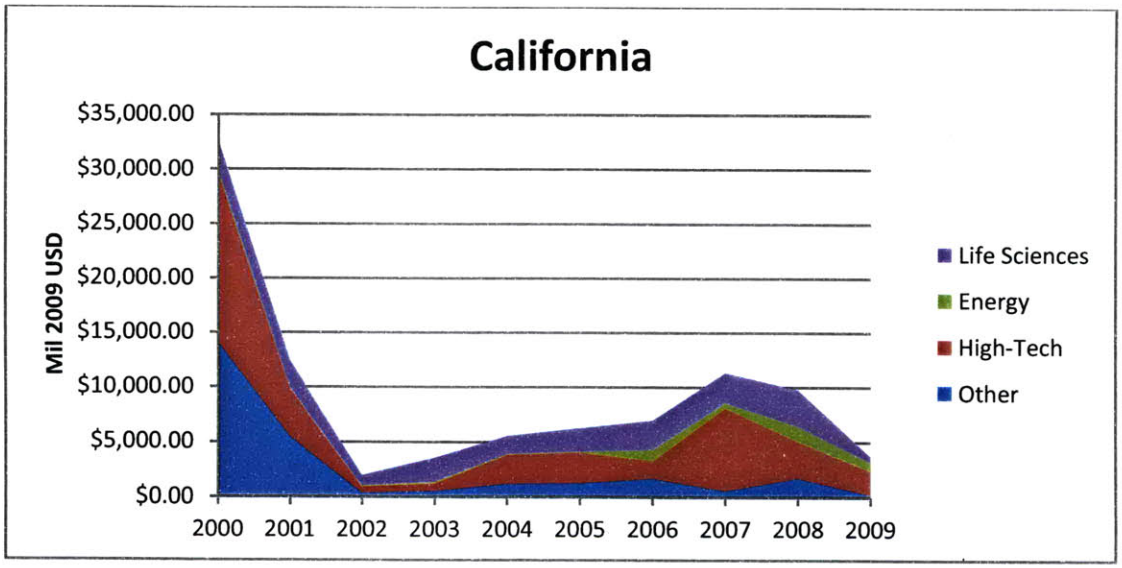

Figure 5: Funding Raised by Industry Focus for California

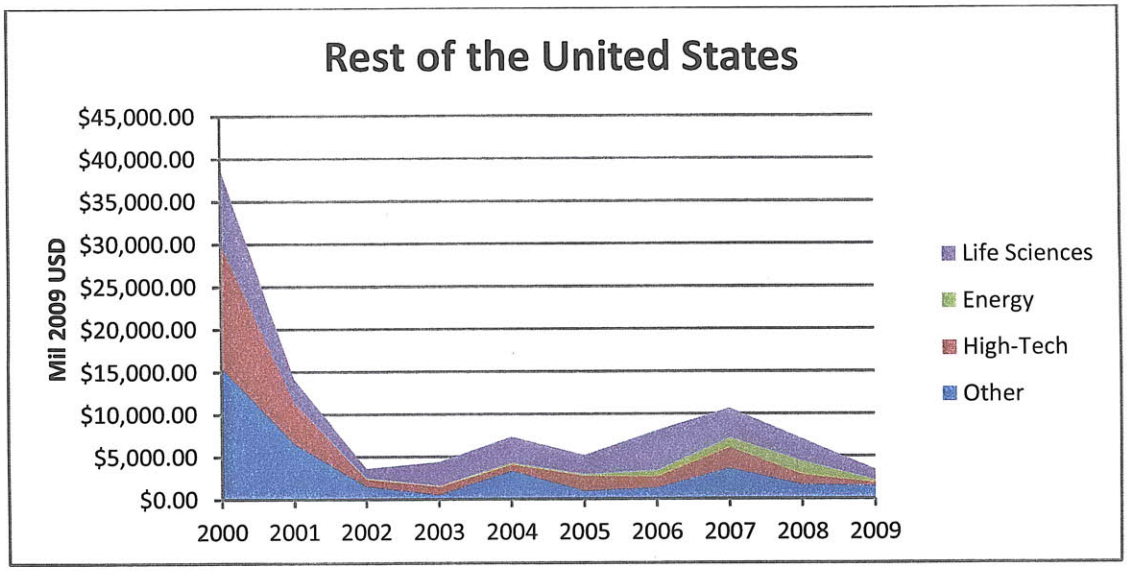

Figure 6: Funding Raised by Industry Focus for the rest of the United States

In analyzing the fundraising by portfolio focus some trends stand out in all three regional cases. First of all, except for one notable exception, funding in all focus areas across all regional cases has declined from 2007 until 2009. Second, energy focused portfolios have not made up a substantial component of any region's venture capital mix, although investment in energy focused funds in California did not fare as badly as other sectors. Finally, in the years following the 2001 technology investment bubble burst, the fraction of investment in venture capital that focused on high-technology investment fell drastically. Life sciences investment then actually grew as a percentage of the overall investment portfolio in each region as a result of not being as adversely impacted.

The exception to the overall decline in funding from 2007 to 2009 is high-technology focused venture capital funds in Massachusetts. In 2009 these funds raised almost six-fold the amount that they did in 2007. This tremendous increase was accompanies by an almost total evaporation of the ability to raise funds for any other industry focused sector. This may be representative in a regional shift in risk perception that high-technology in Massachusetts is the only safe bet in downturn. Figure 7, Figure 8, and Figure 9 present the fraction of the entire industry targeted venture capital fundraising portfolio represented by each meta-category for clarity.

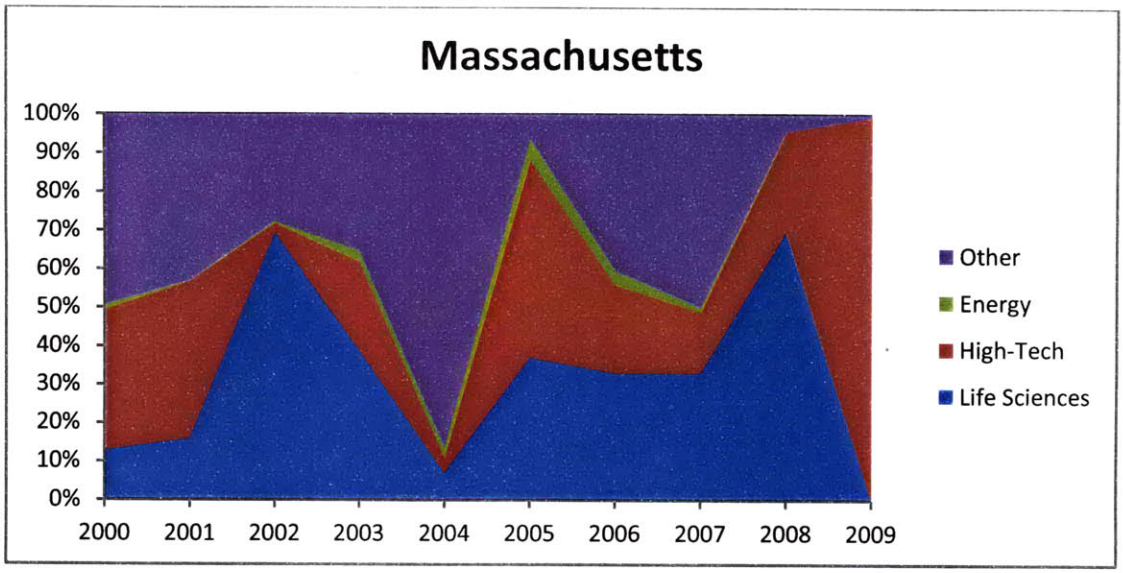

Figure 7: Percentage of Funding Raised by Industry Focus for Massachusetts

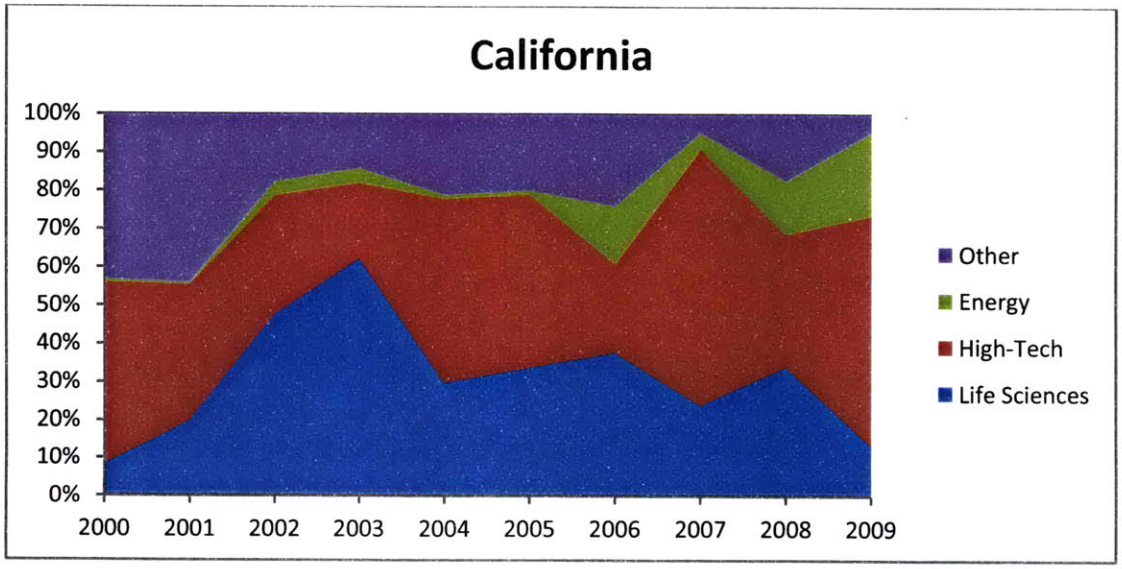

Figure 8: Percentage of Funding Raised by Industry Focus for California

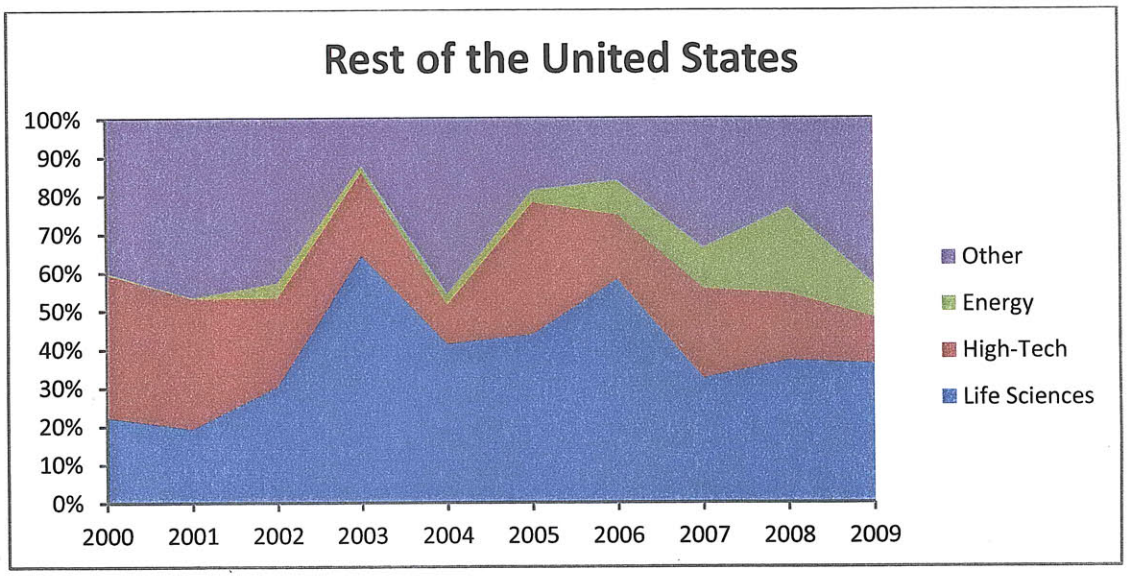

Figure 9: Percentage of Funding Raised by Industry Focus for the Rest of the United States

Since life sciences is the primary area of interest to this work, Figure 10, Figure 11, and Figure 12 treat life sciences venture capital focused fundraising explicitly. The figures each display three data series. First is the percentage of the region's overall investment in sector-specific venture capital going to life sciences portfolios. Second is the fraction of overall venture capital funding raised relative to the amount raised in calendar year 2000. Finally the fraction of life sciences specific venture capital investment raised relative to the amount of life sciences specific venture capital investment raised in calendar year 2000 is included.

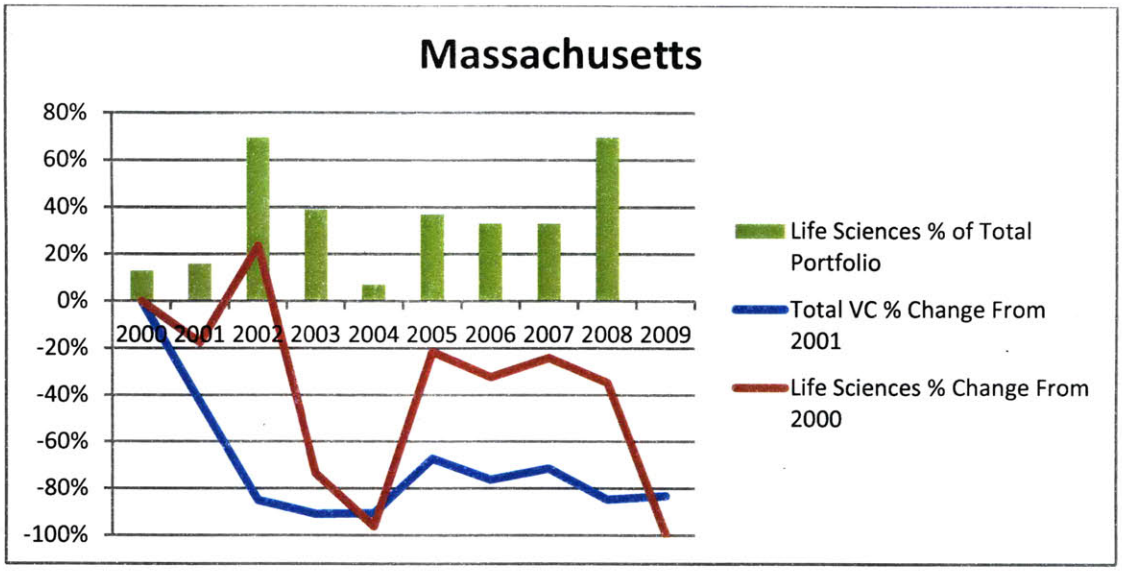

Figure 10: Investment in Massachusetts Life Sciences Focused VC Funds

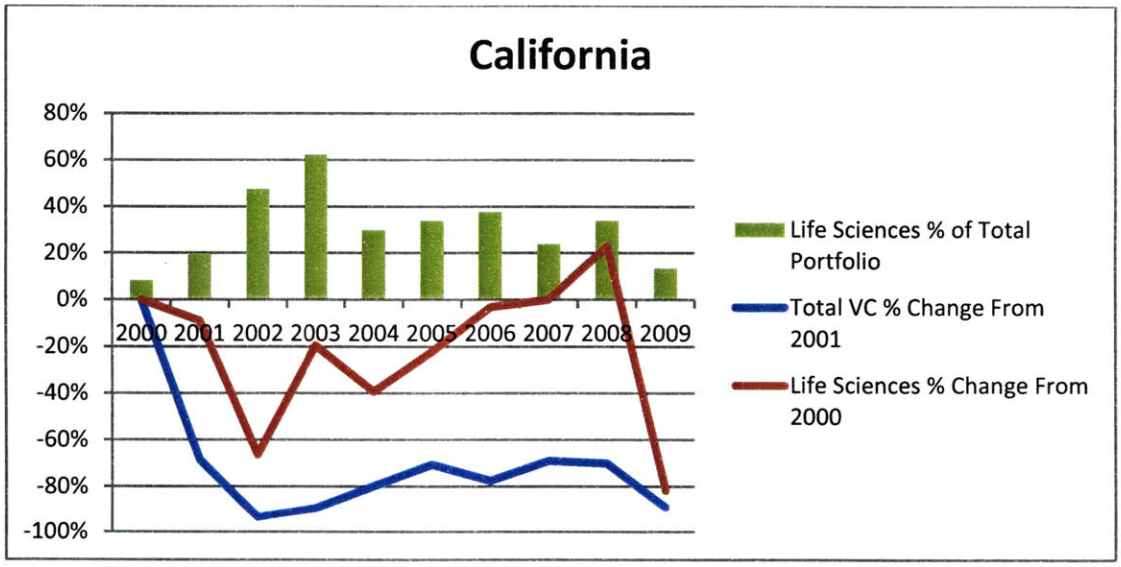

Figure 11: Investment in California Life Sciences Focused VC Funds

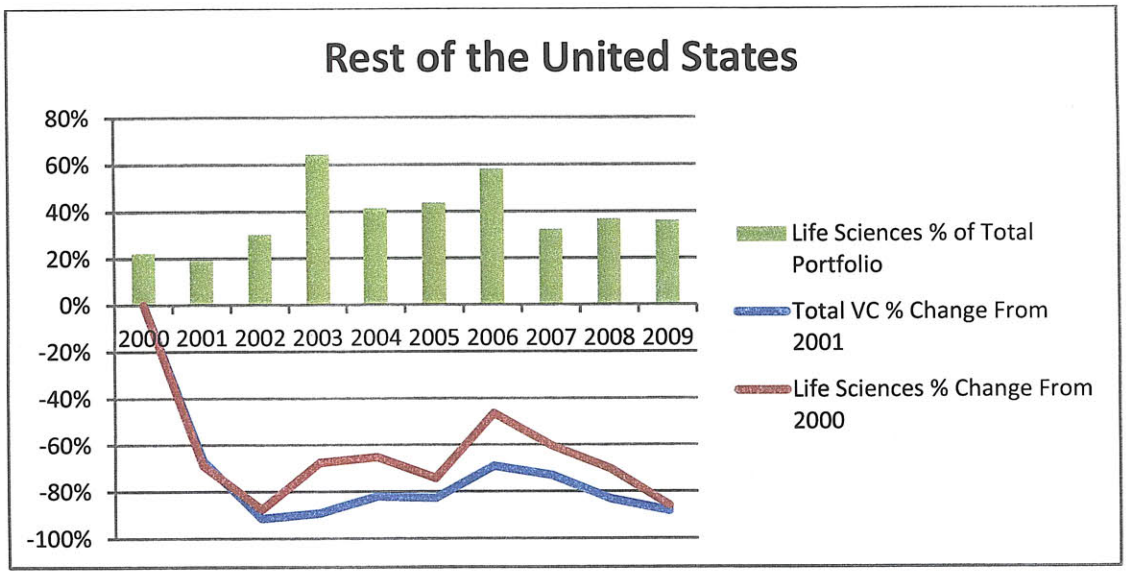

Figure 12: Investment in Life Sciences Focused VC Funds for the rest of the United States

The rest of the United States shows life sciences being impacted over the entire decade at about the same rate as overall venture capital investment. Life sciences portfolios grew from receiving about a fifth of total investment in venture capital to over a third by the end of the decade. That fraction has stayed roughly constant. This accounts for the slight outperformance by life sciences focused venture capital over total venture capital fundraising in 2002 and 2003 followed by life sciences venture capital trending with overall venture capital for most of the rest of the decade and only a slightly worse fundraising performance in 2009 than in previous years.

In the two life sciences heavy regions of the country, though, investment in life sciences focused venture capital portfolios has languished since 2008 after a dramatic increase earlier in the decade. Massachusetts demonstrates this trend with the greatest clarity, having had life sciences investment represent some 70% of total sector targeted investment in 2008 and dropping to zero within a year.

Table 2 below presents statistical analysis to determine whether any sector, including life sciences, behaves differentially year-on-year from another sector. For example, the category "MA Energy" is the data set of the year-on-year changes from year 2000 through year 2009 for energy specific venture capital funds within Massachusetts. The test was performed between each category pair that was thought to behave in a similar manner. Specifically we tested every fundraising category within a region against every other category within that region and we tested every fundraising category against that same fundraising category for every other region. It shows that over the course of the decade there

were no statistically significant differences in the mean year on year change in any of our region-fundraising category pairs. That is to say statistically year on year changes throughout venture capital fundraising, including the relationship between life sciences funding and overall VC funding, were not differentially impacted.

Table 2: P-values for difference-in-means test for year on year VC funding

		All VC			Life Sciences			Energy			High Tech			Other		
		MA	CA	Rest of the United States	MA	CA	Rest of the United States	MA	CA	Rest of the United States	MA	CA	Rest of the United States	MA	CA	Rest of the United States
All VC	MA		0.880	0.753	0.434			0.533			0.294			0.766		
	CA			0.832		0.896			0.330			0.488			0.747	
	Rest of the United States						0.816			0.177			0.930			0.477
Life Sciences	MA					0.427	0.423	0.598			0.473			0.501		
	CA						0.945		0.341			0.530			0.821	
	Rest of the United States									0.223			0.779			0.557
Energy	MA								0.545	0.779	0.339			0.751		
	CA									0.637		0.464			0.371	
	Rest of the United States												0.175			0.620
High Tech	MA											0.321	0.283	0.312		
	CA												0.415		0.667	
	Rest of the United States															0.466
Other	MA														0.847	0.861
	CA															0.683
	Rest of the United States															

*: Result significant at 10% level
**: Result significant at 5% level
***: Result significant at 1% level

Table 3: Year-on-year change investing in venture capital

	2008 Change in Investment From Prior Year	2009 Change in Investment From Prior Year
Massachusetts All VC	-47%	+10%
Massachusetts Life Sciences VC	-14%	-100%
California All VC	-3%	-64%
California Life Sciences VC	+23%	-85%
Rest of the United States All VC	-38%	-30%
Rest of the United States Life Sciences VC	-25%	-53%

Contrary to the finding of no decade long differential impacts, the special case of 2008 suggests that this most recent economic downturn has had a more severe impact on life sciences venture capital funding than overall venture capital. Table 3 shows that life sciences venture capital investment in fact was differentially impacted from overall venture capital fund raising in the post-second downturn timeframe. For the entire part of the decade from 2000 through 2008, life sciences focused venture capital funds had far greater success in fund raising than other sectors and as recently as 2008 life sciences venture capital was faring moderately better in fund raising than venture capital as a whole. 2009 brought on a complete reversal. Life sciences venture capital performed far worse than overall venture capital. Considering the prior success that life sciences venture capital firms had been used to this was a tremendous plunge. Table 4 reinforces this conclusion.

Table 4: P-values of one sided t-test of mean of pre-downturn years being greater than amount raised in post-downturn years

	2008 Funding Raised	2009 Funding Raised
Massachusetts All VC	0.100*	0.138
Massachusetts Life Sciences VC	0.675	0.025**
California All VC	0.899	0.006***
California Life Sciences VC	0.988	0.003***
Rest of the United States All VC	0.077*	0.021**
Rest of the United States Life Sciences VC	0.114	0.012**

*: Result significant at 10% level
**: Result significant at 5% level
***: Result significant at 1% level

In 2008 two out of the three regions of interest show that the amount of overall venture capital funding was reduced from pre-second downturn levels at a 10% confidence level. However in all cases life sciences funding raised was not clearly different from the mean of funding raised pre-second downturn at the 10% confidence level. In 2009, however, across all three regions there is greater statistical evidence suggesting that fundraising for life sciences in that year was lower than life sciences funding

raised in the pre-second downturn years than there was evidence supporting that same conclusion for overall venture capital fundraising.

Hypothesis 2: The number of life sciences focused companies being invested in by venture capitalists has declined significantly

From this point onward in this chapter, all results will pertain solely to life sciences companies and life sciences venture capital investment.

This hypothesis supposes that with fundraising constricted the number of companies that venture capitalists invest in will decline. This question has been explored along two dimensions: total number of companies invested in and companies receiving first time investment. To further put this measure of innovativeness into context, the following charts show companies receiving first time investment as a percentage of all companies receiving investment. In time periods when tolerance for risk is high this ratio should also be high. The converse should be true as fear of risk begins to take over and most investments made go into already pre-existing companies.

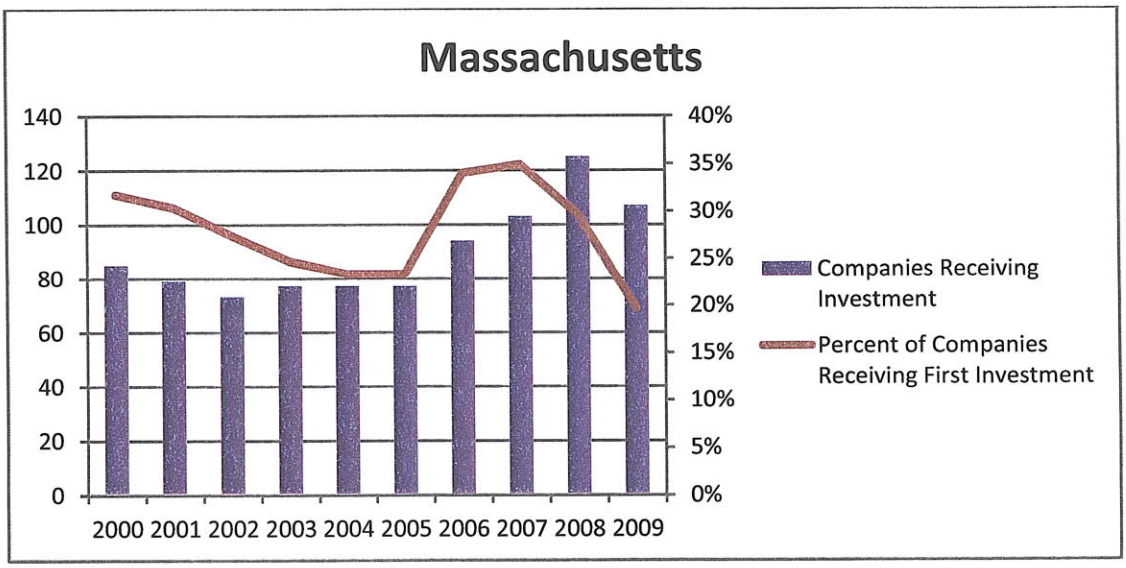

Figure 13: Companies Receiving VC Investment in Massachusetts

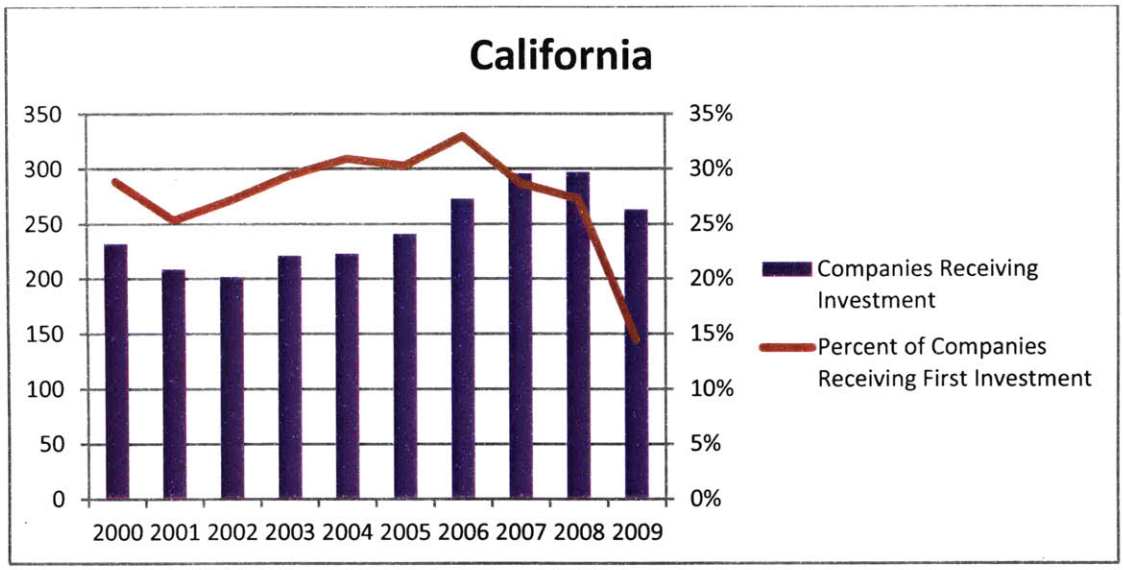

Figure 14: Companies Receiving VC Investment in California

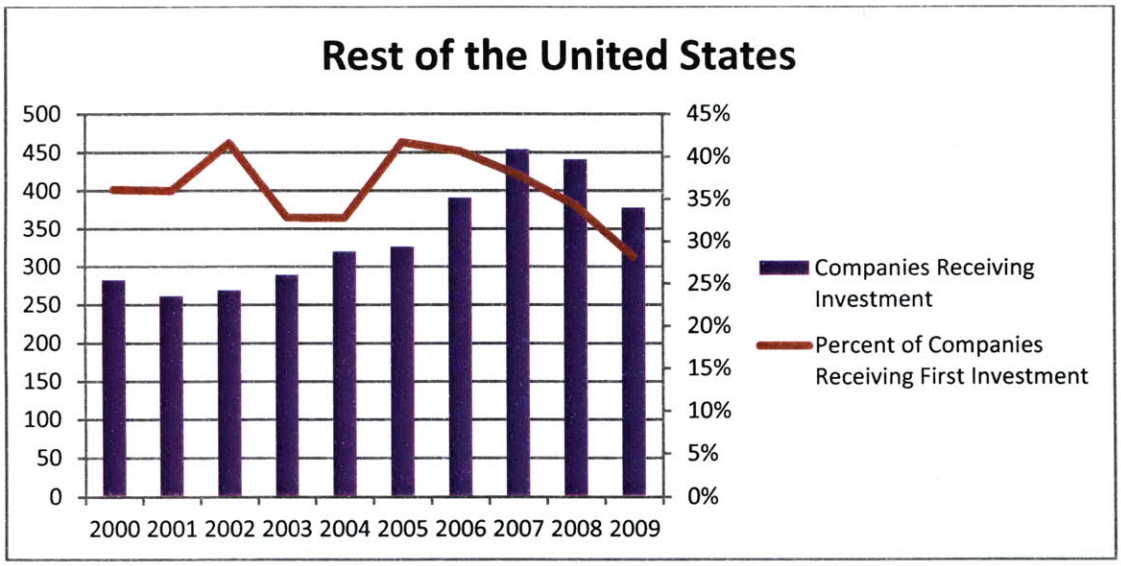

Figure 15: Companies Receiving VC Investment in the Rest of the United States

Figure 14, and Figure 15 all tell the same very interesting story. Over almost the entire decade the number of life sciences companies receiving funding had been on the increase. The downturn of 2001 saw two years of slight decline in companies funded (less than a 10% decline year-on-year within each region) followed by six years of modest to substantial increase. 2009 was only the third time all decade that each of the three regions saw a decline in the number of companies funded. Although it was the most drastic decline all decade, the impact thus far has not been all that substantial. Each region saw no

worse than a 15% decline in the number of companies funded; a relatively small decrease when compared with the tremendous decreases in funding demonstrated in Table 3.

Table 5: P-values of one sided t-test of mean of pre-downturn years being greater than number of companies funded in post-downturn years

	2008 Companies	2009 Companies
Massachusetts Total Funded Companies	0.995	0.971
Massachusetts First Time Funding Companies	0.950	0.182
Massachusetts First Time Companies as Percent of Total Companies	0.619	0.035**
California Total Funded Companies	0.951	0.605
California First Time Funding Companies	0.627	0.002***
California First Time Companies as Percent of Total Companies	0.012**	0.0002***
Rest of the United States Total Funded Companies	0.941	0.549
Rest of the United States First Time Funding Companies	0.688	0.043**
Rest of the United States First Time Companies as Percent of Total Companies	0.061*	0.007***

*: Result significant at 10% level
**: Result significant at 5% level
***: Result significant at 1% level

What is more startling is the decline in the relative share of companies receiving first time funding. Table 5 shows there is statistical evidence to suggest a drop in the relative percentage of new companies receiving funding in California and the rest of the United States as early as 2008 although the difference in the number of total companies funded and the number of new companies funded is not statistically different. 2009 saw a clear and significant decline in the funding of new companies. All three regions of interest showed highly significant evidence of decline in the rate of new companies being funded and two of the three regions, again California and the rest of the United States, demonstrated evidence of decline in the number of new companies being funded also. Interestingly, again no region showed significant evidence in a decline in total number of companies receiving funding.

Hypothesis 3: The amount of money invested into life sciences focused companies that are receiving investment has declined significantly

The previous hypothesis demonstrated that the number of companies receiving venture capital investment has not been severely impacted but it has been noted that investment in venture capital has declined substantially. One possible way to reconcile these two findings is if each company invested in has received substantially less funding. This can be explained in two ways. As venture capital funds have themselves received less funding they may simply have less money to distribute. Alternatively, the decline in funding has caused a significant decline in venture capitalist optimism. This has translated into

VC firms keeping more of their money in reserves because they worry that their current decline in revenue will affect their future ability to invest and so it is more important that they retain a rainy day fund. This second scenario is more likely because venture capital funds rarely invest the money they raise immediately. Raising a full fund can take years and then investing it also occurs over the life of the fund. Therefore the fundraising issue faced by venture capitalists in today's market probably affects their optimism towards investing more strongly than it does their actual ability to invest.

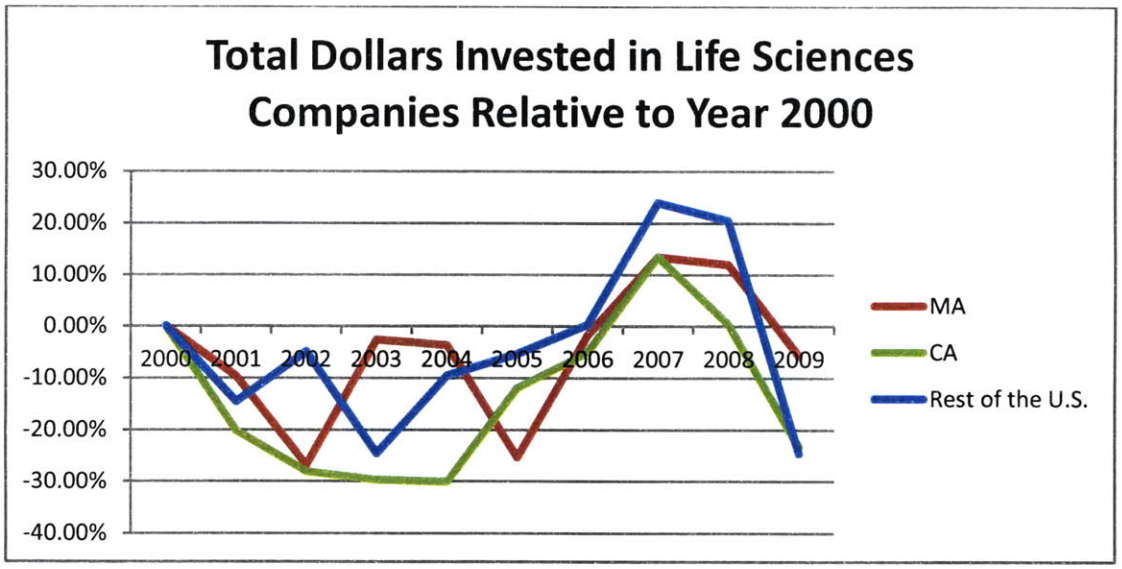

Figure 16: Venture Capital Dollars Invested in Companies Located in the Regions of Interest

Figure 16 shows that the market crash of 2000 saw a rapid and marked conservatism in VC investment in life sciences companies. Similar to what was seen in venture capital fundraising trends, California companies saw the most rapid and severe decline in funding. Massachusetts life sciences companies and the rest of the country fared relatively better. As economic optimism returned mid-decade life sciences companies received record levels of funding across all regions of interest, but California and Massachusetts companies were outpaced at the peak of investment by the rest of the country.

The most recent downturn, however, has had a sobering effect on venture capital investment in life sciences companies. In only two years investment dropped from the 2007 peak by 17% percent in Massachusetts, 33% in California, and 39% in the rest of the United States. Funding for the industry was lower in 2009 than it had been in four years for California and lower than at any other point in the decade for the rest of the United States. Massachusetts appears to have performed better than the other regions of interest. While indeed declining in investment in life sciences companies,

Massachusetts has done so at a slower rate than the other regions and 2009 funding levels are still near 2006 levels. Table 6 verifies this finding. It shows that there is little statistically significant evidence to show that the total funding of Massachusetts life sciences companies was decreased in either 2008 or 2009 relative to pre-second downturn levels but there is evidence supporting the finding that California and the rest of the United States saw a decline in 2009.

Table 6: P-values of one sided t-test of mean of pre-downturn years being greater than dollars invested in life sciences companies in post-downturn years

	2008 Dollars Invested	2009 Dollars Invested
Massachusetts	0.933	0.433
California	0.799	0.099*
Rest of the United States	0.954	0.018**

*: Result significant at 10% level
**: Result significant at 5% level
***: Result significant at 1% level

Figure 17 and Table 7 show that there has been a very mixed impact on the average amount of funding received per life sciences company being funded. By 2008 Massachusetts average funding had dropped by a third from a relative peak in the 2004 timeframe. However this decline began before the economic downturn of 2007 and in contrast to the other two regions of interest, Massachusetts companies saw an increase in average funding in 2009. California has been the most stable of the three regions in terms of average funding. Although it has seen declines in this parameter in 2008 and 2009, those declines have been a more modest 14%. The rest of the United States saw yet a different trend. Funding per company was relatively stable in 2008 from 2007 but there was a sharp drop of 21% in 2009. Each region also had a different response to the downturn of 2000. Massachusetts had funding levels remain stable, California saw a drastic decline that continued for four years and the rest of the United States fluctuated while overall trending downwards. Table 7 shows that these mean measurements must be taken with a caveat. The standard deviations, and thus the variations in amounts received by different companies, are quite large relative to the means. This large spread means that although there have been changes in the mean investment amount, the actual amounts that individual companies receive varies wildly.

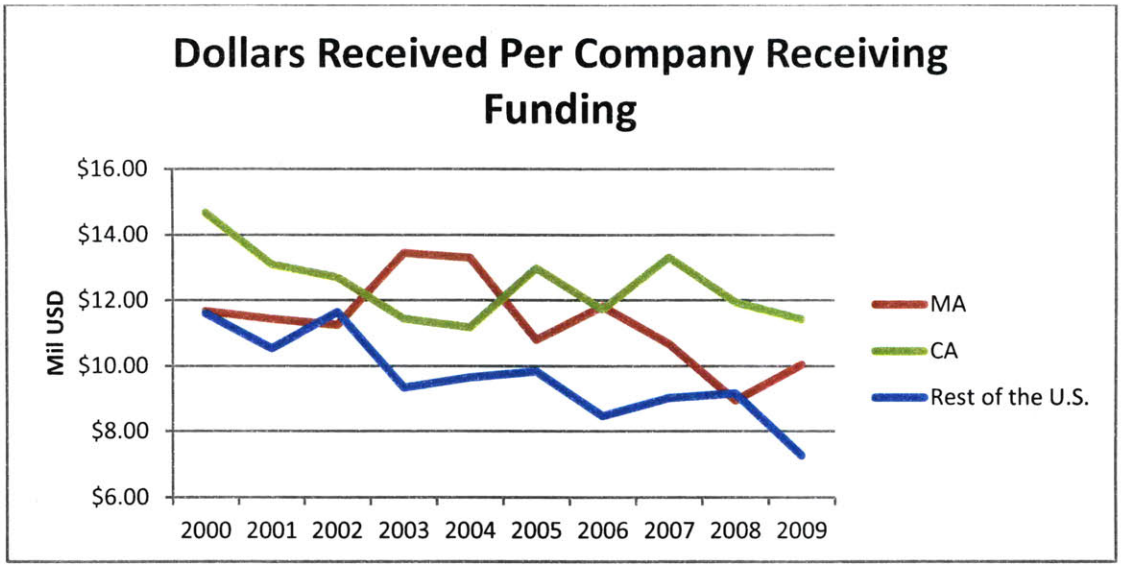

Figure 17: Average Dollars Received per Company Receiving VC Funding Located in the Regions of Interest

Table 7: Mean (standard deviation) for average amount of funding received by life sciences companies

Year	MA	CA	Rest of the U.S.
2000	11.681 (17.980)	14.677 (17.531)	**11.608 (19.365)**
2001	11.440 (13.734)	13.100 (15.179)	**10.535 (15.633)**
2002	11.257 (12.684)	12.702 (14.222)	**11.642 (20.023)**
2003	13.442 (14.372)	11.440 (14.916)	**9.332 (18.484)**
2004	13.301(14.494)	11.183 (13.077)	**9.646 (14.904)**
2005	10.797 (9.535)	12.974 (16.058)	**9.824 (20.824)**
2006	11.817 (15.145)	11.722 (14.575)	**8.454 (13.311)**
2007	10.683 (11.170)	13.309 (15.737)	**9.015 (14.373)**
2008	8.952 (10.869)	11.946 (14.114)	**9.161 (23.135)**
2009	10.040 (10.405)	11.423 (13.287)	**7.252 (11.897)**

Figure 18 presents the average investment received by companies receiving their first investment round. While one might expect that the funding that these earliest stage companies receive would show the same type of decline as overall corporate funding, the data tell a different story. Each region has behaved slightly different with respect to the funding of first time companies. Massachusetts life sciences companies receiving their first investment saw mild declines in the amount they received from 2007 to 2009. California companies have experienced a small gain over this period and the rest of the United States, while experiencing a sharp decline from 2007 to 2008 actually recovered quite a bit in 2009.

The above two trends, with the exception of the 2009 spike experienced by California, suggest that there may be flexible funding and non-flexible funding for life sciences companies. The amounts received for all companies have a year-to-year variation of about $5 million while new companies exist with a year-to-year variation of about $3 million. Newly founded companies may require a well-known amount of money (seemingly about $7 - $8 million) to get started and prove themselves regardless of what macro-economic conditions are. Venture capitalists wishing to invest in new companies would need to provide this amount of funding in order for these companies to have a chance of succeeding. Although fewer such companies may be invested in, a trend demonstrated by Hypothesis 3, the amount of money they receive is more constant. Existing companies, on the other hand, may have more flexibility in the amount of money they receive. It may be possible for these companies to operate on leaner budgets by cutting their development pipeline or focusing on specific applications of existing products. This would make existing companies an easy target for cost savings by cash-strapped venture capitalists. Table 8 suggests that these results should be considered with the same funding per company caveat as total average funding because of the company-to-company standard deviation compared to the funding mean.

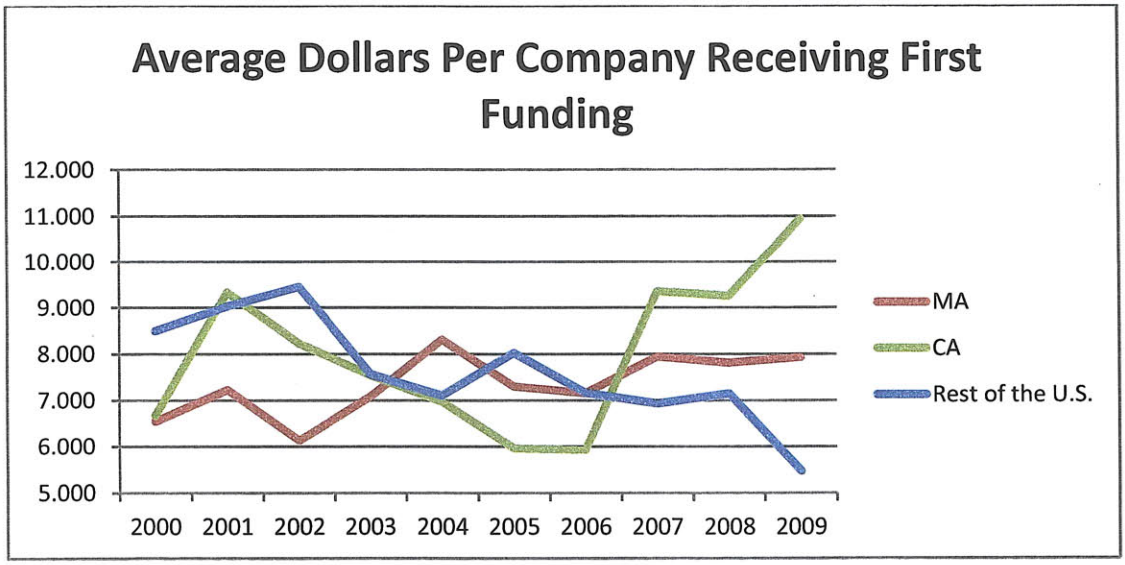

Figure 18: Average Dollars Received per Company in First VC Round Located in the Regions of Interest

Table 8: Mean (standard deviation) for average amount of funding received by first time funding life sciences companies

Year	MA	CA	Rest of the U.S.
2000	$6.539 (9.818)	$6.665 (10.621)	$8.487 (15.834)
2001	$7.230 (7.821)	$9.337 (20.017)	$9.026 (18.844)
2002	$6.123 (5.432)	$8.223 (10.399)	$9.447 (18.434)
2003	$7.082 (7.996)	$7.540 (16.220)	$7.562 (20.531)
2004	$8.306 (10.059)	$6.961 (8.105)	$7.095 (13.650)
2005	$7.293 (9.999)	$5.954 (7.791)	$8.008 (27.225)
2006	$7.148 (7.895)	$5.919 (6.868)	$7.150 (14.101)
2007	$7.934 (7.376)	$9.346 (12.986)	$6.917 (12.866)
2008	$7.804 (10.032)	$9.246 (15.526)	$7.139 (11.665)
2009	$7.924 (10.453)	$10.948 (12.867)	$5.457 (10.885)

Hypothesis 4: The types of life sciences companies (i.e. molecule development, medical devices, other biotechnology) that venture capitalists are funding is changing in an attempt to lower exposure to "risky" industries

Medical device companies are thought to be safer bets to invest in than drug development or other biotechnology companies are. Devices have a lower regulatory burden than drugs do and so require less time and money spent on clinical testing. The research and development costs are also often lower. The electrical, computational and/or mechanical needs of devices are often less complex to develop, verify and scale up than the advanced chemistry necessary for the other industrial subsectors. For these reasons it might be expected that in a period of high risk and low optimism investors would allocate a greater share of their portfolio to devices or make other resource allocation decisions in response to a funding shock.

Figure 19, Figure 20, and Figure 21 below show that movement towards the perceived safety of medical device investment has not happened in response to either the downturn of 2008 or the downturn of 2001. In each geographic region of interest the portfolio mix has maintained roughly the same level of proportional representation for medical devices, drug discovery, and biotechnology projects not encompassed by drug discovery.

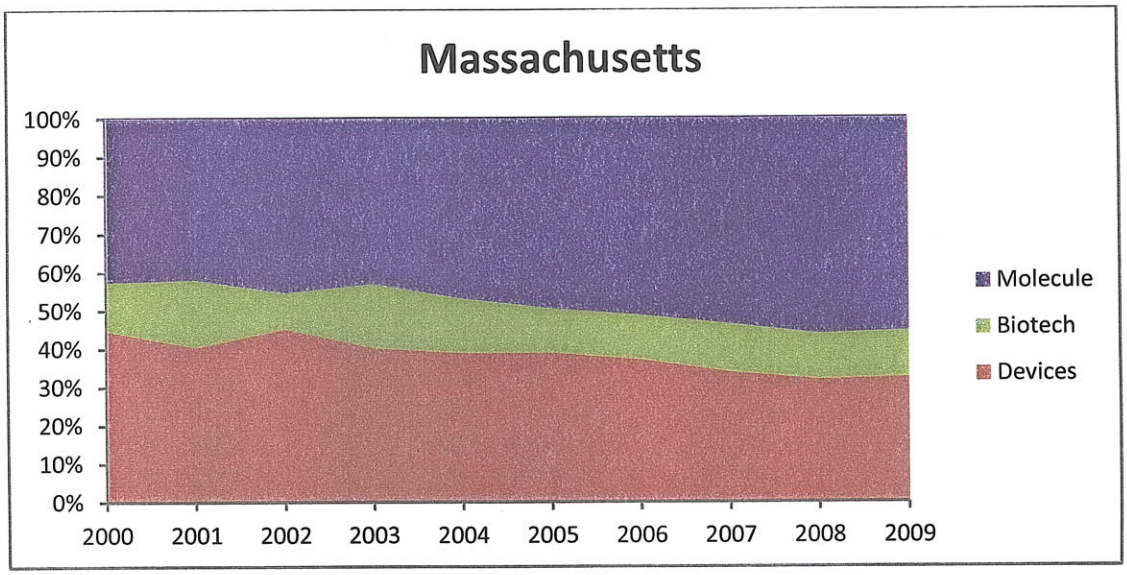

Figure 19: Massachusetts Life Sciences Investment Mix

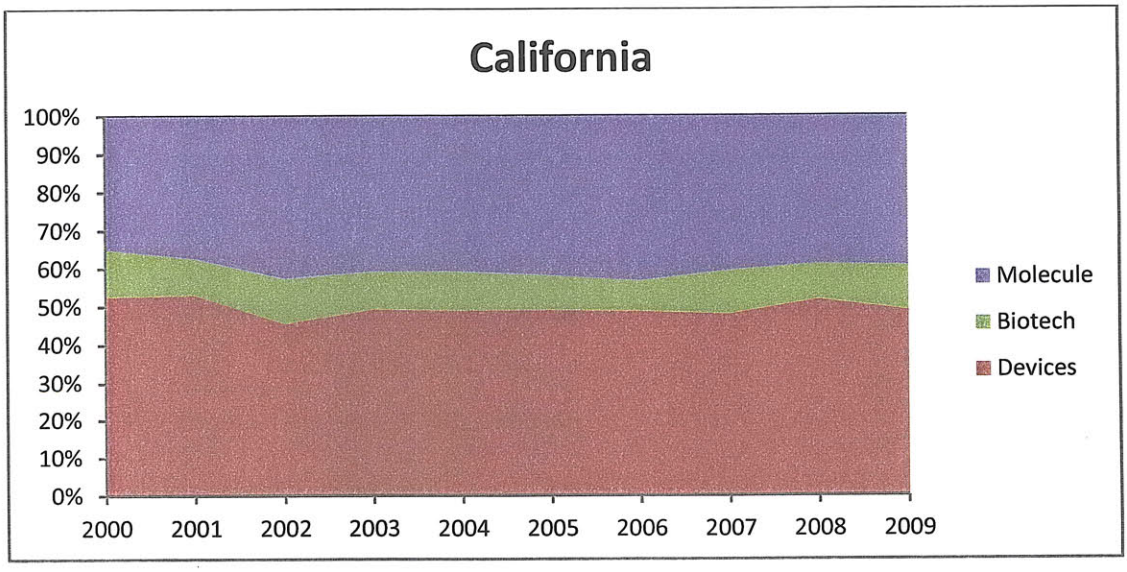

Figure 20: California Life Sciences Investment Mix

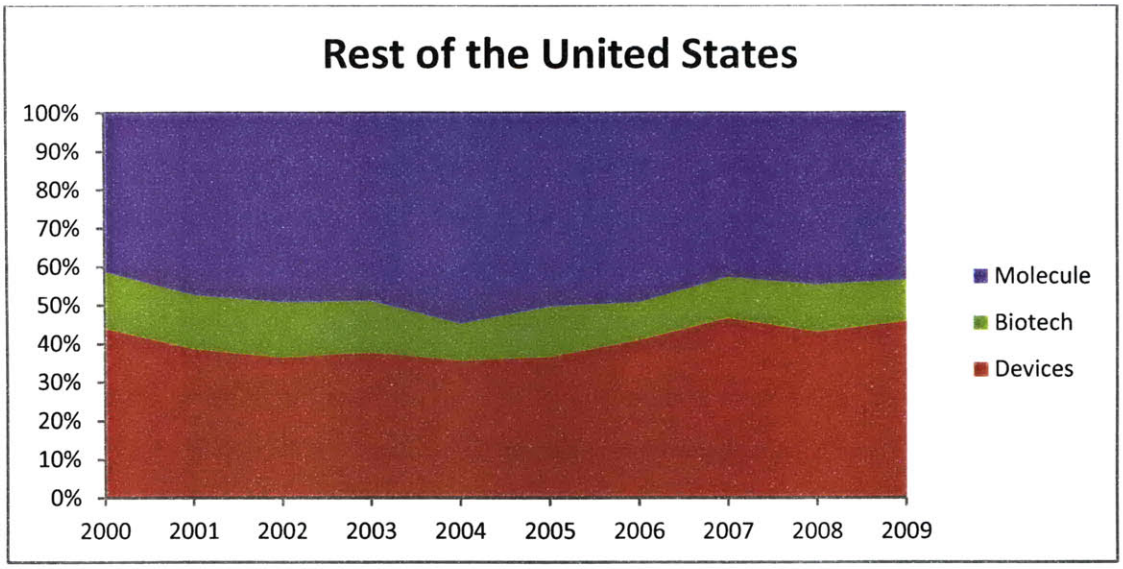

Figure 21: United States Except for Massachusetts and California Life Sciences Investment Mix

Table 9 shows that even though changes in portfolio allocation were not large, because of the stability of pre-downturn times the minor variations of post-downturn years actually were statistically significant. Massachusetts saw allocation changes in both 2008 and 2009 in molecule and medical device sectors. Interestingly these changes were the opposite of those hypothesized. Devices fell to 33% of the state portfolio from a pre-second downturn average of 37% while molecule development rose to 56% from 50%. California demonstrated the opposite trend and made a slight move towards devices and a slight decrease from molecule and biotech companies. There is only slight evidence that the rest of the United States saw these types of changes. 2009 is the only year in which any such evidence exists at a statistically significant level and even then the p-value is very close to the 10% threshold.

Table 9: P-values of two sided t-test of mean in pre-downturn years being different than portfolio composition in post-downturn years

		2008 Percentage of Portfolio	2009 Percentage of Portfolio
Massachusetts	Molecule	0.025**	0.040**
	Biotech	0.416	0.416
	Devices	0.020**	0.036**
California	Molecule	0.023**	0.023**
	Biotech	0.387	0.056*
	Devices	0.001***	0.203
Rest of the United States	Molecule	0.133	0.092*
	Biotech	0.264	0.918
	Devices	0.313	0.097*

*: Result significant at 10% level
**: Result significant at 5% level
***: Result significant at 1% level

The smooth, unchanging behavior exhibited by the above figures may simply be an artifact of the investment cycle of venture capital firms. As has been previously established, most of the investments that venture capitalists make are reinvestments in pre-existing companies. Reinvesting over and over in the same companies could, then, hide the impact that the economic downturn would have on the new companies that venture capitalists choose to fund. Figure 22, Figure 23, and Figure 24 test this by analyzing the investment mix of only companies receiving their first time funding in a given year.

Again, this test does not appear to indicate any large shifts in portfolio composition strategy. Although the focus of companies receiving first time funding does have greater variance than does the analysis of all portfolio companies, two of the three regions (California and the rest of the United States) have allocation changes of less than ten percent in any of the investment focus areas over the entire decade. Massachusetts is more volatile than the other two regions but it is neither medical devices nor drug development companies that lose out in this volatility. In certain years relatively fewer non-drug biotechnology companies are funded. These spurious years do not appear to be related to either the economic downturn of 2000 or the more recent downturn.

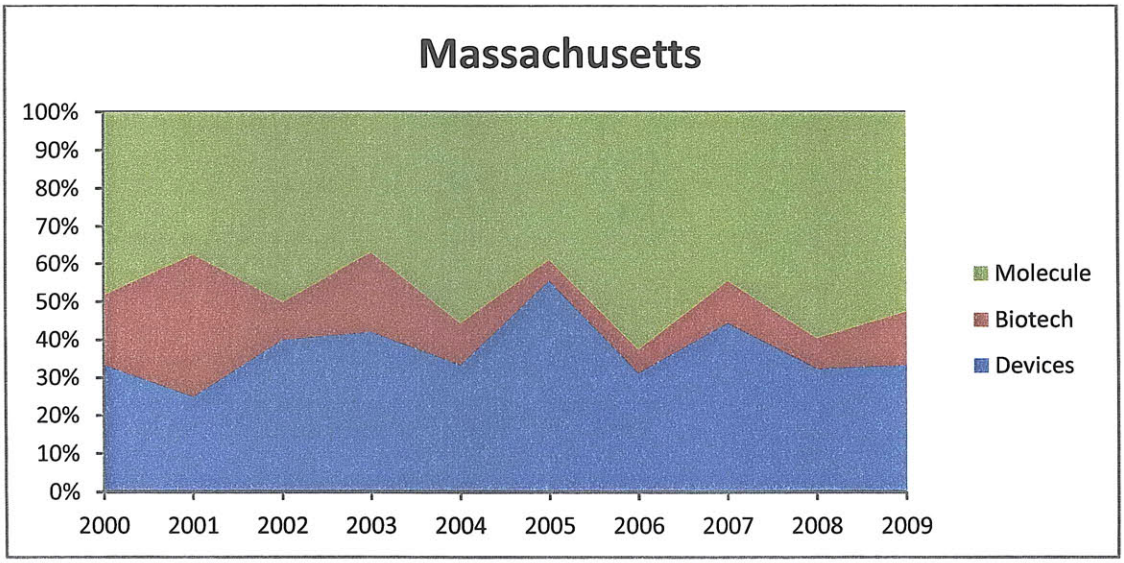

Figure 22: Massachusetts Investment Mix of Companies Receiving First Funding

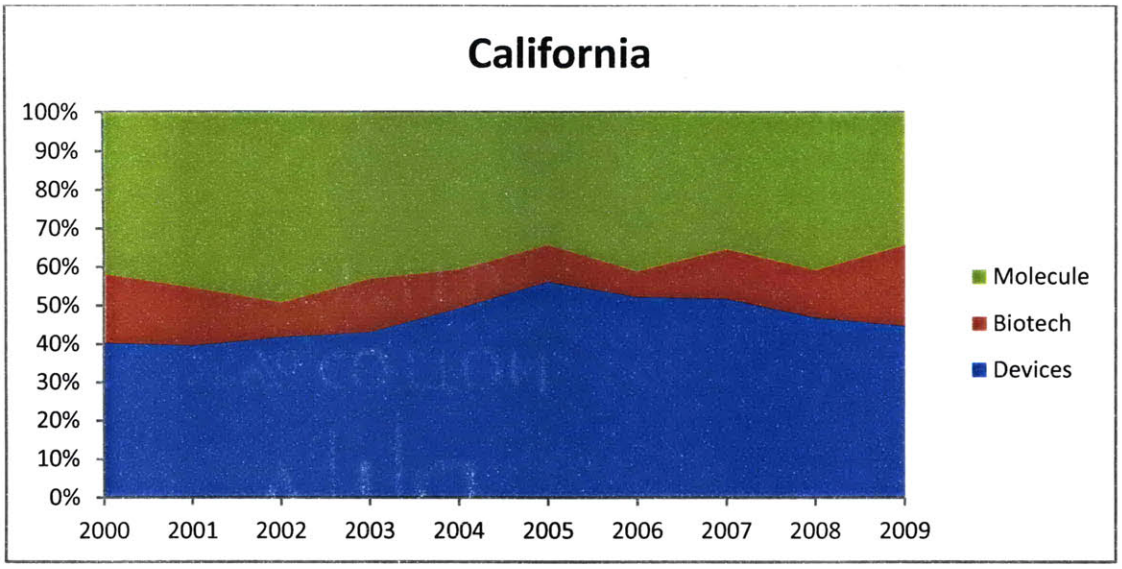

Figure 23: California Investment Mix of Companies Receiving First Funding

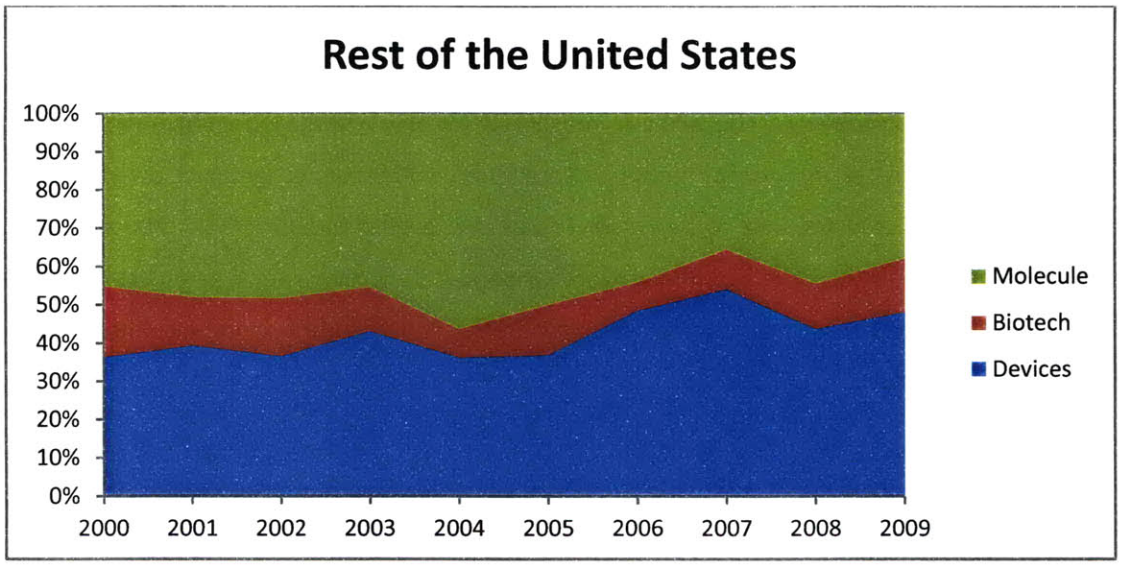

Figure 24: United States Except for Massachusetts and California Investment Mix of Companies Receiving First Funding

Because there is more historical variation in the types of new companies receiving funding there is less statistical evidence of a change in resource allocation to new companies. Table 10 shows that Massachusetts has seen no significant change in resource allocation during post-second downturn years while California saw a decline in new device companies in both 2008 and 2009 and an increase in biotech companies in 2009. The rest of the United States saw a slight increase in new biotech companies in 2009.

Table 10: P-values of two sided t-test of mean in pre-downturn years being different than portfolio composition in post-downturn years for newly funded companies

		2008 Percentage of Portfolio	2009 Percentage of Portfolio
Massachusetts	Molecule	0.203	0.777
	Biotech	0.759	0.036
	Devices	0.202	0.242
California	Molecule	0.169	0.121
	Biotech	0.191	0.003***
	Devices	0.033**	0.014**
Rest of the United States	Molecule	0.622	0.153
	Biotech	0.191	0.051*
	Devices	0.977	0.418

*: Result significant at 10% level
**: Result significant at 5% level
***: Result significant at 1% level

Hypothesis 5: A greater portion of the VC portfolio is being allocated to later stage, less risky companies than higher risk early and seed stage companies

Investments made in later stage companies are usually less risky than investments made in earlier stage companies. Later stage companies have proven themselves by meeting early stage milestones and may even have revenue streams. As the analysis presented for Hypothesis 4 demonstrated, later stage companies require greater amounts of money invested than earlier stage companies do. However, later stage companies are also thought to be closer to liquidity events because their products should be further developed than the offerings of younger companies. Because later stage investments are less risky than earlier stage ones it might make sense that in times of downturn more investments are made in later stage companies.

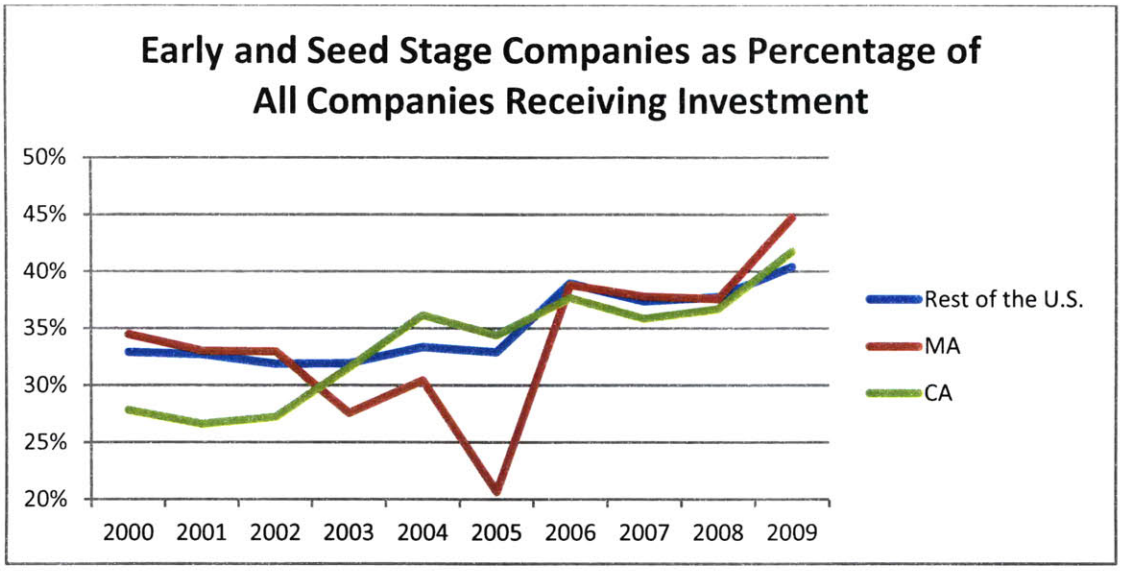

Figure 25: Early and Seed Stage Companies as a Percentage of all Companies Receiving Investment

Figure 25 indicates that this hypothesis is also not correct. This figure plots the fraction of investments made in companies that VentureXpert identifies as seed stage or early stage companies as a percentage of all companies invested in for a given year. With very little exception the decade has seen a steady increase in early stage investment. If anything, the downturn of 2008 has seen an acceleration of this trend. It is important to note that investment in early stage companies is different from investment in companies receiving first time funding (which has been shown to have been reduced in 2009). Early stage companies can have received reinvestment whereas first time funded companies cannot have by definition. Table 11 verifies that there is no statistically significant evidence to support the initial hypothesis in any region of interest for any time period.

Table 11: P-values of one sided t-test of mean in pre-downturn years being greater than rate of early and seed companies funded in post-downturn years

	2008 Percent Early and Seed	2009 Percent Early and Seed
Massachusetts	0.121	0.978
California	0.884	0.999
Rest of the United States	0.806	0.806

*: Result significant at 10% level
**: Result significant at 5% level
***: Result significant at 1% level

Hypothesis 6: A greater portion of the VC portfolio is being reinvested in existing portfolio companies to help these companies "weather the storm"

A venture capital portfolio is developed over a number of years and is relatively illiquid. Companies that venture capitalists invest in must be protected until they either fail or reach a liquidity event. As economic conditions make venture capitalists more conservative it is hypothesized that they would be more protective of existing portfolio companies and less interested in investing in new companies. Hypothesis 3 provided some evidence of this by demonstrating the relative decrease in the fraction of companies receiving funding that is comprised by companies receiving their first funding round.

Figure 26 explicitly looks at the fraction of all investment deals that are follow-on investments. A deal is defined as one venture capital firm funding one company. A funding round that involves a syndicate of several VCs funding one company is treated as containing several deals; one for each VC involved in the round. A follow-on investment is a deal in which the venture capital firm has invested in the company in question previously. This figure reinforces the hypothesis that reinvestment is more frequent in downturn. Reinvestment increased drastically in Massachusetts and the rest of the United States following the downturn of 2001. From 2003 through 2007 reinvestment behavior was mixed amongst the different regions of interest. After 2007, though, the reinvestment rate began to rise and this increase happened at a faster rate in 2009 in Massachusetts and California.

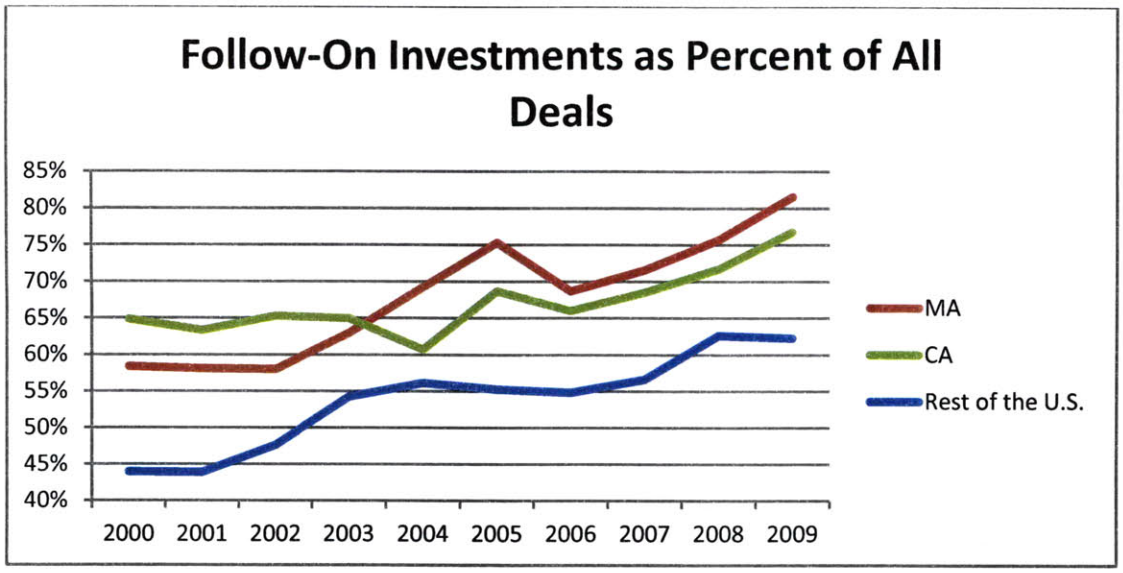

Figure 26: Fraction of Venture Capital Deals that are Follow-On Investments

This final hypothesis has the greatest amount of statistical support. Table 12 shows that in every region of interest and for both post-second downturn years there is highly significant evidence in support of rejecting the null hypothesis that there has been no change in follow-on investment in favor of the alternative hypothesis that follow-on investment has increased.

Table 12: P-values of one sided t-test of mean in pre-downturn years being lower than rate of follow-on investment in companies funded in post-downturn years

	2008 Percent Follow-On	2009 Percent Follow-On
Massachusetts	0.024**	0.003***
California	0.024**	0.005***
Rest of the United States	0.0002***	0.0003***

*: Result significant at 10% level
**: Result significant at 5% level
***: Result significant at 1% level

5 Impact

The previous chapter presented data on the impact of financial downturn and how the life sciences venture capital industry has responded. This chapter explores the effects that the venture resource allocation has had on life sciences commercialization activity in Massachusetts. These effects are understood through the lens of interviews with seventy-six venture capitalists, entrepreneurs, philanthropic foundation directors, technology transfer office directors, community organization directors, and executives from both large and small companies and from across each of the life science domains focused on by this project.

Lemma 1: Ultimately venture capital is an industry that is slow to change strategy in the short run

The data analyzed in the last chapter indicated that contrary to prediction, venture capital investment strategy did not change in the short run in response to constrained capital. This conclusion was supported by interviews, but more strongly by what was not said than by what was said. Fourteen venture capitalists were asked (1) whether they had changed the focus of their target investment either in terms of the sector mix or stage mix of their portfolios, and (2) whether they had changed the rate at which they made investments. In the case of this first question, 85% of respondents (all but two) said that their strategy was unchanged. The other two indicated a slight favoring towards investment in medical devices. 77% of respondents said that they were not changing their rate of investment. The three who said they were changing all said that they were increasing their investment pace because they see a greater number of opportunities.

This finding supports an aspect of the venture capital ecosystem stressed in the literature: its inflexibility. The value of a good venture capitalist is built up over a long period of time. They bring not only capital to a successful investment but also a robust interpersonal network, and deep experience in troubleshooting the types of problems that their portfolio companies may encounter. These traits are particularly important for life sciences companies as many of these ventures need shepherding through a very high risk early stage. Even when downturn conditions occur, venture capitalists do not appear to change direction. This is likely due to the fact that their expertise and experience does not change. If a venture capitalist's network and operating experience is predominantly in medical devices or biopharmaceuticals, then that may be the area that they are most well suited to invest. In fact, it may be

more risky for a venture capitalist to invest in an area that he or she does not understand well because of a market downturn.

This brings up another reason explanation for the constancy of VC portfolio composition. Venture capitalists take a very long range perspective of their business. As one venture capitalist noted, "In a good environment startups are really hard and in a not good environment they're even harder. Anyone who thinks that the field has gotten much more difficult has not been in it." The nature of long term investing in companies requires a degree of focus on and adherence to strategy. Experienced venture capitalists have been in their industry for decades and have experienced capital market ebbs and flows. The business of guiding startups is never easy. With portfolios that last for up to a decade there is no reason for venture capitalists to overreact to economic conditions that are far shorter than that.

Lemma 2: Venture capitalists have become much more conservative in an effort to protect current holdings

Although venture capitalists take a long run approach to the types of companies that they invest in, they do appear to have a pragmatic (if not slightly panicked) approach to making new investments in periods of downturn. Another venture capitalist told us that he "Shifted reserves to existing companies pretty significantly. We assume that there is no follow-up capital out there so we want to make sure we have enough capital out there for our companies." As the previous chapter showed, investment in new companies appears to drop drastically during these times. 56% of the venture capitalists who were asked about these trends acknowledged decreasing investment in new companies to focus on their existing portfolio. Those who said they were making such a reduction cited a change of from 15% - 33% reduction in resources to new companies in favor of companies currently in their portfolio. This level of change is consistent with the drop in new companies funded observed in the data.

While 56% of respondents said that they were decreasing investment in new companies, the other 44% anticipated that their investment strategy was unchanged from the pre-downturn environment. These were venture capitalists that for whatever reason still had large amounts of cash on hand or that were directors of corporate venture funds (and therefore associated with a large company with cash set aside for the purpose of venturing).

Reinvestment in portfolio companies is just one conservative strategy employed by venture capitalists. Several other respondents said that they were placing more of an emphasis on forming syndicates and

choosing the right partners to co-invest with. "We would also be looking to put together larger syndicates than we were previously. We have to survive an uncertain economic period can't count on raising new money. We want other groups that have deep enough pockets that can continue to fund the company. Looking to other larger VCs from both coasts but that was always the same" said a venture capitalist echoing the sentiments of others. This points to another trend highlighted in the literature on venture capital investing. As an atmosphere of fear replaces one of greed, venture capital firms look to one another for reassurance. Larger syndicates are formed to double check investments and to provide a back-up source of capital should more money need to be raised.

Venture capitalists have also become more open to opportunities to exit their current portfolio than they were prior to 2008. The allure of obtaining a positive return, even if that return is at a lower rate than would be hoped for previously, has increased. Our interviews yielded many stories like this one: "We are working more with pharmaceutical companies and making creative deals using options on products and companies. It used to be that VCs didn't want to partner with big pharma because it capped their upside. We'll take capped upside now so long as we're getting reasonable return and think we'll get a higher chance of getting it released. "

The fear that many general partners find themselves haunted by today was what happened after the downturn of 2000. "There were a lot of funds that got started up in 2000, 2001 and 2002 and they had negative returns so they're not able to raise capital anymore" explained a long time venture capitalist. Capital markets will return eventually. When this occurs VCs will scramble to raise capital again so that they can launch new portfolios. Those whose portfolios did poorly during this downturn will find raising new money challenging. Because of this venture capitalists are anxious not only because of their need for funding now but because of their expected ability to raise new funds in the future. Protecting their current portfolio from destruction is a venture capitalist's best way to protect their own ability to raise funds when access to capital returns.

Lemma 3: VC conservatism combined with capital market trends has created a "buyers market"

The combination of constricted capital markets and reduced venture capital activity appears to have put downward pressure on private company valuations. As described above, many venture capital firms reduced their interest in funding new ventures in favor of reinvesting in their current portfolio. Startup

companies felt this pressure in terms of their own access to funding. A medical devices start-up executive told us that "people were slower to respond, because they were overwhelmed w/ many more opportunities than they could handle. Certainly some of the funds we approached had financing issues of their own. We certainly felt the ones that did express an interest in us were certainly using the economic times to their advantage when negotiating better terms." This experience was quite common amongst heads of small companies. The challenges that venture capitalist faced in raising money trickled down to entrepreneurs. Those VCs who did set aside money to invest were using it to negotiate favorable terms (equity stakes, liquidation rights, etc...) for themselves.

Venture capitalists are not the only group negotiating favorable terms, though. Ultimately big companies with available cash have been able to acquire smaller companies at reduced prices from 2007 levels. Another start-up CEO provided one instance of a story experiences by many small companies. "The offer [for acquisition] was 100% driven by the price and the dilutive nature of raising money. If the economy had been better, they would have had to offer a better alternative." Some interviewed entrepreneurs would say that this individual was lucky to even have received an offer for acquisition. A Boston investment banker focused on the healthcare sector pointed out that "there is a structural change going on in a lot of deals. The sales are beginning to look more like partnerships, meaning that the buyer will make milestone payments on assets they acquired as the results are achieved. And that's because the buyers have the capital and therefore the leverage." A biotechnology CEO and former venture capitalist said that big pharmaceutical and big biotech companies told him "We used to buy companies with platforms like yours but now we just buy the platforms or options on them." They pay for what works and don't take risks on things that don't, he explained.

Lemma 4: The economic downturn has had a strong and negative impact on innovation at many levels

The ultimate reason that there is an interest in studying the impact of the economic downturn on venture capital is because of the link between venture capital and innovation. The combination of venture investment data and interview results suggest that in the final analysis, economic downturn and the venture capitalist response has a strong and negative impact on innovation. That is to say, by impacting venture capital, economic downturn harms the translation of science into commercial applications.

The first step to validating this conclusion is to show that the production of good science that could turn into commercial products has not declined. If the production of ideas had been impacted, then any impact on commercialization could have been a factor of fewer ideas available to commercialize. This does not appear to be the case. For life sciences, most basic research is supported by United States federal agencies, and in particular the National Institutes of Health (NIH). Not only was NIH funding not negatively impacted in 2008, but it was increased by a stimulus from the American Recovery and Reinvestment Act of 2009. Total NIH grant funding in 2009 for Massachusetts was $2.8 billion, for California was $3.8 billion, and for the rest of the country was $19.1 billion (United States National Institutes of Health).

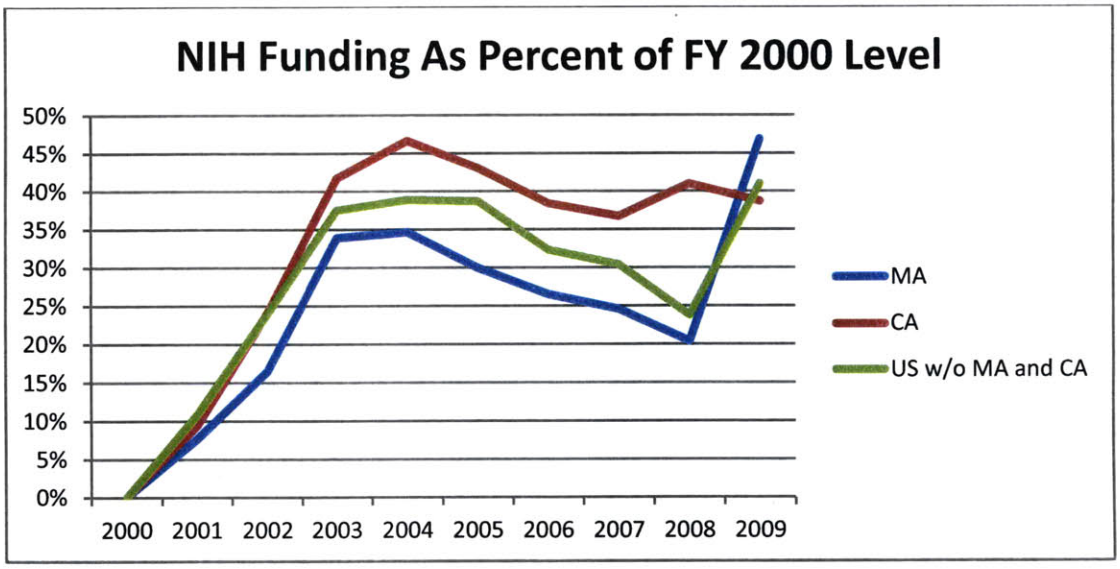

Figure 27: Change in NIH grant funding from FY 2000 levels

Another measure of scientific output that indicates production of ideas has not been majorly impacted is the rate of university technology licensing office activity. These offices are the interface between academic discovery and commercial markets. Under the Bayh-Dole act of 1980 allows universities to own the intellectual property developed from federal funding (such as from NIH grants). When faculty invent a process or product they are supposed to disclose details of the invention to their technology licensing office. The licensing office then decides whether or not to pursue patent protection for the invention and how to commercialize it. Figure 28 and Figure 29 demonstrate that at several leading institutes of scientific ideas neither the volume of invention disclosures or patents filed has been significantly impacted from the years prior to the economic downturn to the years after it.

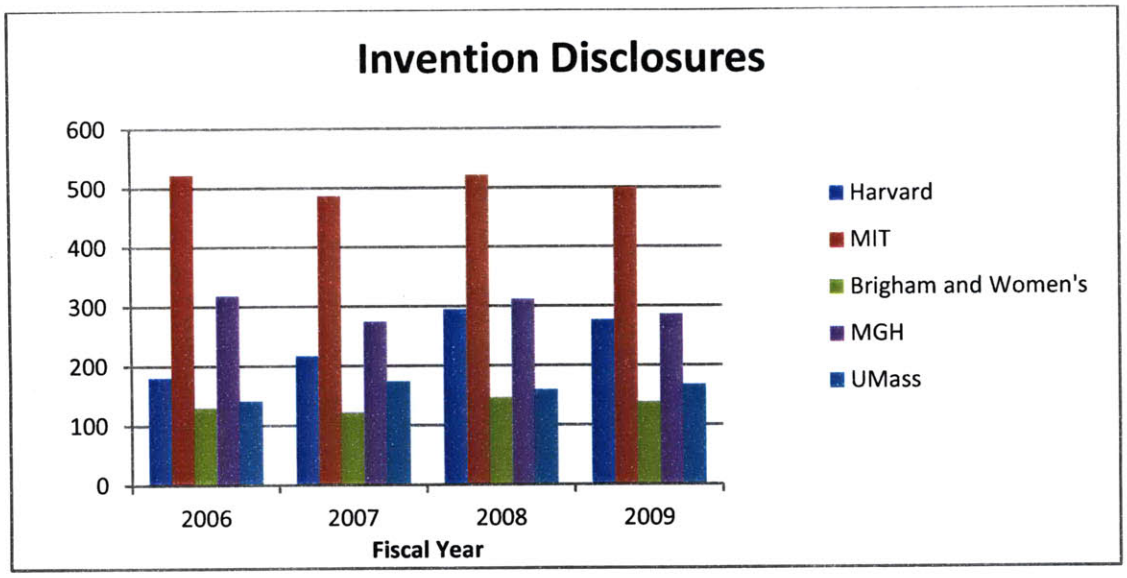

Figure 28: Invention disclosures from select universities

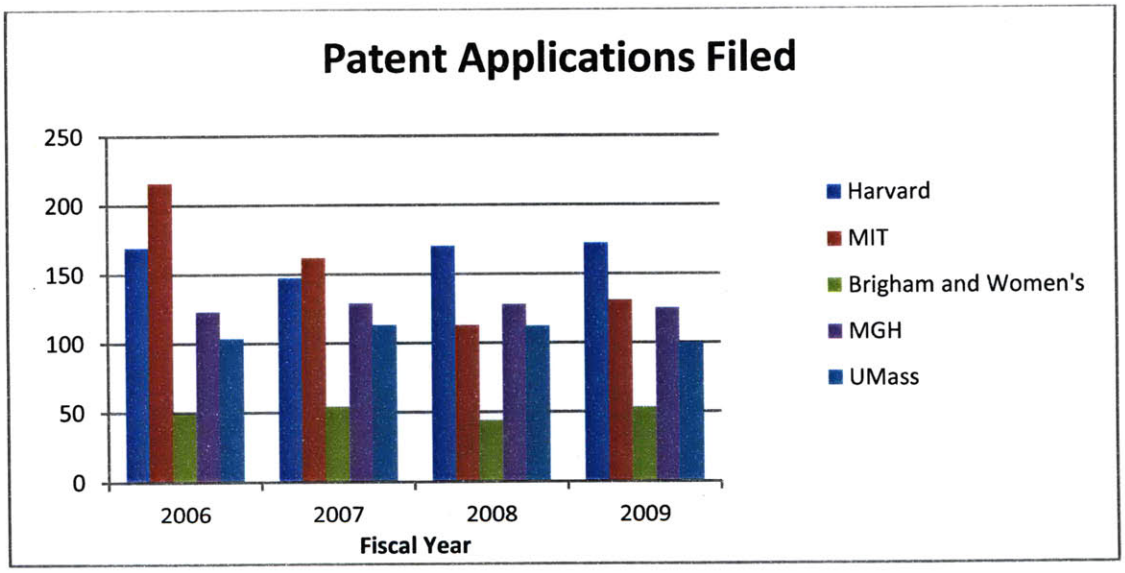

Figure 29: Patent applications filed from select universities

Given the sustained levels of scientific production but the reduction in new venture creation, it seems fair to conclude that innovation as translation from science to product has been impacted negatively. A technology licensing professional told us that "Companies are having a dreadful time. New companies are having trouble paying the bills. We are implementing bill collecting plans and we have even dropped patents that companies could not continue to pay."

Direct translation of university research is not the only area that innovation has been hindered in. With reduced access to capital, existing companies have had to make cuts that affect their own ability to innovate. Product pipelines have been pared back to include only the most essential products and experiments. A co-founder of a pharmaceutical startup explained that "We took out non-critical experiments, people, and value-added work." The CEO of another startup related that although she is able to pursue a basic course of action, "If I had greater access to capital I would probably be pursuing both technologies simultaneously and I would probably be taking one of them into three or four indications simultaneously...now we're basically saying one molecule very focused in one disease." These types of stories were very common amongst all entrepreneurs interviewed.

Finally, hiring of scientists and business professionals has been impacted. The CFO of a life sciences services company, summed up the sentiment expressed by many companies. "We have been undertaking a more rigorous philosophy with regard to hires vs. 2006 or 2007. We're on a need-to-have basis." However, he added that there is a potentially bright consequence of tightened hiring and the reductions in force that many companies have taken: "On the positive side, there are a lot of talented people in the market."

6 Policy Recommendations

We have established that the venture capital industry has responded to the most recent economic downturn in ways that are detrimental to new venture creation and the associated innovative activity. Many stakeholders depend on these innovations in different ways:

- Big life sciences companies rely on a steady stream of small companies to supplement their own internal R&D pipelines
- Local governments benefit from the job creation and tax revenues that comes with venture formation
- Universities and researchers benefit from the financial gains and mission-fulfilling aspects of technology commercialization
- Society benefits from the life saving and life sustaining innovations that come out of life sciences companies

We believe that just as capital markets have exhibited cyclicality since their inception, economic downturns will continue to occur and the funding of venture capital will have peaks and troughs. Policies in the public, private and academic space should be implemented in order to mitigate the impact on innovation during these troughs.

Strive for steady-state venture formation: an investment strategy

Before carrying on further it is important to discuss the limitations of new venture creation. First, successful ventures require a supply of limited resources. Many life sciences companies require a combination of good ideas and the right people for translating those ideas into products. While there is no magic formula for how to find such combinations, we only make the point that the number of viable businesses is finite and belief in the converse is likely to cause more problems than it solves. We also believe, as other authors have suggested (Gompers & Lerner, 2000, and Kannianinen & Keuschnigg, 2004), that there are a limited number of venture capitalists with the expertise required to practice their trade competently and that each of these venture capitalists has a limited amount of time to dedicate to portfolio companies. Based on our results we believe that this leads to the creation of "start up bubbles." When capital is easily available for a particular type of industry, in our case life sciences, many new companies are founded and an abundance of ideas are tested in the market. The converse of this is true when capital availability is constricted.

In a seminal work, Benjamin Graham explained that investing the same amount of capital regularly at discrete time periods mitigates some degree of portfolio risk (Graham, 1974). This dollar cost averaging ensures that an average price is paid for the investment in the long run as troughs and peaks are balanced. We recommend taking a cost averaging approach to supporting new ventures. Rather than over investing in new companies during certain periods and under investing during others, the same rate of investment should be made year-on-year. This avoids several problems. First it balances the voume of new companies created and by stabilizing supply it will have a stabilizing effect on prices paid by acquirers (and therefore IRR generated by VCs). Second, it stabilizes the benefits produced by new venture creation. Governments would have a more consistent idea of how many jobs will be created by new ventures each year and how much tax revenue can be raised. Universities would have a better idea of how much technology they can expect to license and be better prepared to support that goal. Finally, "venture cost averaging" will balance the ideas taken to commercialization. Classical economics would propose that if ideas are produced at a relatively constant rate over time, then the best ideas are funded first and then the ideas that receive funding become progressively less good. In this model when a funding bubble exists, several sub optimal ideas will receive funding. Once a bubble bursts fewer good ideas receive funding. If we could identify a reasonable desired amount of new ventures that could be commercialized then a known amount of "best ideas" per unit time could be brought to market.

This proposal faces two challenges. The first challenge is how to set the desired rate of new venture creation. One approach is to look at historical highs and lows and to assume that a longterm average is sufficient. Judging from our work an overall rate of new venture formation would be approximately 30% of all companies receiving VC funding in a given year. Alternatively, further research could be done to study the rate of new company formation that can be supported by a specfied amount of the resources needed to create such ventures. Because these resources are not evenly distributed geographically this may be a more effective approach.

Lower barriers to venture creation

The second challenge facing our proposal is to undertsand the mechanisms by which new venture creation can be managed so that this rate can be maintained at a stable rate or amplified in specific arenas. We believe that this can be accomplished by controlling the barriers to creating new ventures but as many studies have shown, the particular details that undergird entrepreneurial capacity are

poorly understood. In simplistic terms accoridng to this analysis, these barriers fall into three categories: ideas, people, and funding.

Many, if not most, of ideas that underpin life sciences companies involve some support from university research. In some instances company founders and advisors come out of university laboratories. Other companies rely on licensing university held intellectual properties. Barriers exist that hinder these activities, though.

One barrier is the way in which entrepreneurial activity is received in the academic sphere. The currency of the academic realm is peer-reviewed publication. Doctoral success, tenure promotion, and individual and institute prestige are all grounded firmly in the quantity and quality of publishing activity. Venture creation is not only not helpful to producing peer-reviewed publications but it is detrimental to it. New ventures require time which means there is less time available to focus on research activity. New ventures also often require secrecy about their technologies and business plans to protect against competitors. This flies in the face of the culture of openness upheld by academia. On top of this, many researchers have personal biases against commercial activity because their passion lies exclusively in basic research.

Academic institutions should be engaged in lowering the barriers to idea flow into commercial activity. One way in which this can be done is through standardization of technology commercialization offices. Per the United States Bayh–Dole act (35 United States Code, Chapter 18, §200-212) universities can retain ownership over the intellectual property discovered within them. Technology licensing offices exist within universities to facilitate the commercialization of this intellectual property. The standard operating procedures by which these offices do business is different from university to university. A study of best practices should be undertaken to learn what processes support successful technology transfer so that they can be embraced and which processes encumber it so that they can be avoided. Simply standardizing the process will go a long way in helping entrepreneurs feel comfortable interacting with academia for the purpose of technology transfer.

Commercialization activity should also be rewarded to a greater degree in academia. Although starting companies is not the primary job for researchers, activity that supports technology transfer could be considered as a component of a tenure application. Researchers who develop commercially useful technologies and processes should be encouraged to sit on scientific advisory boards for companies utilizing their products and students at all educational levels should be exposed to some amount of

entrepreneurial mentorship. Certainly not all researchers will engage in or even care for commercial activity but universities can help their communities be aware of entrepreneurship as an option.

Arguably the most critical part of new venture success is having the right people involved. Life sciences ventures in particular require access to a diverse skill set including scientists, business people, lawyers, clinicians and others. Joining a new company represents a risk to everyone involved. Skilled individuals who choose to found or join a start-up often do so at the expense of taking a more secure position in industry with a guarateed salary and benefits. New ventures have less money available to pay employees than large companies and there is a greater perceived risk of the small company failing.

Institutions should be organized to mitigate the risk to talented individuals to join a new company. Public policy could be better aligned to support working in a new venture. For example, tax advantages might be offered to individuals whose sole employment is for a small company of twenty or less people for the first year that they spend with that company. A more radical proposal is for the private sector to act in some way that mitigates this risk. Because large companies benefit from cross-fertilization of ideas and ultimately wind up as partners, investors and acquirers of promising small companies, big industry should consider taking a larger role in sharing resources, such as talented people, with these companies. Large companies should experiment with programs such as encouraging their own staff to take rotational assignments with innovative new ventures or even offer employment guarantees in case of the start-up failing to promising staff that might otherwise shy away from a new company. We acknowledge the legal challenges regarding protecting intellectual property protection that stem from this proposal though. We do believe that figuring out a way to address those concerns in a fair manner is possible and would be exceedinlgy useful.

Use Cashflow to control corporate formation

The final barrier to venture creation is the one focused on in this thesis: availability of financing. This barrier receives special treatment because it is both the most challenging barrier to overcome in clever ways, and at the same time it is the one barrier that public policy can take advantage of to exercise some control over new venture creation. At a first order level, cash flow will be dictated by market forces. As has been proven in this thesis, when capital markets are robust venture capitalists will have funding to invest in new ventures. When capital markets recede, there will be less money invested in VC.

Providing or restricting capital is a blunt public policy lever but in this instance it may be effective. As the rate of new company formation picks up, venture capitalists or new ventures themselves can be taxed in order to slow down activity that later could lead to a crash. Revenues from this tax should be saved in an innovation "rainy day fund." When markets fail to provide enough capital to support the pre-determined target level of new venture formation then this fund should be used to support activities that lead to venture creation. These could include tax subsidies for venture capital firms that invest in new companies or, again, direct subsidies to the companies themselves. While many parties will find this system of balancing new venture formation unpalatable, the reward for accepting the burden is a more stable and more lucrative long term market for new ventures (and for liquidity events for existing ventures).

A final word of caution is needed when discussing the role of government in venture formation. This recommendation and several others presented in this chapter recommend public policy interventions in a long-term, high risk-high reward, private sector affair. Policy makers must be cognizant of the fact that nurturing an environment conducive to a sustainable rate of venture creation will take far longer than average political cycles. The short term political gains that can be won by carelessly taxing, subsidizing, or otherwise affecting new ventures pale in comparison to the long term consequences. Regions where public policy and private activity interact well are rewarded with superclusters of employment, technology transfer and economic growth in cutting-edge sectors. Regions that fail to appreciate that these results cannot be replicated overnight may never accomplish them. For this reason it is recommended that any public sector activity that has an effect on innovation be housed in a politically isolated government agency, in as far as creating such an entity is possible.

When downturn does occur, put efficiency first

The work that this thesis was based on was commissioned in response to an economic downturn. Therefore we will conclude with a recommendation on how to respond to economic downturns that do occur. A well-functioning supercluster can be thought of as a well-oiled machine. Confident people and great ideas are fueled by ample capital and new ventures are produced, liquidated at high valuations and the capital generated from these liquidity events is used to re-stoke the furnace. When an economic downturn occurs the fuel supply for this machine is restricted. Trying to find more fuel is one approach and should be pursued in as much as it can be. The reality of the situation, however, is that in a bad

downturn there may just not be enough capital available to achieve previous levels of supercluster functionality.

We believe that the more productive approach is to make the rest of the venture creation machine operate as efficiently as possible. An accounting should be taken of all capital equipment that has been made redundant as a result of small company research and development cut backs. A system should be implemented for sharing this equipment amongst all parties who need it. Communities that are usually isolated by industry focus or academic discipline should be encouraged to interact more both among themselves and with other communities. This will generate new ideas and allow for new strategies to be developed for how to treat existing product lines. A system should be developed for catching and recirculating the ideas that fail or are abandoned as a result of the downturn. This might take the form of well publicized auctions of intellectual property similar to what is done with real estate that is foreclosed on. Going a step further, government might purchase orphaned intellectual property at a deep discount and then make it publicly available.

Regardless of which recommendations are implemented, we urge that they be implemented irrespective of macroeconomic conditions. Although it is easier to fix systems under the urgency of crisis, it is more effective to take a preventative approach. When all appears to be functioning well, that is when various stakeholders should make an extra effort to collaborate, set resources aside, and prepare for a time when prospects are not as bright. As nursery rhymes and fairy tales from cultures around the world teach us when we are young (seemingly to be forgotten with age), only by preparing in times of plenty can we truly remain strong in times of wanting.

7 Conclusions

The Massachusetts life sciences supercluster is a source of tremendous innovation. The Commonwealth's academic and industrial institutions produce a consistent stream of cutting-edge scientific research and the region has a well-developed professional and financial infrastructure to support the translation of these ideas into useful products. Venture capital plays a particularly important role in this ecosystem as VC funding is essential to most life sciences companies due to their high research and development costs and long time to market.

The economic downturn of 2008 saw capital markets constrict. This effect spread from public markets to private equity markets and venture capital was similarly impacted. As the limited partners who invest in venture capital realized their need for greater access to liquidity combined with the attractiveness of depressed prices in other markets (i.e. real estate, stocks, bonds, etc...), venture capital firms saw their ability to raise funding greatly diminished. We used this setting to evaluate the impact of economic downturn on venture capital resource allocation. We also conducted extensive interviews with stakeholders in the Massachusetts life sciences community to better understand the impact of these changes in resource allocation. Our findings are as follows:

Life sciences targeted venture capital funds have been particularly hard hit

Not only did overall funding into venture capital decline, but life sciences focused venture capital funds have found the environment especially challenging. While 2008 saw life sciences funds show greater resiliency to the downturn than other sectors of venture capital, 2009 saw this trend reverse and there is evidence to suggest that life sciences funds were impacted more severely than other sectors.

This has led to a decline in the amount of funding companies have access to

With less new capital coming in from investments, the average investment size in two of the three regions of interest has dropped significantly after the economic downturn. New companies appear to have shown more resilience to this effect. We believe that this is because for a new life sciences company to have a chance at success a minimum amount of money must be invested in them irrespective of macro-economic conditions.

Fewer new companies are being funded as VCs attempt to protect existing investments

Having restricted access to capital has led to VCs behaving in a more risk-averse manner. While the total number of companies invested in has not changed drastically the rate of new company formation has dropped significantly. This has been accompanied by an increase in the rate of reinvestment into existing companies in an attempt to see them through the downturn so that that they can reach liquidity events in the future.

These points have had a negative impact on innovative activity

The above findings hinder the translation of ideas into useful products. Pipelines have been cut and the technology transfer associated with new company formation is down. As large companies take advantage of the situation by acquiring technology on favorable terms the returns to venture capital are reduced. This puts even more downward pressure on future venture capital fundraising prospects.

Economic periods are cyclical and so events like this downturn are likely to happen again both in the life sciences industry and in other areas. Take for example the energy industrial sector. The combination of increased financial interest, scientific output, and general excitement make this sphere a likely candidate for over-investment followed by the same consequences that have been chronicled herein. When downturns do occur we urge an increased emphasis on community efficiency. With depressed capital available to support venture formation, communities need to be more collaborative with the resources that are available. An effort should be made to ensure that equipment, space, people and ideas do not go under-utilized.

Generally we recommend taking a preventative approach to the impact of downturn. Lowering the barriers to new venture formation while controlling cash flow into new ventures can lead to a steady state rate of new company creation. Controlling the supply of new ventures produced should then stabilize the value of liquidity exits. This approach has the added benefit of dollar cost averaging investment in innovation.

7.1 Future Work

While we have answered important questions regarding how venture capital responds to a downturn, there is still more work for future research to address. As venture capital funding returns to peak levels, analysis should address whether trends discussed herein reverse themselves. This thesis also treats the

link between public market behavior and venture capital fundraising qualitatively. It would be worth taking a data driven approach to this issue. Finally, our policy recommendations assume that venture capital funds innovative companies linearly. That is to say the most innovative companies are funded first and then the marginal amount of innovativeness declines for each additional venture supported. Research evaluating the veracity of this would help illuminate the actual value of venture capitalists to supporting innovation.

7.2 Final Remarks

We believe that this work has shed useful insight into the behavior of a fundamental piece of the technology innovation and commercialization system. Learning from the Massachusetts life sciences super cluster, both as an engineering system and as a collection of fascinating individuals, has been incredibly exciting and intellectually rewarding. We realize that the work that this supercluster supports is not just an academic abstraction. The life sciences technologies developed in Massachusetts and elsewhere extend and improve the quality of life of people everywhere. We conclude simply by stating our hope that these breakthroughs continue to be supported and that the communities that support them remain robust. The author thanks readers of this work for their time.

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Appendix A: Interviews Performed

Name (Last, First)	Title
Amariglio, Leon	Rhythmia Medical, co-CEO
Aspinall, Mara	On-Q-Ity, CEO
Barrow, Abigail	Massachusetts Technology Transfer Center, Director
Beall, Robert	Cystic Fibrosis Foundation, President and CEO
Behr, Daniel	Harvard University, Director for Business Development
Berke, Carl	Partners Innovation Fund, Associate Director
Bird, Jerry	Massachusetts Technology Development Corporation, Vice President
Brauns, Tim	Boston BioCom LLC, Vice President for Strategic Planning
Cameron, Charley	Hub Angels, Managing Director
Casey, Kevin	Harvard University, Associate Vice President for Government, Community and Public Affairs
Celniker, Abbie	Taligen Therapeutics, CEO
Chalek, Mark	Beth Israel Deaconess Medical Center, Chief of Business Ventures
Chmura, Tom	University of Massachusetts System, Vice President for Economic Development
Chowdhury, Sohini	Michael J. Fox Foundation for Parkinson's Research, Team Leader
Citron, Paul	Medtronic, Retired Vice President of Technology Policy and Academic Relations
Constantine, David	MassChallenge, COO
Creeden, Robert	Partners Innovation Fund, Managing Partner
Crowley, Robert	Massachusetts Technology Development Corporation, President
Csimma, Zoltan	Genzyme Corporation, Senior Vice President for Human Resources
Dagi, Teo	HLM Venture Partners, Partner
Douglas, Richard	Genzyme Corporation, Senior Vice President for Corporate Development
Elton, Jeff	Novartis Institute for BioMedical Research, Senior Vice President of Strategy and Global COO
Erenburg, Irina	Partners Healthcare, Director for Strategic Transactions
Ertel, Steve	Acceleron Pharma, Vice President for Corporate Development
Fasman, Ken	Adelson Medical Research Foundation, Vice President and CSO
Flemming, Jonathan	Oxford Bioscience, Managing Partner
Fredrick, Amy	MedTech Ignite, Director
Galakatos, Nick	Clarus Ventures, Managing Director
Galliher, Parrish	Xcellerex, CTO
Garvey, Jim	SV Life Sciences, Managing Partner

Gottleib, Gary	Partners Healthcare, CEO
Gottschalk, Adrian	Biogen Idec, Senior Director of Global Oncology and Cardiopulmonary Commercialization
Greeley, Michael	Flybridge Capital, General Partner
Green, Nina	Tufts University Office for Technology Licensing, Director
Greene, Barry	Alnylam Pharmaceuticals, President
Hallinan, John	Cytel, CFO
Higgins, Bob	Highland Capital Partners, General Partner
Holtzman, Steve	Inifinity Pharmaceutical, CEO
Hunter, Michael	Commonwealth of Massachusetts, Undersecretary for Business Development
Hyman, Steven	Harvard University, Provost
Judson, Matt	Leerink Swann, Managing Director
Knight, Stephen	Fidelity Biosciences, Managing Partner
Kohlberg, Isaac	Harvard University, Chief Technology Development Officer
Kolenbrander, Kirk	Massachusetts Institute of Technology, Vice President for Institute Affairs
Leonard, Reid	Merck Research Laboratories, Director for External Research and Licensing
Leuchtenberger, Mark	Targanta Therapeutics, CEO
Levin, Mark	Third Rock Ventures, Partner
Littlechild, John	Healthcare Ventures LLC, Partner
Lomedico, Peter	Juvenile Diabetes Research Foundation, Director of Strategic Alliances
McNary, Chris	Thermo Fisher Scientific, General Manager
Moore, Jeffrey	MP Healthcare, Vice President
Moses, Jean	Harvard Clinical Research Institute, Treasurer
Mukohira, Tak	MP-Healthcare, Vice President
Muniz, Stephen	Puretech Ventures, Partner
Nasrullah, Imran	Massachusetts Biotechnology Council, Chief Business Officer
Nelsen, Lita	Massachusetts Institute of Technology, Director for Technology Licensing
Ochoa, Rosibel	University of California at San Diego von Liebig Center, New Commercialization Director
Oyler, Catherine	Johnson & Johnson, Senior Director for Emerging Technologies
Rosen, Jonathan	Boston University Institute for Technology Entrepreneurship and Commercialization, Executive Director
Rosenberg, Bill	University of Massachusetts System, Executive Director for the Office of Commercial Venture and Intellectual Property
Ryan, Una	Diagnostics for All, CEO
Sandoski, Aaron	Norwich Ventures, Managing Director
Shanahan, James	SynDev Rx, Vice President for Business Development

St. Peter, Steven	MPM Capital, Managing Director
Steinenger, Robert	Acceleron Pharma, Senior Vice President for Manufacturing
Stevens, Ashley	Boston University, Executive Director for the Office of Technology Transfer
Summers, Nevin	Harvard-MIT Health Science and Technology Program, Director of Corporate Development
Taunton-Rigby, Alison	RiboNovix, CEO
Termeer, Henri	Genzyme Corporation, CEO
Toneguzzo, Frances	Massachusetts General Hospital, Director for Corporate Sponsored Research and Licensing
Trusheim, Mark	Co-Bio Consulting, President
Villa-Komaroff, Lydia	Cytonome, CSO
Vogel, Jean Marie	Pluromed, CEO
Walts, Alan	Genzyme Ventures, Managing Director
Wolfe, Janet	Wolfe Labs, President
Wong, Ling	Bill and Melinda Gates Foundation, Program Officer