

Innovation as overlapping scientific and technological trajectories: exploring tissue engineering*

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ABSTRACT

The question of exactly how science is transformed into technology and reaches the market is an old and important one. While the social structures of “science” and “technology” are quite different, recent work suggests that science and technology may in fact co-evolve through a much more bi-directional interaction than was originally thought. These findings raise a number of important unanswered questions regarding the dynamics of science-technology interactions. In first place are the networks through which science is created are similar to the networks of technological progress? In the second place are scientific networks deeply interlinked or co-mingled with networks through which technology is created? In the third place what is the nature of the interaction between the two networks?

In this paper we explore these important questions in a detailed study of an emerging area of biomedicine – tissue engineering. We use a novel methodology that traces the network of patents and papers that cite the foundational patent and paper in the field. We combine this with in-depth qualitative interviews with the focal inventors/authors and members of the network.

Our results show that for this case there exist quite well defined scientific and technological networks. However their underlying logic is distinctive – the scientific network is dense, broad and characterized by collaboration while the technological network is sparse and more competitive. Furthermore, while we find evidence of overlap it does not take the co-publishing and cross-citation form that might be predicted from the current literature. Our results suggest that by quantitative measures few star scientists participate across academic-industry boundaries and firms do not participate in extensively in science. We argue instead that considerable overlap exists between the two networks that is not captured in traditional quantitative measures. These processes of overlap range from firm founding and licensing to consulting, mentoring and informal scientific advising – mechanisms that have not traditionally been explored by scholars of technical change.

Our findings highlight the importance of scientific as well as technical networks in technological progress. They also have implications for our understanding of the processes through which spillovers arise. Our preliminary results suggest that the traditional focus on one or two mechanisms of overlap is limited and that in fact the overlapping networks involve a wide range of exchanges. Finally our findings raise intriguing questions regarding the determinants of productivity in bringing science-based ideas to market.

1 INTRODUCTION

The question of exactly how science is transformed into technology and reaches the market is an old and important one. Early work has modeled this process as a linear, “waterfall” but more recent work has considerably completed the picture. While the institutional structure of “science” and “technology” are quite different¹, the old view that “science” was an exogenous, self-contained process has been replaced by a growing awareness that science may be, to a considerable extent, endogenous. Moreover much work suggests that science and technology may in fact co-evolve and that nature of interaction may be much more bi-directional than was originally thought.

These more recent findings raise a number of important unanswered questions regarding the dynamics of science-technology interactions. In first place, does the finding that there is bi-directional communication between science and technology imply that the networks through which science progress is made are deeply interlinked or co-mingled with networks through which technology is created? Are the boundaries between the two blurred? Recent editorials on relationships among physicians and businesses suggest that these two communities are overlapping and that some people are intensely worried about the effect of these overlaps on the social structure of science². Secondly, if there is interaction what are the processes and ties that characterize this overlap? Although a number of fascinating studies in the network literature suggest that being part of both the scientific and technical networks is crucial to driving technological and/or scientific progress, to our knowledge no one has focused explicitly on the range of ties that define the overlap³.

In this paper we draw on a detailed qualitative and quantitative study of the development of tissue engineered cartilage to explore these issues. Drawing on in-depth interviews and a detailed analysis of 76 patents and 158 papers we show that in this particular case there exist quite well defined scientific and technological networks. Communication between the two networks is bi-directional, as expected. But it does not take the co-publishing and citing form that is described in the literature on spillovers (Henderson and Cockburn 1994). Our findings suggest that at least as measured by quantitative measures: i) few key scientists participate across academic-industry boundaries and ii) firms do not participate in science.

¹ This view has been put forward by Merton (1957) among others that the institutions and norms of science are unique. Dasgupta & David contrast science and technology.

² In November 2000 the New England Journal of Medicine declared its support of stringent rules on equity ownership by clinical research scientists and physicians (Angell 2000).

³ While Podolney & Stuart (1995) and others have explored patenting networks to our knowledge there have been no systematic studies of scientific and patenting networks.

However, our qualitative interviews highlight that considerable informal and formal overlap exists between the two networks that is not captured in traditional quantitative measures of patent and paper citations. These processes of overlap range from firm founding and licensing to consulting, mentoring and informal scientific advising and play a potentially significant and previously unexplored role in transforming scientific progress into technical, commercial and healthcare benefits.

Thus our approach not only describes the overlapping networks but also aims to develop a more nuanced understanding of the processes that they embody. Our paper makes three useful contributions to scholarship on technological change. First it develops a richer description of the networks that embed technological and scientific progress. Second by focusing on the overlap between science and technology it reintroduces the scientific trajectory into the debate on technological change. Finally drawing on it takes a closer look at the range of ties that characterize the processes that are associated with trajectories and examines the contemporary context in which these networks overlap from one trajectory to the other.

2 LITERATURE REVIEW

We draw upon a distinguished research tradition for this detailed study of the overlapping networks of science and technology. In particular we revisit the enduring issue of the relationship between science and technology that has animated scholars of history, the economics of technical change, and science studies as well as policy makers for many years.

In the field there is general agreement with the influential stream of research developed in the 1970s by Rosenberg (1982), Nelson and Winter (1977) and others suggesting that science is closely linked to other innovative activities and its direction shaped by everyday considerations rather than a special entirely separate world driven by its own norms and interests. This so-called “endogeneity of science” has highlighted the importance of economic interests, commercial activities and a range of different institutions in the direction of scientific progress. While scientific progress was recognized as strongly shaped by its social and economic context, many continued to conceptualize the link between science and technology as a “waterfall” process with ideas in science moving seamlessly into the technological domain. However scholars have come to replace this with a more nuanced view of the individual domains of science and technology, and a few empirical studies have highlighted that the overlap between the two activities is complex (Garud and Rappa 1994).

A great deal is known and understood about the individual networks in which scientific and technical progress takes place. Scientific progress is characterized by the significance of institutions, practices and

communities (Jardine 1998, Lenoir 1995, Kohler 1976). More recently the science studies provides rich exploration of the social structures and networks shaping the scientific trajectory (Kuhn 1970; Gieryn 1983). For example the so-called laboratory studies provides remarkable detail regarding the practices of science (for example Latour and Woolgar 1986) and scholarship on the “career” of scientific discoveries highlight several important features of scientific progress: institutional and professional boundaries collaboration and competition evidence and interests (Merton 1957).

Likewise, technological progress has been explored from a number of dimensions. Dosi (1982) and others conceptualize technological progress as moving along an S-shaped curve with performance limits driving individuals and firms to eventually explore alternative approaches to a problem⁴. However research has shown that these trajectories are deeply embedded in a series of institutions and networks that shape the development and progress of a particular technology (Bijker et al. 1987, Blume 1992, McKelvey 1997). Likewise the recent work of Podolny and Stuart (1996) has highlighted the importance of centrality in the technical network for overall firm performance.

The breadth of scholarship outlined above focuses on the networks in which either science or technology are embedded. However our understanding of the connections and overlap between these two networks is quite limited: it typically highlights only one or two dimensions of overlaps and ties and therefore gives us only a partial view of the interconnections between the two networks. Empirical evidence developed by Mansfield and others provides empirical support for the importance of university science for firms making progress along the technological trajectory. In the biomedical arena the influential studies of Comroe and Dripps (1976) documented that scientific research of a diverse nature were crucial to medical innovation and often many years apart. A related research stream had found a link between high citation rates and the references of scientific papers in patents (what has been referred to as “science linkage”)⁵.

These studies point to the fact that a connection to “science” and scientific networks leads to improved technological progress. Indeed this proposition has lead to a stream of research in the tradition of Cockburn and Henderson (1986) and Zucker (Zucker Darby and Brewer 1998) that asks how a firm’s ties to the scientific network influences its overall economic performance and more specifically its progress

⁴ Dosi (1982) has expanded the Kuhnian notion of a scientific paradigm to suggest that distinctive technological paradigms exist that bound the nature of the questions that are asked and the methods used to solve them and drive progress along a relatively narrow and well-defined trajectory.

⁵ The idea of “science linkage” or the number of scientific articles to which a patent refers in its “Non-Patent References” section has been explored extensively by Narin and co-authors (for example Narin and Olivastro 1992).

along the technological trajectory, particularly in instances when the trajectory is new and emerging from a different paradigm. The general findings of this research are that three types of ties and modes for spillovers exist: Publication and co-authorship, proximity to star scientists and movement of scientists. With respect to publication, it has been argued that particularly in periods when there is a shift in technological paradigm and the new paradigm is closely linked to science, such as the biological approach to drug development, publications by the leading firms are crucial in making a successful transition (Henderson and Cockburn 1994, Arora and Gambardella 1994, Liebeskind et al. 1996)⁶. The second type of tie is the link to “star scientists”: Zucker et al (1998) argue that ties to science arise largely through the proximity and participation of “star scientists” in firms who are active in commercializing novel technologies. A third tie is the movement of human capital. David and Dasgupta (1994) comment that the “export of scientists and engineering from the academy to industrial research is potentially the most important and salutary among the mechanisms available for effecting knowledge transfers” (p. 511).

This literature has contributed to our understanding of the impact of involvement in science on technical productivity. And yet it is based on two assumptions: Firstly that there are only simple ties and singular modes of connection and secondly that these two networks are densely interconnected through these ties. To our knowledge there have been no studies that explore the breadth of the ties and the interconnections between the scientific and technical communities. In the light of our understanding of the two separate networks of science and technology as complex and deeply embedded these studies raise a number of intriguing questions and unexplored issues particularly around: How is the two network constructed? What is the extent of overlap? What are the processes that shape the interaction between science and technology? Therefore in this study we develop a systematic analysis of the networks of science and technology and explore how they interrelate building on the tradition of quantitative research methods but also using qualitative methods to explore the processes whereby the networks overlap arises.

3 DATA AND METHODS

In this paper, we explore the overlap between scientific and technical networks in one setting - tissue engineering. This field is recognized to be one of the most active and promising arenas for scientific and medical advance in the twenty first century (Nathan 2001). Also, as a new biomedical paradigm it is complementary to but not repetitive of much of the research on spillovers and networks undertaken in biotechnology. While the foundations of tissue engineering rest in part on molecular biology they also

⁶ Publication is taken as a sign of participation in the “republic of Science”, early access to novel insights through conference participation and suggestive of a deeper understanding of the scientific foundations of the new technological trajectory.

draws on chemical engineering, cellular biology and materials science. Within tissue engineering we have undertaken a narrow quantitative study and followed this with a more in depth qualitative analysis. This research approach allows us to explore the wide range of different ties – some of which can be easily found in quantitative data while others are harder to uncover. The narrow scope of our quantitative research reflects the preliminary nature of our research but provides an important foundation for future quantitative analysis. The quantitative study maps and analyzes the citation networks for a matched paper and patent published in 1991 that are widely cited and among of the foundational works of tissue engineering. This pair was chosen for the close match between the science and technology. It provides a natural experiment in the early development of a biomedical trajectory. Our qualitative analysis is complementary and designed to explore the nature of the networks within science and technology and the interconnections between the networks. It included interviews and a broader analysis of the publications, patents and relationships of key scientists in the tissue-engineering field.

3.1 INDUSTRY SETTING

Tissue engineering provides a particularly fascinating setting in which to explore this question because it is a field with active scientific and technical communities and is active both for basic research and a wide range of potential applications. It has also been identified as one of the key medical research opportunities for the twenty-first century with the potential to revolutionize tissue loss and organ failure – a problem that afflicts 8 million patients each year in the United States alone (Niklason and Langer 2001).

The scientific basis for tissue engineering is broadly focused on understanding the way in which multiple cells are assembled into larger scale organs and tissues in the developmental progress. Scientific progress has been built on a range of disciplines including molecular and cell biology, pathology, biochemistry and chemical engineering. The technical trajectory has also seen significant progress over the last fifteen years. It is driven by a set of clearly articulated technical goals: A recent review article described the field as “*an interdisciplinary field in which the principals of engineering and the life sciences are applied toward the generation of logic substitutes aimed at the creation preservation or restoration of lost or decreased function [of organs]*” (Vacanti and Mikos 1995). Recent advances in materials science, molecular biology and medicine have led to an entirely new technological trajectory in the development of biomaterials to solve the problem of tissue loss. Technical progress in tissue engineering is believed to have many applications for a range of different organ systems including blood vessels, corneas, skin, cartilage, liver, pancreas, spinal cord and bladder. Technical advance is therefore shaped both by its commercial and its healthcare potential: current treatments for organ failure and tissue loss are costly and inadequate. Over eighty *de novo* firms have been founded to take commercialize the developments in

tissue engineering. Many of these are in the United States although more recently firms in Europe have been founded to exploit tissue engineering.

In this paper we focus on the scientific and technical progress around tissue engineered cartilage. While some applications of tissue engineering such as the replacement liver still require years of technical work and their scientific basis remains unclear, tissue engineered skin and cartilage of different types are currently in clinical use. Tissue engineered skin is more established and there is less active research in this area. In contrast, the area of cartilage is extremely active. Cartilage is of great commercial interest because hundreds of millions of people around the world suffer from arthritis, which in part arises from damage or degradation of the cartilage - a tissue in the body that does not repair or heal itself. The scientific fascination with cartilage lies with its complex structure and the ability of the body to engineer load-bearing materials.

3.2 QUANTITATIVE DATA

In this paper we undertake a preliminary analysis of the scientific and technical networks engaged in cartilage-based tissue engineering. Our perspective borrows from Granovetter's (1985) notion that industries get established as economic relations become embedded in social relations. Our quantitative methodology follows in the tradition of studies that explore patenting and publication activities by individuals and firms and studies such as Podolny and Stuart (1995) that map the patent citation networks of firms. However, our quantitative approach is highly focused and narrow: we analyze the first generation citation networks of a single paper and a single patent. We have taken this narrow quantitative focus for two reasons. First we view this quantitative approach as a preliminary exploration that will help shape a more extensive quantitative analysis in the future. Second we are interested in understanding the process of overlap between the scientific and technological trajectories and therefore we need to explore the networks in depth. By using a single patent-paper pair there is considerable scope for a full exploration of the overlap between the two networks including inventors, institutions, other co-authorship and co-inventorship activities, and educational affiliations in addition to complementary qualitative work.

Our aim is to explore how the scientific and technological trajectories develop and what individuals and institutions encompass the network in which these trajectories are embedded. We assume that the scientific trajectory can be mapped through a series of scientific papers and that the citation network to a significant early paper can map a part of that trajectory. Likewise, building on patent citation research we assume that a highly cited patent makes a significant contribution to the technological trajectory and its citation network represents incremental technical progress along the trajectory (Flemming and Sorenson

2000). Our research design is to take as a starting point a patent and a paper that represent as closely as possible the same idea, with the paper providing the scientific evidence and the patent describing a particular embodiment of the idea. We then trace the first generation of patents that cite the focal patent, papers that cite the focal paper and patents that cite the focal paper.

The choice of this first patent-paper pair is critical to our quantitative strategy. Our criteria for choosing the patent-paper pair are three fold: First both patent and paper should be widely cited, second the pair should be substantially overlapping in content, time and authors and third the authors must be academics prominent in the scientific or technical community. A widely cited patent has been shown to be an important contribution to technical progress and to be of economic significance (Trajtenberg 1986). Likewise, widely cited papers are typically those that make a seminal contribution to the scientific literature (Albert et al. 1991).⁷ The requirement for overlapping content in the patent and paper is not a well-explored notion but our concern is to use a common starting point for the exploration of the two networks. If the paper and patent incorporate the same ideas and are created by the same individuals then we suggest that at least at this point, the two trajectories intersect. Similar and overlapping information is incorporated into both documents but they are used in different ways and mark a point along two trajectories – the paper marks progress along the scientific trajectory while the patent is a point on the technological trajectory. Our third criterion, academic prominence is used to ensure that the patent we choose was developed at an academic institution. This allows us to trace the technical network from an academic starting point and thus focus on academic-industry spillovers. In addition it allows us to exclude competitive interactions as an explanation for participation in the technical network. In choosing prominence we can also make a link to our qualitative work that interviews key individuals in the tissue-engineering field. To our knowledge, this patent-paper pair methodology has only been used in one previous study to explore differences in authorship when individuals are participating in the scientific and the technical community (Ducor 2000). In that case the pairs were linked through common amino acid sequences that were both patented and published.

We explored patents using a series of key words: chondrocytes (234 patents), cartilage (921 patents), tissue scaffold (128 patents). The top academic assignees were the Massachusetts Institute of Technology, Children's Hospital University of Texas, the Massachusetts General Hospital (MGH), U. Penn, University of California System and University of Texas. MIT and Children's Hospital represented

⁷ Quality of a paper linked to citations – ref the norms of science are the get promotion through publication – Dasgupta & David, Research Policy.

significant co-assignment collaboration on most of their patents. In this set of patents, the most prolific inventors were J. Vacanti (Children’s Hospital) and R. Langer (MIT). Our preliminary qualitative work also identified Langer and Vacanti as key individuals in the development of tissue engineering. We therefore looked for research (rather than review) papers by these authors early on in the development of tissue engineering that might be a matched candidate for our quantitative research. We developed a search of all joint research publications, which included Langer and Vacanti. We found 53 joint publications and tried to match these with the eleven co-invented patents. These matches were made using information on the date, abstract, authors and claims. From the set that was well matched for content, we chose the pair with the highest combined citations.

Both the patent and the paper were published in 1991 (the inventors applied for the patent in 1989 but it was granted in August 1991). The patent in the pair is one of the earliest for tissue engineering and cartilage in particular.⁸ The patent chosen is cited 76 times, which is high by most comparative measures and suggests that it is an important contribution to the field of tissue engineering. It is the first co-patented research between Vacanti and Langer and was jointly assigned to their two institutions – Children’s Hospital and Massachusetts Institute of Technology. It included a third co-inventor, Dr. Charles Vacanti (Joseph’s younger brother who was then a Resident at the MGH). Later that year, the three scientists, together with Dr. B. Schloo published a paper that represents the pair in the *Journal of Plastic and Reconstructive Surgery*. The paper details their experimental evidence for in vivo tissue engineered cartilage and is cited 158 times (Vacanti et al. 1991). This pair forms the starting point to capture data on the scientific and technical networks that build on the ideas in the paper and patent. Our methodology is to trace all the citations to the patent following its granting using data available on the U.S. Patent Office database. We then trace citations to the paper through the Web of Science (Table 1).

	Focal Patent	Focal Paper
Date published	8-21-91	11-1-91
# of citations in patents	76	5
# of citations in papers	0	158
# scientific references	4	18
# patent references (cited)	13	0

Table 1 Basic data on the focal patent and paper

⁸ Patent No. 5041138 “Neomorphogenesis of cartilage in vivo from cell culture” granted August 1991.

For each citation we gather four variables: i) the inventor(s) or author(s), ii) the assignee(s) or affiliation(s), iii) the year of citation, iv) the number of citations to that paper or patent. We then analyze the set of individuals for affiliation⁹, whether they have been co-authors or co-inventors of the focal individuals (in this narrow set of citations), and whether they are graduate students at the focal institutions (through the Michigan Dissertation Abstracts database). For inventors we also gathered data on the total number of patents that they have been granted and the number of papers that they have authored (according to the Web of Science). The set of institutions is coded for geographic location (state or country) and its type according to three categories – university, industry, other.

3.3 QUALITATIVE DATA

The purpose of our research is to explore the social networks underlying the scientific and technological trajectory and the complex relationships between the two. Our qualitative research strategy is therefore to uncover the nature of the relationships among individuals in the scientific and technical communities and also between the two communities. Qualitative data is fundamental to this study for two reasons: First there may be key interactions within and among the two networks that are not captured by quantitative metrics – indeed one of the goals of this study is to explore whether and to what extent this is the case; second we are exploring questions of process – the processes through which two networks influence one another is probably only accessible through qualitative analysis.

Our qualitative approach was to identify the key players in the scientific arena of tissue engineering. We had already ascertained from our quantitative analysis that Professors Langer and Vacanti had prolific joint publications (53) in the field and long lists of independent publications (209 for Vacanti alone in Web of Science mainly in tissue engineering). However we supplemented our list of key individuals in three ways: from review articles in the six most prestigious scientific and medical journals, from the contributors to the Handbook on Tissue Engineering (second edition published in 2001), and thirdly from the Agenda of the Tissue Engineering Society Annual conferences which have been held biannually for the past six years. The tissue engineering review articles published over the past decade were gathered from six journals: Science, Nature, Scientific American, the Journal of the American Medical Association (JAMA), The Lancet and the New England Journal of Medicine. We then identified leading scientists in cartilage tissue engineering key references in the review articles. In addition we asked Langer and Vacanti to identify for us the individuals that they believed to be central to the scientific network.

⁹ For the authors of papers their affiliations cannot always be matched to specific authors and in this case we include only the first and last authors and their affiliations in our counts of institutions.

Our methodology was to request in person or telephone interviews with these leading individuals. In this paper we present only our preliminary qualitative findings based on interviews with five of the top ten authors in the paper citation network and five other individuals identified as being key scientists in the field. Each interview lasted between one to three hours. The interviews took the form of semi-structured conversations, which follow three lines of inquiry. First they include a series of questions on the nature of the scientific challenges in tissue engineering, the contribution of the individual scientists and the peer group with similar interests in the scientific community. The second area of conversation focused on the technical applications of tissue engineering – the particular applications of interest to the scientist, the approach taken to products currently available, their limitations and future technical directions, and finally the leading members of the technical community. The third focus of discussion was on the interactions between the scientific and technical communities. This section of the interview asked individuals about i) their own direct activity in the technical community - whether they were engaged in patenting and licensing, ii) their typical types of interactions with the technical community – consulting, sponsored research, informal advising etc. iii) the specific firms with which they had interacted and iv) their general views on the link between scientific and technical communities. We have supplemented these interviews with informal discussions with graduate students in the laboratories and observation of weekly laboratory group meetings over a two-month period.

4 FINDINGS

Our key findings fall into two areas. Our first set of findings related to the individual scientific and technical trajectories. We find that they are distinctive both quantitatively and qualitatively. Our qualitative data reinforces our quantitative findings that scientific and technical communities have striking different networks: the scientific networks are dense and broad, with the focal scientists Langer and Vacanti working with numerous co-authors. The technical networks are narrower and more sparse – scientists do participate but make fewer connections through co-invention. Our second set of findings relate to the overlap between the two networks. Here our quantitative and qualitative findings diverge. Our quantitative data suggest that contrary to previous analysis in the biotechnology and pharmaceutical industry, there are very few industry-based individuals publishing in addition to patenting and only a few scientists actively pursuing both publication and patenting. Thus in quantitative terms the networks show very little overlap. However our qualitative results suggest that there is in fact a dense overlapping community but that these overlaps take forms that have not been explored in much of the previous literature on spillovers: licensing, consulting, Scientific Advisory Board membership, sponsored research and graduate students.

We organize our findings into three sections. First we present our understanding of the two different trajectories based on interviews and analysis of the papers and patents in the patent-paper pair network. Second we outline our qualitative and quantitative findings regarding the scientific and technical trajectories and the networks that encompass them. Thirdly we turn to our conflicting quantitative and qualitative results on the nature of the overlap between the two networks.

4.1 TRAJECTORIES

Our understanding of scientific and technical progress has been strongly influenced by the notion that a trajectory or path emerges along which progress and knowledge building take place and by the idea that the scientific and technical trajectories are distinct but complementary. Using qualitative interviews and patent-paper analysis we have attempted to examine the differences between the scientific and technical trajectories in the field of tissue engineering. This understanding provides a foundation for our analysis of the networks of individuals and institutions that contribute to the different trajectories. In interviews with scientists who are pioneers in tissue engineering, they describe the scientific and technical dimensions of tissue engineering as strongly reinforcing: Both paths are driven by the desire to improve human health and yet the paths have distinctively different foundations (Figure 1).

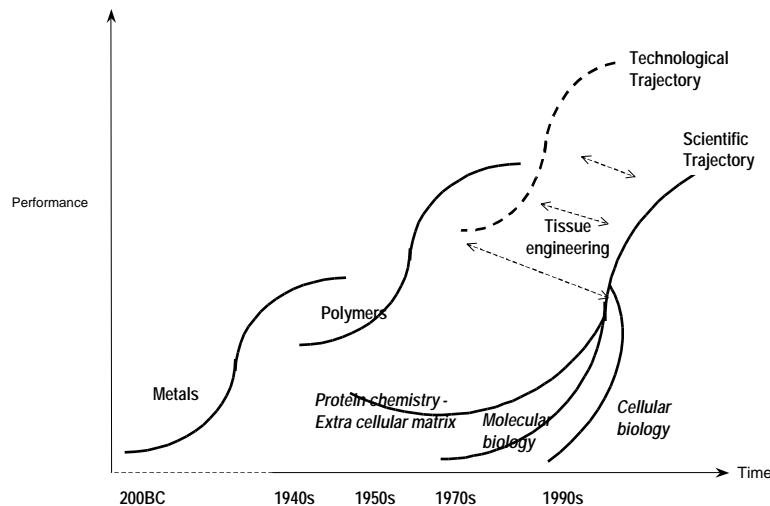


Figure 1 Origins of the Scientific & Technological Trajectory in Tissue Engineering

The long history of experimentation and interest in understanding, managing and ultimately remaking our organs dates back to the use of metal in teeth by the Aztecs and can be traced through the first heart transplants and early hip replacement experiments in England in the 1950s. While physicians may have

been the chief architects of these experiments they brought into the operating room many years of knowledge from scientists and engineers and occasionally the individuals themselves. In the past decade a new approach emerged called tissue engineering: engineering a tissue that can be used in the body to repair and renovate injured cartilage, blood vessels, liver and so on. This approach poses significant technical challenges because the body has lent complex and refined properties to natural tissues that are hard to imitate. Significant scientific challenges also exist because of our limited scientific knowledge of the ways in which groups of individual cells together form entire organs and systems with complex properties and functions. In these different views of the challenge we can find the foundations of the scientific and technical trajectories of tissue engineering.

For those primarily engaged in science the backdrop of unmet medical needs translates into a series of deep scientific questions and problems. The trajectory of solving these questions builds on molecular and cellular biology, protein biochemistry and biomechanics. On the other hand technologists see unmet medical needs and practical challenges as directly shaping the contours of the technical challenge and the market opportunity. For them the tissue-engineering approach is new: This technology trajectory represents a discontinuity from the old metal and polymer-based approaches to organ repair.

4.1.1 Scientific Trajectory

A fundamental question drives the scientific trajectory. How do cells organization, develop and function at the level of living systems and organs rather than individual cells and molecules?(Lanza, Langer and Vacanti, 2000). Building new knowledge about how the body builds and repairs organs and systems rather than isolated cells drives the scientific trajectory. Interest in these questions has risen rapidly over the past decade and there has been an explosion of scientific activity in the field. This is difficult to quantify but is exemplified by the rise in NIH funding, the increase in the number of large and active research groups and an exponential increase in the number of papers in the area. A 1993 review article in the prestigious journal *Science* by Professors Vacanti and Langer has been cited 513 times providing just some indication of the growth in this field (Langer and Vacanti 1993). The field has also developed its own professional bodies such as the Society for Tissue Engineering formed in 1996.

This endeavor rests in part upon the foundations of molecular biology. But it represents a significant shift away from the core concerns with genes and their proteins had come to dominate biology, medical science and much scientific funding with the rise in modern molecular biology and genetics (Morange 1998) towards interest in a higher-level architecture of cells and systems. In exploring the scientific trajectory, scientists rapidly discovered that a focus on cells alone or the molecular biology of growth

factors was inadequate to understand the development of organs. Instead the trajectory builds on the intersection of the disciplines focused on three core aspects of biologic tissues: cells, the extra-cellular matrix and signaling systems.

Combining insights into these three components of tissue has led scientists from different disciplines to contribute a range of techniques, a range of disciplines and a breadth of professions – surgeons, endocrinologists, molecular biologists, and chemists - to the scientific trajectory. Nevertheless, basic scientific research asks questions that remain core to the original disciplines. For example molecular biologists remain focused on growth factors and their role in signaling cell growth using the tools and techniques that spurred the biotechnology revolution. Cell biologists continue to explore the cellular component of tissues but now incorporate the burgeoning field of stem cell biology. This could provide profound scientific breakthroughs if we can understand the genetic changes that switch on and off during the process of cell transformation and differentiation. It also contributes to an understanding of how cells might be transformed into nervous system, internal organs and the musculo-skeletal system (Solter and Gearhart 1999). The third element of the tissue – the extra-cellular matrix is traditionally the domain of chemists and biochemists with an interest in bone chemistry and the biochemistry of collagen. Scientific progress is focused on how chemical properties give these structures their unique mechanical properties. The role of the extra-cellular matrix appears to lie in supporting the macro-organization of cells as well as the translation of mechanical and chemical signals. Scientific progress continues around understanding how the materials of the matrix itself are formed into complex scaffold-like architectures.

Engineers who bring the rational principles of engineering to be the problems of to living systems have shaped the scientific trajectory (Vacanti and Vacanti 2000). Engineers including Langer bring skills in chemical engineering and a deep knowledge of the ways in which materials behave in the body. Others like Professor Alan Grodzinsky have spent years studying the basic science and mechanical properties of the cartilage system (Quinn et al. 1999). But many, particularly chemical engineers have become engaged in tissue engineering through their more traditional role in the technology trajectory of biomaterials that has long been concerned with tailoring the properties of materials to meet human therapeutic needs.

4.1.2 Technology Trajectory

The technical trajectory of tissue engineering can be constituted as exploring combinations of scaffolds, cells and factors to meet specific medical needs. The two trajectories of scientific and technical progress are closely linked: for example many scientists are focused on the basic question of understanding

differentiation among stem cells but this question is also relevant when applied to the formation of new tissues. However the origins of the two trajectories are very different. The technical trajectory has its history in biomaterials. Biomaterials are defined as substances other than food or drugs contained in therapeutic or diagnostic systems that are in contact with tissue (Pappas and Langer 1994). Tissue engineering represents a new approach to the development of biomaterials for implantation and regeneration. Many of our interviewees described three distinctive periods in the development and use of biomaterials: metals, polymers and cells, with cells representing the current tissue-engineering paradigm. This takes biomaterials away from its traditional roots in materials science into the world of biology.

The first paradigm or S-curve is based on metals and dates back to the ancient Chinese but continues today with over 11 million people in 1988 having an implant of some kind the most common being metallic artificial joints (Moss 1998). While metals have the great advantage of being highly inert substances and not reacting or raising an immune response in the body they fail to integrate with the biological environment –with bone or soft tissue (Agrawal 1988). This has led to a second paradigm based on polymers: silicones, Teflon, PMMA, collagen, PGA and hydrogels. Polymers have become substitutes for total joint prostheses in some instances particularly some forms of ultra-high-molecular weight polyethylene introduced by surgeon Dr. John Charnley in the 1960s (Charnley 1972). The major problem with polymer joints is the process of wear and tear, which seems to lead to a lot of debris and bone resorption. This paradigm of biomaterials continues as polymer chemists and engineers become more adept at manipulating chemical composition to match functional needs and bioabsorbability¹⁰.

The tissue engineering approach to biomaterials create a new trajectory that builds on advances in polymer engineering to create polymer scaffolds that can be used in vitro but then combines cells and growth factors in such a way as to mimic the more complex architecture of human tissue. The emergence of this practical, technological and commercial construct came with the idea of fabricating living replacement parts in the laboratory from biological rather than man-made components. The technological framing of tissue engineering is exemplified in this excerpt from New Scientist: “*a single tube of cells could be turned into enough tissues to treat hundreds or thousands of patients filling freezers with ready-to-use immune cells, neurons, heart, or liver tissue*” (Cohen 1999). Unfortunately this technological paradigm is fraught with a range of complex problems some of which are congruent with the scientific

¹⁰ This is exemplified by implant healing research at the University of Washington Engineered Biomaterials Center where scientists have developed a polymer coating process that creates tiny indentations to facilitate binding of proteins and thus promoting natural healing rather than scar tissue creation.

trajectory while some are more related to specific clinical applications and the ability to undertake tissue engineering on a widespread and cost-effective scale. Once again, the scientific and product architecture help define and shape the nature of the technical challenges that fall within the three elements (cells, growth factors and matrix) of the proposed products. Techniques are borrowed from the commercial domain of molecular biology, semiconductors and elsewhere. New micro-fabrication techniques are needed to create scaffolds for arteries and islets and other formations. Cells must be grown on a sufficiently large scale and in a form that does not change to the more general fibroblast form from the specialized form. The growth factors require genetic engineering approaches to their production.

Many firms have been created to develop the new biomaterial trajectory in tissue engineering¹¹. Many are *de novo* and some like Restore Therapeutics, Osteobiologics and Advanced Tissue Sciences are founded by academics. Some academics have moved to the business community while others remain in academia. This together with the congruence of many problems between the scientific and technical trajectories suggests that the scientific and technical networks will be highly overlapping and are certainly complementary rather than competitive in nature. However little is known about the exact content, nature and process of this overlap.

In the following two sections we outline our results regarding the two separate networks and then our results concerning their overlap.

4.2 SCIENTIFIC & TECHNICAL COMMUNITIES

Our quantitative results suggest that the communities engaged in building the scientific and technical trajectories are distinct – there is limited overlap between them and firms make the predominant contribution to the technological trajectory (patenting) whilst all the papers are authored by academics (99%). We also find that patents do not cite the foundational scientific publications in tissue engineering. Rather they cite the patent of the focal authors/inventors. Our qualitative results reinforce the finding that the two communities and their knowledge building are distinct but in addition they provide several insights into the process of making scientific and technical progress. There are distinctive networks around the two trajectories. In addition we find that particularly important features of the scientific network include graduate students becoming independent academics, competing groups and extensive co-authorship. In contrast technical progress is more closely confined and guarded by competitive strictures.

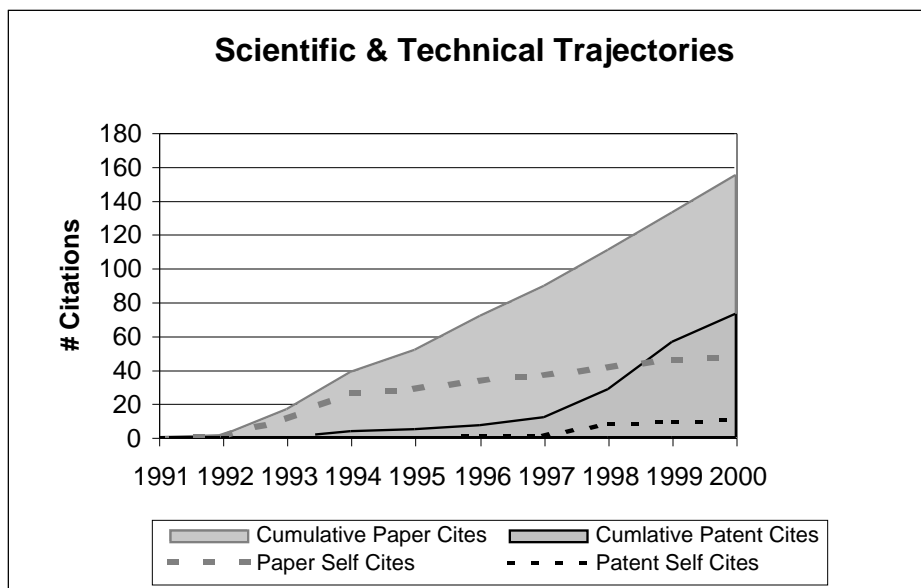
¹¹ We have generated a database of eighty-two firms in the US and Europe, based on the database of the Pittsburgh Tissue Engineering Initiative.

In addition to the distinctive scientific and technical communities and their processes there is a third community – the medical community that in tissue engineering plays a crucial and overlapping role with both scientists and technical experts.

4.2.1 Quantitative Results

Our quantitative analysis of the networks that are created by papers and patents citing the original paper-patent pair highlights the nature of knowledge building along each trajectory: The scientific network that is created along the scientific trajectory is dense, closely linked to the focal authors and is extremely wide – it encompasses over four hundred scientists over a ten year period for a single paper. In contrast the technical network is smaller, narrower and less closely connected to the focal inventors. The scientific paper builds on prior scientific work – it cites 18 scientific references (this is relatively low in this type of literature). In contrast the patent cites only four non-patent references – three scientific articles and one textbook, suggesting that at the time of the patent there was limited current literature to draw on¹².

We explore three key quantitative aspects of the trajectories of scientific and technological progress that build on the focal patent-paper pair: their shape, the individuals and their links to the focal authors or inventors, and finally the institutions engaged in the trajectory.



What is the shape of the network? The scientific network of citations that has been built on the focal paper in the past decade is extensive; it numbers 158 papers completed by over 450 authors from 59 first and last author institutions (Figure 2)

Figure 2 Patent & Paper Citations form the Trajectory

¹² This individual finding runs counted to the accepted notion expressed by Fleming and Sorenson (2000) among others that patents that are strongly science-based and that make a foundational contribution to a new technology trajectory build heavily on scientific literature.

The scientific trajectory also starts to develop soon after the paper is published with a peak in citations in 1994 and a steady flow in later years. The patent citation network (citations to the patent in future patents) has a much greater lag – the maximum year for citations is 1999. The patent network is also smaller – there are only 76 citations to the patent, which is high for a patent but almost half the number of citations to the paper pair. The patent network is also smaller – it includes only 99 authors and 32 institutions (Table 2). While nine of the patents are single inventors, only 10 are jointly assigned (this includes 7 that are jointly assigned between MIT and Children’s Hospital for the focal inventors).

	Number of self citations	Number of inventors/ authors	Number of co-authors/inventors of the focal individuals	Number of assignee/ affiliation institutions
Patent Citation Network	11	99	11	32
Paper Citation Network	50	190 1 st & last (>450 in total)	79	76 (1 st & last authors)

Table 2 Characteristics of the patent & paper citation networks

Who is contributing? The focal scientists – Vacanti and Langer - have made a significant contribution to the scientific trajectory through the papers that they have authored together and with others that build on their foundational research. Vacanti and Langer build heavily on their 1991 experimental paper. They have authored fifty of the 158 papers that cite their 1991 paper and this is only a fraction of their overall research output for the period. This suggests that for this case, scientific progress relies on detailed and cumulative knowledge building by key individuals building their own scientific path but drawing on the literature and findings of others. The network is also characterized by collaboration. Only nine of the papers are single authored. Of the remaining 64% are collaborations within the same institution and 36% are collaborations between at least two institutions.

The contribution of Vacanti and Langer to the technology trajectory is more limited. In the patent citation network they have twelve patents that cite their 1991 patent – 16% of the patents in this set. This reflects not only a lower relative contribution but also a much lower degree of inventorship than authorship activity of the focal authors/inventors. It underscores the role of the focal individuals primarily in the scholarly scientific community rather than in the commercial technical community. But perhaps more pertinent than their absolute contribution to either trajectory are the networks that they create in building upon their early scientific and technical breakthroughs (Table 3).

	# self citations pats/papers	Co-pat & co-pub generates	Of remaining pats/pubs: # by co-inventors	Of remaining pats/pubs: # by co-authors
Patent Network	12	11 co-inventors	5/64	0/64
Paper Network	50	79 co-authors	8/108	15/108

Table 3 Ties in the patent & paper network

The entire network of individuals who are part of the scientific community that built on the focal paper is significant: there are over 450 authors in total and 190 first and last authors¹³. Langer and Vacanti have worked with a significant number of these authors as scientific progress is made. In the fifty papers they have authored that cite their work on new cartilage formation they have created a co-authorship network of 79 different co-authors, some of whom have worked with them on multiple papers. Many co-authors then go on to cite the focal paper in papers they write alone, suggesting that co-authorship is part of a closely related process of building the trajectory. Thus the scientific network is broad with the focal authors densely connected to the network of many but not all of the citing authors through co-authorship.

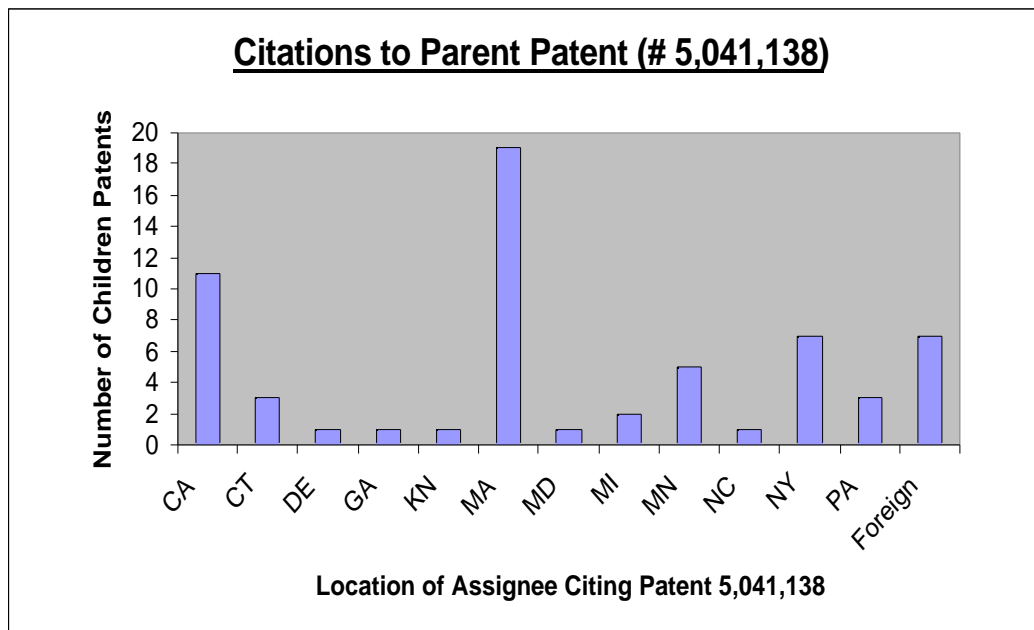
In the technological network Langer and Vacanti co-invent with only 11 additional co-inventors. All these co-inventors are individuals with whom they have published at least six co-authored papers. This suggests that while a high status individual such as Langer is willing to create a broad network of co-authors to build the scientific trajectory along his path, his co-inventorship network is only open to a few key individuals. Several of their co-inventors have also gone on to patent alone, citing the focal patent.

These data highlight a key difference in the networks from the perspective of the focal scientists – their scientific network is wide and they are densely linked to a range of co-authors. In the technological network they are not densely connected. Instead they have few co-inventors – they have no *technological* link to the remaining 91 inventors. This however does not imply that the focal inventors are not connected within the technical network. Rather that the connections are not through co-invention.

¹³ The co-authorship convention that is typically followed in this and other scientific fields is that the primary researcher is the lead author and the most senior academic in whose laboratory the research is performed is the last author. These two positions are considered to be the most significant in the collaboration

What institutions build the trajectories? We have analyzed the institutional affiliations of the first and last authors on the 158 papers in the scientific network and find 76 institutional affiliations (for first and last authors alone). These institutions are geographically dispersed (Figure 3). However they are predominantly academic – only 2 of the 158 paper citations are authored by industry – one is authored from a single firm and the other is co-authored with an academic. The technical network is quite different. The patents are also relatively more concentrated among a smaller number of assignees. The overall size of the institutional patenting network is also smaller. It includes a mix of industry and academic institutions. There are six academic institutions and three hospitals in addition to the institutions that were assigned the focal patent. There are 21 firms in the assignee network. However as we might anticipate 60% (of the non-self citing patents) come from industry.

Figure 3 Geographic Dispersion of Patents



These basic quantitative results suggest that there are two communities – scientific and technical and that there are distinctive patterns might characterize the network in these two communities – one dense and collaborative and one sparse and competitive. Our qualitative findings reinforce these results but explore in more depth the nature of the processes that drive progress in the two settings.

4.2.2 Qualitative Results

Our interviews suggest that there are in fact three distinctive communities that constitute the scientific and technical trajectories of tissue engineering. The two traditional communities that we might expect are scientific and technical. Our interviews highlight a third community of physicians. Our qualitative

results also suggest a number of features of the different communities, their practices and networks that the quantitative analysis cannot capture. Each of these features may have important implications for spillovers, participation in overlapping communities and productivity in science-oriented fields. First the scientific community is highly inter-disciplinary and crosses departmental boundaries. Progress is made through a network dominated by hierarchical ties from graduate student and former graduate student to advisor. Second, there exists an important medical community of physicians who seem to play a crucial role in spanning both the technical and scientific networks. Third while a technical community exists its network is sparse and highly competitive.

4.2.2.1 Interdisciplinary & Hierarchical Scientific Progress

The scientific community in tissue engineering is largely engaged in peer-reviewed publishing, received much of their funding from public sources and exists mainly within the traditional University institutions¹⁴. The field is emerging, taking on a more formal structure and identity over time. In 1996 Vacanti founded the Society for Tissue Engineering. This embeds the scientific community in a more structured institutional environment and brings legitimacy to the field outside of the originating disciplines. These originating disciplines are diverse and unlike more established arenas of science tissue engineering is constituted as a highly inter-disciplinary community. The backgrounds of scientists in tissue engineering reflect the many different disciplines whose insights are the key to continued scientific progress. These diverse scientists not only bring a different perspective to the problem, they also bring new tools, techniques and models from these arenas into tissue engineering. Scientists we interviewed described being part of the tissue engineering community but also integral and closely tied to their discipline. Their description of the field parallels the emergence of molecular biology in the 1950s (Morange 1998)¹⁵. Key laboratories have been built in tissue engineering on the basis of biochemistry, chemical engineering, mechanical engineering, molecular biology and surgery. Some scientists take a basically discipline-oriented approach: Professor Grodzinsky has over a twenty-year period developed a series of model systems that allow his laboratory to measure the influence of mechanical forces on the growth and biochemistry of cartilage (Lee, Grodzinsky et al. 2000). Others cross disciplinary-boundaries within their own laboratories: Professor Ingber is a molecular biologist and physician who has developed

¹⁴ The scientists we interviewed described the scope of their activities as traditional scientific practice and limited observations suggest that have been studied in more depth following ethnographic methodologies in molecular biology, biochemistry and physics following the studies of La Tour and Woolgar; cancer biology studies; Anderson and others.

¹⁵ At that time there was no recognizable discipline of molecular biology but rather a collection of physicists, chemists, and cell biologists interested in the fundamental mechanisms through which the cell encoded and translated its information. Gradually a new legitimate discipline with its related practices, problems and techniques emerged.

theories and models to explore the way in which mechanical forces shape the extra cellular matrix and influence biochemistry. However the quantitative results suggest that the need for a multi-disciplinary approach seems to lead to significant collaborations across disciplines and institutions.

Building on our quantitative evidence we explored the nature of different network ties as scientists make progress along the scientific trajectory. Our discussion of networks with scientist and technical experts in academia and industry focused on the different individuals and groups with whom they were collaborated formally and informally. We found that in this setting, academic scientists form a range of different ties to one another within their scientific communities. We discussed different modes of connection- our evidence suggests that they include ties to colleagues with complementary disciplinary expertise, to former graduate students now in independent laboratories and to their own changing set of students and fellows. Scientists were also aware of and influenced by much of the work of others – competing groups taking a similar approach and others following different scientific approaches to the same problems and questions. However some groups particularly those that are international were rarely mentioned even though they made a significant contribution to the scientific network in terms of citations.

Building Collaboration: Our interviews and participation in laboratory group meetings underscored the awareness of scientists of the need to combine different arenas of expertise into the scientific trajectory. Collaboration was driven both by the scientific challenges of tissue engineering but also by the nature of the review process: in a recent laboratory group meeting one senior professor commented to his group: “*we need to get more molecular biology expertise.*” He pointed out that the traditional reviewers at the National Institutes of Health were molecular biologists critical of the relative lack of sophistication of the group’s approach. The Professor went on to point out that “*although the molecular biologists do not know how to make anything useful, they do have valuable techniques to pin-point exactly what tissue has been made*”. Collaboration creates ties across different research groups and often institutions. While some are made for complementary expertise, collaborations are often built on personal relationships: The Langer-Vacanti collaboration of fifteen years was built on a shared post-doctoral research experience with Professor Judah Folkman and brought together Vacanti’s surgical understanding of new organs with Langer’s expertise in creating polymer scaffolds for therapeutic applications. Personal (academic) ties often overcome geography: in one group meeting, a professor suggested that his group collaborate with a

West Coast institution he had just been visiting. He said, “*we should work with Prof A – he was in the Griffith lab before going out to the West Coast*”¹⁶.

Doctoral Students: Prof A was linked to the Professor we interviewed through his time as a graduate student in a collaborating laboratory established by one of Langer’s former doctoral students. This highlights a pervasive finding in our qualitative work that can be traced through the quantitative data: A crucial and often overlooked aspect of the scientific network seems to be the relationship between scientists, their graduate students and former graduate students who are now academics. The substantial National Institute of Health (NIH) grants together with some industry money fund research laboratories with a significant number of doctoral and post-doctoral students: many of the laboratories supported upwards of twenty-five students at different stages of their training. These individuals continue to be important collaborators when they lead the laboratory to follow similar lines of enquiry but who must (by virtue of the tenure process) develop their own distinctive contribution to the scientific trajectory¹⁷.

Alternative Paths along the Trajectory: When we asked scientists about other leading figures in the field of tissue engineering, to date we have found a relatively small, overlapping group of individuals. The interviewees mentioned a number of scientists who were not always collaborators. Some of these groups were in the same institution or cluster of institutions others were international. The different groups were distinguished by the fact that they approached scientific progress in a different way: Langer-Vacanti work across many tissues, focusing on the underlying scaffolding and the *in vitro* development of tissues while others focused almost exclusively on cartilage and skin and on *in vivo* approaches. Thus while the contours of the scientific trajectory shape collaboration and scientific debate the networks are dense and shaped by the academic career path and inter-disciplinary interactions.

4.2.2.2 Loosely Networked Technical Community

In contrast, the technological network that was described in our interviews had sparse connections and the technical trajectory is shaped by competing groups taking different approaches to a series of well-defined applications of tissue engineering. The technical network is defined by organ systems. This organization of applications also maps to the organization of ideas in at least of the academic laboratories which used

¹⁶ Professor Linda Griffith was a post-doctoral student with Professor Langer (a focal individual) who now has an independent laboratory at MIT.

¹⁷ This is exemplified by Professor Anthony Atala now director of tissue engineering at Children’s Hospital has taken the research he developed in Vacanti’s laboratory and developed expertise in building artificial bladders with muscle and lining cells over a polymer scaffold. Langer also continues to collaborate with former doctoral student David Mooney now a faculty member at Michigan with a research group in Chemical Engineering.

the “organ” boundaries to present their research at group meetings. Firms also define themselves using the categories of tissues that they are engineering (Table 4).

Firm	Organs & Systems
Advanced Tissue Sciences	Skin, cartilage, blood vessels, heart valves
Organogenesis	Skin blood vessels
Osteobiologics	Bone, cartilage
Genzyme Surgical	Skin, cartilage

Table 4 some de Novo Firms in Tissue Engineering

Although they approach the same market, the approach to tissue engineering among these firms is often radically different – some pursue *in vivo* solutions while others taken an *in vitro* approach. In addition, their origins typically lie in different technical approaches. Like the scientific “roadmap” of cells, growth factors and extra-cellular matrix, one scientist who had interacted extensively with the technical community commented on the different cultures of firms founded on each of these three domains. Growth factor firms are basically in the business of biotechnology and their technical network is mainly with molecular biologists. Cell-based firms were founded to promote cell therapy and are based on culturing different types of cells. Their technical network is cell biology. The third group is interested in the ECM and has developed from the traditional biomaterials approaches to medical devices, within a network of physical scientists and engineers. Not only are their approaches different, but the groups are tied through different industry networks – the Biotechnology Association for the growth factor oriented firms and the various medical device groups e.g. MassMedic in the MA area for the matrix-based firms. The more recent firm founding are of firms, which are not as easily identified as one of these three domains – they encompass a more broad-based, but tissue specific approach. Many of the firms come together at conferences like the Orthopedic Tissue Engineering conferences but these seem to be focused on industry-academic collaboration rather than interaction and collaboration among firms.

4.2.2.3 Medical Community

While the inter-firm technical networks are sparse many firms have close ties with a community of physicians. The role of the medical community in the technical network is highlighted in a recent review of tissue engineering: “*what stands out from the past, and remains with us in the present, is the role played by surgeons in creating one body part or another to meet the needs of individual patients...it was in the tradition of innovative surgical borrowing to rebuild a body part that new materials were sought to*

substitute for what the patient's own tissues might provide" (Bell, 2000). The boundaries around certain organ systems shapes the technical network to include ties between firms working with particular organs and the related medical specialists – dermatologists, orthopedic surgeons, and in the more pioneering applications to heart valves, cardiovascular surgeons. The network ties firms to surgeons are crucial in the technical context because physicians have specialist knowledge and access to patients for clinical trials and demonstration.

The medical community is also an integral part of the scientific network. The challenge for the medical community is to response to the needs of more than 70,000 patients currently awaiting organ transplantation with fewer than 11,000 donors (cadaveric and living) available annually¹⁸. There are also 8 million surgical procedures performed annually in the United States to treat tissue loss and organ failure. (Vacanti and Langer 1999). This has led to the close involvement of a community of surgeons. In sharp contrast to the arms length role of physicians in molecular biology in which the experimental systems were isolated cell lines, the medical community and particularly surgeons are key participants in the tissue engineering scientific community. Interest among physicians is highlighted by the recent increase in articles in leading medical journals on the subject of tissue engineering. A recent JAMA edition on medical opportunities for the twenty first century also featured articles on organ replacement, stem cell therapy and biomedical engineering amongst other topics (Niklason and Langer, 1999). Tissue engineering demands the knowledge and experimental systems of surgeons who have a deep understanding of the nature of injury and regeneration of human organs. Interviewees like Professor Spector a scientist specializing in orthopedic engineering now find themselves in the operating room to really appreciate the intricacies of cellular systems and the surgical challenges they pose. The institution he joined shaped his collaboration with physicians¹⁹. He came to the Brigham and Women's Hospital to lead orthopedic research and found a context in which he could "scrub-in" to learn about the *"real problems that surgeons confront...it is very different to hearing them describe the challenges they face and the way that cartilage behaves."* This collaboration highlights the role of the physician community and importance of medical knowledge in shaping scientific networks. The integration of medical knowledge also exists when the scientist is a practicing surgeon: Vacanti himself is a practicing pediatric transplant surgeon who thus combines both experiences and works across multiple professional networks.

¹⁸ United Network for Organ Sharing. Critical Data for 2000: U.S. facts about transplantation. Available at <http://www.unos.org>

¹⁹ This follows the idea proposed by Lenoir (1995) that organizational and institutional changes arise to reflect the changes in interactions among disciplines and professional communities and that institutional change can also lead to greater interdisciplinary collaboration.

Physicians who run large laboratories expressed a drive to search for new scientific knowledge as well as treating the patients they see on a daily basis. The medical community is tied to the technical community through its care of patients. Thus the medical community plays an important role in the overlap between the scientific and technical communities. Likewise, our interviews have highlighted that far from being an ivory tower, the scientists in tissue engineering are closely tied to the technical trajectory and are strongly motivated by patient care. Our qualitative findings suggest that there is considerable activity and a multitude of ties in the overlapping networks of science and technology.

4.3 OVERLAPPING SCIENTIFIC & TECHNOLOGICAL NETWORKS

Our quantitative analysis of the overlap between institutions, individuals and activities suggest that the scientific and technological trajectories are quite distinct. There is some patenting activity among individuals in Universities, but for the most part it is confined to firms. Likewise, some individuals in firms publish but this activity is extremely limited. An analysis of the overlap of individuals finds only one individual who has crossed the boundary from academia to industry. Only five individuals participate in co-authorship or co-patenting. Thus our quantitative results imply that there are two large distinctive and separate networks. However our qualitative results are strikingly different even for the small number of individuals interviewed: they reveal significant overlap, dense communication, joint participation in conferences, and multiple modes of interaction. This suggests that our current quantitative measures do not adequately capture the actual extent and nature of overlap between the two trajectories.

4.3.1 Quantitative Findings

Our findings regarding the quantitative overlap of the two trajectories are defined by a number of different metrics: i) individuals who participate in both networks and ii) institutions that participate in both networks and iii) overlapping activity across industry and academic individuals or institutions.

There are only two out of 158 papers that are authored or co-authored by individuals in firms rather than in academic institutions. This is unexpected since the empirical and conceptual literature on spillovers would lead us to expect that numerous firms would also participate in the scientific network (Henderson and Cockburn 1994). In contrast, 29 of the 76 patents invented or co-invented by individuals in Universities or hospitals, thus emphasizing the growing role of academics in the generation of intellectual property. Our findings also suggest that the scientific and technical networks are distinctive and largely made up of *different* individuals and institutions.

We find that only a small number of individuals and institutions participate in both citation networks. However at the overlap these individuals are predominantly academics who publish and patent, while very few individuals in firms follow this path in our network²⁰. In addition very few participate in co-authorship or co-invention across the institutional boundaries of the two networks (Figure 4).

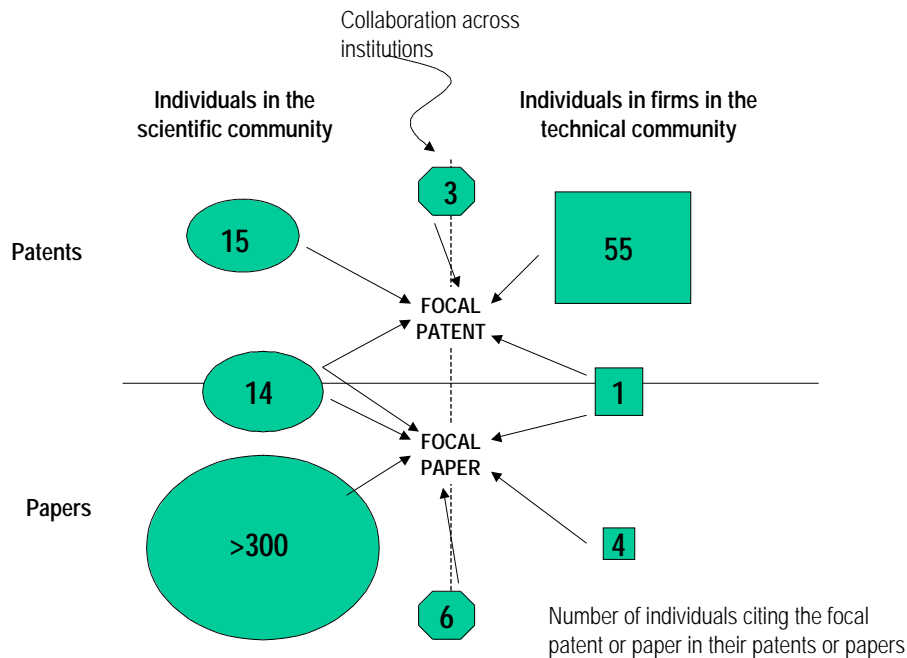


Figure 4 Individual Overlap of Scientific & Technological trajectories

If we explore who these individuals are, obviously Langer and Vacanti participate in both the scientific and technical trajectories at the start. In addition there are 11 other individuals who participate in both networks in collaboration with Vacanti and Langer. A number of these co-inventors also have patents invented alone but part of this trajectory. There is only one individual based in industry that both patents and publishes (one paper). These academics are not unusual in combining publication with patenting. The link to medicine provided an important rationale for patenting among the scientists we interviewed. One scientist described patenting as a “necessary evil” to get his research through clinical trials. When speaking of Professor Langer, MIT’s Head of Technology Licensing noted: "He says, 'I want every one of my inventions to get used to help people,'" she said. "He doesn't see this as an interruption of his academic work²¹." This suggests that at times the worlds of science and technology have closely

²⁰ Note that the number of individuals in the patenting network does not sum to 99 because some cannot be assigned to either academic or industry institutions.

²¹ MIT Enterprise Forum, Inc., satellite broadcast on May 21 1998.

connected norms and incentives particularly in the early development of the scientific and technological trajectories. This suggests that the two communities will be overlapping in the early period and may gradually diverge over time²².

Our results are similar for institutional participation (Table 5). In the tissue-engineering network around the focal patent and paper there are eight academic institutions that participate in both the scientific and technical networks but only one firm that engages in patenting and publication -Advanced Tissue Sciences based in California and they have only published two papers in this network.

	Patents only	Papers only	In both networks Patents & Papers
Academic Institutions	3	62	8 (2 focal)
Business Firms	20	1	1

Table 5 Institutional Overlap for patenting and publishing activities

If we turn to overlaps that lead to co-authorship and co-inventorship across institutional boundaries we find very limited activities. Only two are co-authored through an industry-academic collaboration. Not surprisingly, only one patent is co-assigned to a University and a firm. In aggregate these results run counter to our expectations regarding significant patenting and publication activity on the part of firms in new, leading edge arenas of technology in which the scientific and technical trajectories are closely linked and mutually reinforcing (Liebeskind et al.1996). This puzzle together with our qualitative research suggests that we ought to conceptualize the overlap of the networks with a more fine-grained analysis and supplement these findings with qualitative insights. This ought to inform our understanding of how interactions are shaped between the scientific communities who build the scientific trajectory and the technical communities who are developing applications and commercializing them.

There exist a wide range of additional mechanisms through which individuals and institutions can cross boundaries and participate in the activities of the scientific and technical communities. The literature on spillovers recognizes a number of these different modes of overlap amongst the scientific and technical networks. This section presents a more detailed analysis of the overlapping networks and then our

²² This pattern mirrors our understanding of the early developments in recombinant DNA: early scientists were closely engaged in both the scientific and the technical communities (Kenney 1986).

qualitative findings. We explore a range of mechanisms of overlap that can be found in the quantitative data on careful analysis: citing of scientific papers in patents by firms, co-authorship and co-patenting of papers by individuals in firms and academic institutions and the movement of individuals from one community to the other. We then explore our interview-based findings of the overlap.

Citing of scientific papers: A noticeable feature of the technical network is that despite the considerable overlap in content between the patent and the paper, there are only five citations to the 1991 paper in any of the patents in the first generation patent network and these are all patents filed by Vacanti and Langer. We are currently gathering data on other non-patent references in these seventy-six patents.

Co-authorship of papers: As noted above, firms neither cite Langer and Vacanti's paper in their patents, nor do they participate in the publication network. Of the two firms who publish in the scientific network one is Organogenesis - founded by Professor Eugene Bell (now an Emeritus Professor at MIT). Their paper is co-authored with academics from Tufts. The second is Advanced Tissue Sciences (ATS) also founded in 1986 by a now former academic Dr. Gail Naughton²³. ATS have two papers – one alone and one that is co-authored with Dr. Daniel Grande, Director of the Orthopedic Research Laboratory, Dept. of Orthopedic Surgery, North Shore. We also found evidence of co-inventorship – a mechanism that has been overlooked in the literature on spillovers the exchange and flow of knowledge.

Co-inventorship of patents: There are a number of examples, even in the limited data set on the patent-paper pair of individuals who co-invent across scientific and technical community boundaries. There are two mechanisms through which this takes place. The first is through co-inventorship with joint assignment and the second is co-authorship with the academic inventor assigning their work not to their academic institution but solely to the firm. Dr. Grande again exemplifies an example of co-inventorship and co-assignment. In 1995 he filed a patent co-invented with Lucas that was jointly assigned to his academic institution and MorphoGen Pharmaceuticals, a New York-base start-up company²⁴. Lucas and another co-inventor Henry Young continue to build on the technology trajectory with their 1996 patent (assigned to MorphoGen alone) that also cites Vacanti and Langer²⁵. The other example of co-invention is by Barbara Boyan, Professor and Director of Orthopedic Research at University of Texas. She remains affiliated to an academic institution but works on patents assigned to either her University or the firm she

²³ Gail Naughton received her PhD in Biology from xxx in 197x and was a member of the Faculty of the School of Nursing of Hunter College in New York City.

²⁴ Patent #5,906,934 Mesenchymal stem cells for cartilage repair, Approved May 25, 1999.

²⁵ Patent #5,837,235 Pluripotent mesenchymal stem cells and methods of use thereof, Approved October 27, 1998.

co-founded. She has four patents in the network one of which is assigned solely to OsteoBiologics, a Texas-based start-up and the other three to the Regents of the University of Texas.

Movement of individuals across networks: While Grande and Boyan appear to work across the boundaries of academia and industry, their primary affiliation seems to be with an academic institution. However another mode of overlap is the movement of scientists from academia to firms. One example of this is evident in these networks. In earlier papers, Ishaug publishes with Professor Mikos and is affiliated with Rice University, Department of Chemical Engineering. Analysis of this author in the Michigan Abstracts Database traces her PhD to Rice with Professor Mikos as her supervisor²⁶. In a 1999 publication, Ishaug-Riley is the first author of a publication solely affiliated with ATS.

4.3.2 Qualitative Results

The movement of individuals from academia to firms and collaboration across boundaries both represent examples of the different modes through which spillovers take place and the networks of science and technical trajectories overlap. However, the overall quantitative results suggest that the overlap between the scientific and technical trajectories is extremely limited and confined to a very few individuals. Nonetheless, even these limited quantitative examples are somewhat suggestive of more rich and complex modes of overlap between networks. We have explored this in more detail in our qualitative work. Our qualitative results contradict our quantitative results: We found that there is a rich overlap between the academic community and the technical community and that progress along the technical trajectory is strongly shaped by the scientific trajectory. Our qualitative evidence suggests that there is considerable and substantive overlap between the two networks but that it typically does not take the form of co-authorship or co-invention.

Our initial evidence is outlined in above (Table 6). This suggests that some overlaps arise between scientists who represent key figures in the scientific network and those individuals to translate that work into commercial applications. However the overlap moves beyond individual links as the table highlights. Further investigation and interviews reveal that the relationships across the scientific and technical networks arise through five key mechanisms: informal links such as conference participation and a series of more formal ties – sponsored research, consulting and Scientific Advisory Board Membership, employment of graduate students and licensing.

²⁶ Susan L. Ishaug-Riley, Ph.D. 1997. Bone Formation By Three-Dimensional Osteoblast Culture In Biodegradable Poly (a-Hydroxy Ester) Scaffolds.

Top inventors in patent network (excluding focal inventors)	Affiliation	# Patents	# Publications	Relationship to focal inventors
Gail Naughton	Advanced Tissue Sciences	7	0	Founder of firm ATS which now has rights to the focal patent
Anthony Atala	Children's Hospital	6	4	Co-author and former member of Vacanti's lab at Children's Hospital, now in Urology
Brian Naughton	Advanced Tissue Sciences	6	0	CSO of firm ATS which now has rights to the focal patent
John Brekke	THM Biomedical	5	0	
Mary-Ann Walter	Osteobiologics	4	0	

Table 6 Links of key inventors to focal inventors

Conference participation: This routinely brings the scientific and technical communities together particularly in the context of medical applications. For example, at the recent Advances in Orthopedic Tissue Engineering conference in January 2000 in Washington D.C. six of the eighteen speakers were from industry. Scientists were among the most central figures in the field. However on closer examination these presentations show significant differences – those from industry speakers are typically concerned with reporting specific results from application-oriented clinical and scientific studies. For example one abstract in cartilage tissue engineering was focused on the firm's new product: *“Numerous animal studies were performed to obtain pre-clinical data that supported two human clinical feasibility studies and, presently, a multi-center trial with the Collage meniscus Implant [ReGen's product]...based on results to date we conclude that the Collagen Meniscus Implant is implantable, biocompatible and resorbable and supports new tissue regeneration as it is resorbed”*²⁷. The practical application in human trials highlights the fact that academic physicians mediate much of the overlap between the two communities. The papers co-authored in the tissue-engineering network we have studied – by Organogenesis and ATS - have an academic co-author that is a scientist-physician in a medical setting.

²⁷ Dr. W. Rodkey, VP Scientific Affairs ReGen Biologics. “Collagen Meniscus Implants: A New Technique to Preserve and Restore Damaged Meniscus Cartilage” Abstract for Advances in Orthopedic Tissue Engineering, January 2000, Washington D.C.

This is not surprising given the potential audience of leading physicians: they can provide significant reputation benefits to the firms, access to patients, and independent clinical trials. Our interviews suggest that co-authorship is often merely a signal of a more formal overlap that might include sponsored research and consulting.

Sponsored research, consulting & students: One professor we interviewed commented that “although patenting is important and useful, what I really enjoy is training my graduate students and watching them establish themselves as academics in their own right....sometimes funding from industry and sponsored research helps us to train more students”. In line with the overall trends in industry funded research, in tissue engineering, sponsored research and consulting were common modes of overlap between science and firms. Many of the professors had done formal and informal consulting for tissue engineering firms. However they occasionally found this challenging with de novo firms because sponsored research budgets were likely to be cut in times of financial difficulty. Nevertheless sponsored research is also an important route to overlap through graduate students. In three instances documented so far, graduate students have moved from the laboratories of key tissue engineering scientists to firms active in the field. In at least one of these cases, sponsored research constituted another tie between the lab and the firm. Graduate students can be thought of as an important “output” of the scientific trajectory in addition to the knowledge that is created. They can participate in further building the scientific trajectory or move to the technical community. Another increasingly critical output of Universities is intellectual property – as our data show this is certainly the case for Universities active in tissue engineering. Such IPR contributes to the technological trajectory but actually influences patient care when it is reduced to practice. This typically takes place through licensing and provides a crucial link between the scientific and technical communities.

Founding & Licensing: Our qualitative interviews suggest that two firms – ATS and Reprogenesis - have extensive overlap with the focal authors. In the case of ATS this is consistent with the number of patents in the technical trajectory but not with their limited co-authorship and publishing. The relationship between ATS and the scientific community is complex. The focal patent was assigned to MIT and Children’s Hospital in 1991 and managed by MIT who licensed it to a start-up firm called Neomorphics co-founded by Vacanti and Langer. In 1992 Neomorphics was acquired by ATS with the sale including many (but not all) of the rights to the 1991 focal patent and related patent portfolio. In the period after the acquisition Langer and Vacanti continued to be closely involved with the business. They were in regular scientific discussions with the firm, one of Langer’s technicians moved to work with them, and Dr. Ishaug, mentioned above, moved to the firm from the laboratory of one of Vacanti and Langer’s close

collaborators, Professor Mikos. For a number of years after the acquisition, the focal authors maintained a close relationship with ATS beyond the formal exchange of control of their intellectual property rights. None of this is evident in the quantitative network data. However the overlap between the scientists and another firm – Reprogenesis – is even less obvious.

Reprogenesis is not linked through co-authorship or patenting to the focal authors in the network. However it is the firm with the closest current ties to the focal scientists²⁸. Indeed the firm was co-founded by the focal scientists. Reprogenesis also has rights to the focal patent for some applications²⁹ and has clinical trials underway at Children’s hospital with Dr. Anthony Atala, a co-author of Vacanti and Langer. In addition the firm’s chief scientist Dr. Frank Gentile is a PhD graduate of MIT in Chemical Engineering and is in communication with the scientists³⁰.

These two firms highlight the close overlapping ties between the scientific and medical communities and firms. Such ties appear to be particularly evident for de novo firms in the early stages of a new scientific and technological trajectory whose intellectual foundations are closely linked.

5 5. CONCLUSIONS

Our broad research agenda is focused on the nature and differences of scientific and technological networks. We are also interested in how these networks overlap and are linked through multiple different ties. In either the literature on spillovers and the networks literature few papers that we are aware of explore these two different but interacting worlds in a parallel setting.

In this preliminary paper we have explored the networks that were built around a single paper and a single patent in a biomedical setting. These two “documents” form a natural experiment because they both transcribe the same idea: the attachment of cartilage cells to a polymer scaffold in order to tissue engineer replacement human cartilage. The two texts are different – the paper describes experimental results while the patent defined the scope of the underlying idea and claims its inventiveness. From this starting point we can trace the networks as the scientific and technical trajectories evolve (in one generation of citations over a decade long period). Our research design overcomes the difficulties typically associated comparing the two networks – the fact that the starting ideas are rarely similar and that the focal authors and inventors rarely contribute to both trajectories.

²⁸ Reprogenesis was founded in 1993 and merged with Creative Biomolecules and Ontogeny to form Curis in 2000.

²⁹ Reprogenesis S1 document.

³⁰ In their paper in *The Lancet* (Langer and Vacanti 1999) they cite a personal communication with Dr. Gentile.

Our preliminary findings are twofold: First they concern the differences between the two networks and second they highlight the nature of their overlap. Our results suggest that for the cartilage case the two networks are characterized by very different logics. Far from being similar in their size, structure, and collaboration (between individuals and institutions), they are quite distinctive. The scientific network is broad, the focal authors continue to make significant contributions and create a wide network of academic co-authors within and across institutions. In contrast the technical network is narrow, incorporates fewer inventors and fewer institutions. The focal inventors play a less significant role and create fewer co-inventors. The range of institutions is also more varied – the technical network includes firms, academic institutions and hospitals.

Our second set of results suggests that the overlap between the two networks is significant but in this instance does not arise through the mechanisms that are described in the literature. Instead of co-authorship and significant participation in the world of “science”, the ties include licensing, consulting on the part of academics, the movement of graduate students, and firm founding. This suggests that at least for tissue engineering, rather than firms moving into the world of science, academics are moving into the world of technology – not entirely but through mechanisms that allow them to participate in both worlds.

These results make a contribution to the literature on technological change and the social context in which science and technology evolve. We provide a detailed analysis of this process in one particular setting. Our findings have implications for our understanding of the nature of scientific and technological networks in the contemporary biomedical setting. They emphasize the importance of the technological network and notions of the market in the scientific network – licensing, patenting and consulting and the overlap with the technological network are part of the modern scientific institution. Our results also inform our understanding of the organization of firms engaged in the commercialization of newly emerging science and technology – specifically that the emphasis on co-authorship and science on the part of firms engaged in the technological network may be only part of the picture .

Our case study of tissue engineering also highlights a point already made in the academic literature but our findings underscore its significance: technology transfer is an extremely complex process that remains poorly understood. The technology embedded in the tissue engineered cartilage patent did not transfer smoothly from academic laboratory to a firm and then into a commercial product. The ideas were licensed to a newly formed firm, which was subsequently acquired, and parts of the rights transferred. Some aspects of the ideas and their application were licensed to a third and fourth firm. In each case the relationship between the inventors and the firms was quite different and varied over time.

Our study is preliminary and has raised some intriguing issues that we intend to tackle in future research.

In the first place are these results generalizable? We will use further matched pairs to explore the scientific and technological networks in other cases. In the second place these findings raise intriguing questions of productivity. Are productive scientists embedded in both kinds of networks? And what about productive firms? Although we do not explore these issues in this paper, our continued research asks the question of whether the interactive effects between the two networks are actually critical?

These results imply that firms must construct a complex web of relationships with scientific institutions and scientists that allow for the exchange of ideas, intellectual property, expertise and human capital. The question of which of these mechanisms is the most important for successful technological productivity and under what conditions remains unanswered. Thirdly, our findings raise important questions regarding the degree to which overlap between science and technology, particularly in the direction of scientists participating in the practices and institutions of technology, is desirable.

6 6. REFERENCES

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