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# Innovation as co-evolution of scientific and technological networks: exploring tissue engineering

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## Abstract

The question of exactly how science is commercialized is an important one. While the social structures of “science” and “technology” are distinctive, recent work suggests that scientific and technological ideas in fact co-evolve. This paper addresses the dynamics of such co-evolution: are scientific networks deeply co-mingled with networks through which technology is created and if so how? It does so in a study of an emerging area of biomedicine—tissue engineering. The research is based on a novel methodology that takes advantage of the fact that an idea is often inscribed in both a patent and paper, thus forming a patent–paper pair. Starting with the pair, it is possible to trace the citation network of patents, papers, inventors and authors, combining traditional bibliometric analysis with in-depth interviews to provide new insights. The results show that for this case there exist distinctive scientific and technological networks. Furthermore, while there is evidence of overlap, it is neither co-publishing nor citation as might be predicted from current literature. Rather co-mingling exists through founding, licensing, consulting and advising. This has implications for our understanding of the processes through which spillovers arise, the way in which commercialization and technology transfer should be structured and for recent debates on conflict of interest in biomedicine. © 2002 Elsevier Science B.V. All rights reserved.

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## 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 improved the picture. While the institutional structure of “science” and “technology” are quite different, the old view that “science” was an exogenous, self-contained process has been replaced by a growing awareness that science may be, to a considerable extent, endogenous.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 unanswered questions regarding the dynamics of science–technology interactions. In the 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 and commercialized? 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

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of these overlaps on the social structure of science.<sup>1</sup> 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 broad range of ties that define the overlap.<sup>2</sup>

In this paper, I draw on a study of the development of tissue engineered cartilage to explore these issues. Using in-depth interviews and a detailed analysis of 76 patents and 158 papers, I show that in this particular case there exist quite distinctive 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). My findings suggest that at least by bibliometric measures: (i) few key scientists publish across industry–academic boundaries; and (ii) firms do not participate in science. However, rich interview and archival analysis highlight that considerable overlap exists between the two networks not typically captured in traditional analyses of science and technology. The processes that shape overlap and co-evolution range from the continued involvement of key scientists in further patenting and technology development in addition to firm founding, consulting, mentoring and informal scientific advising. These appear to lay a potentially significant and previously unexplored role in transforming scientific progress into technical and commercial benefits.

This research not only describes the overlapping networks but also aims to develop a more nuanced understanding of the processes that they embody. My 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 community into debates on technological change. Finally, it takes a closer look at the processes that are associated with spillovers and examines the contemporary context in which networks overlap to shape co-evolution of science and technology.

## 2. Literature review

I draw upon a well-established research tradition for this detailed study of the networks of science and technology. In particular, I revisit the enduring issue of the relationship between science and technology that has animated scholars of technical change and science studies, as well as policy-makers, for many years. Nonetheless, the distinction between science and technology is difficult to operationalize. Furthermore, in research universities and firms alike, the boundary between the two is becoming increasingly fuzzy and not always be recognized by those engaged in the various activities. For the purposes of this paper, I use Dasgupta and David's (1994) definition as a starting point. They draw a distinction between the social organization of the worlds of science and technology. Whilst a body of scholarship in science studies has recognized that these views greatly simplify reality,<sup>3</sup> the distinction allows for useful comparative analysis. Science they argue is characterized by publication, supported by a priority-based reward system and exists predominantly (but not exclusively) in research universities.<sup>4</sup> This is in contrast to the world of technology in which ideas are produced for economic ends and encoded in patents and other modes of protection to facilitate appropriability. This simplified distinction provides a starting point from which to explore how the individual scientists, scientific and technical communities and their institutions shape the co-evolution and co-production of new ideas.

We gain some insight into co-evolution by considering three distinct arenas of scholarship: (1) the nature of the institutions and practices that separately shape the evolution of science and technology; (2) the nature of co-evolution and spillovers as it applies to

<sup>1</sup> 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).

<sup>2</sup> While Podolny and Stuart (1995), Podolny et al. (1996) and others have explored patenting networks, to our knowledge there have been no systematic studies of scientific and patenting networks.

<sup>3</sup> See, for example, the studies of Latour (1987), Latour and Woolgar (1979) and the review of Callon (1994).

<sup>4</sup> This is not to say that all ideas are shared publicly immediately and that there exist no tacit knowledge that forms the basis of scientific advantage. Rather, the overarching and simplified view of the system is shaped around publication practices.

technological progress; and (3) the existing, although limited, literature on the intersection of science and technology.

A great deal is known about the individual networks that shape scientific and technical progress. Scientific progress is characterized by the significance of institutions, practices and communities (Merton, 1957; Jardine, 1999; Lenoir, 1995; Kohler, 1976). More recently, science studies provide rich explorations of the social structures and networks shaping the scientific controversy and have explored “laboratory life” in great detail (Latour and Woolgar, 1979; Gieryn, 1983; Mulkay, 1972). 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 problem.<sup>5</sup> However, research has shown that progress is deeply embedded in a series of institutions, communities and networks that shape the choice and path of particular ideas (Almeida and Kogut, 1999; Bijker et al., 1987; Blume, 1992; McKelvey, 1997). More recent work has highlighted the importance of position in the technical network for overall firm performance (Podolny and Stuart, 1995; Rosenkopf et al., in press).

While these studies typically highlight science or technology, the notion of co-evolution forms an important part of scholarship on the economics, history and sociology of technical change (Rosenberg, 1982). Such evolutionary theories focus on the dynamic processes behind changes in a particular variable over time (Nelson, 1995). Nelson (1995) has surveyed different approaches to the proposition that science and technology both evolve and make progress. He notes that progress in science may in part “reside in the connections between science and technology” (p. 63) with a “market like environment stimulating research on various topics” (p. 77) and that universities may play a crucial role in the development of modern technology, thus leading us to the notion that science and technology co-evolve. This so-called “endogeniety of

science and technology” highlights the importance of economic interests, commercial activities and different institutions in the nature and direction of scientific and technical progress.

In particular, the suggestion that spillovers represent the free flow of ideas among different individuals and institutions also underscores the inter-relationship between the development of ideas in one setting and their assimilation and use in another. This is particularly salient where the dynamics of science–technology interactions are concerned. That spillovers arise in the course of technological progress (when ideas developed in scientific context spillover into the technical domain) and create positive externalities for innovation is not a new insight (see, for example, Freeman, 1992; David, 1993; and the empirical evidence from Mansfield, 1995). In the biomedical arena Comroe and Dripps’ (1976) influential study documents that diverse scientific research is crucial to medical innovation. A related research stream had found a link between high citation rates and references to scientific papers in patents (McMillan et al., 2000). However, while technical progress is recognized as strongly shaped by scientific progress, until recently many conceptualized this link as a “waterfall” process with ideas in science moving seamlessly into the technological domain. A few studies exemplify the more nuanced view of the overlap between the two activities as mutually reinforcing and each shaping the other (Garud and Rappa, 1994; MacKenzie, 1992). This raises a number of critical questions regarding how the complex social organization of science and technology interact and overlap in the spillover of ideas.

Our understanding of such overlap is limited: quantitative studies typically highlight only one or two dimensions of overlap and therefore, give only a partial view of the interconnections between the networks. However, they point to the fact that a connection to “science” and scientific networks shapes technological progress. Indeed this proposition has led to a stream of research in the tradition of Henderson and Cockburn (1994) and Zucker et al. (1998) that asks how a firm’s ties to the scientific network influences its overall economic performance and more specifically its technological progress, particularly in instances when the technology is new and science-based. The general findings of this research are that three types of ties and modes for spillovers exist: publication and

<sup>5</sup> 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.

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 to one 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).<sup>6</sup> 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. Dasgupta and David (1994) comment that the “export of scientists and engineering from the academy to industrial research is potentially the most important and salutory 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: first that these networks are densely interconnected and second that the connections are simple and singular. While such studies represent one way to make the transition from studies of laboratory life to behavioral models of interaction, they have done so by defining only one or two indicators or traces of interaction. To my knowledge, there have been no studies that explore the more multiplex nature of the ties that might better capture the traces of interconnections between the scientific and technical communities. And yet in the light of our understanding that separately the networks of science and technology are rich and deeply embedded there exist a number of intriguing and unexplored issues: what is the extent of overlap between science and technology? What are the processes that shape the interaction and how do they co-evolve? What quantitative traces partially but more realistically capture such interactions? Therefore, in this empirical study I develop a narrow but systematic analysis of the inter-relationship between networks of science and technology. To do so, I use a new patent–paper pair

methodology outlined below, building on traditional bibliometric research methods but incorporating rich qualitative methods to overcome some of the limitations of the trace-oriented approach.

### 3. A novel methodology: patent–paper pairs

An exploration of the co-evolution of science and technology poses particular methodological challenges. First, which elements of science and technology are relevant and second, which individuals and institutions? To overcome this problem, I exploit the fact that in periods when scientific and technical constructs become intertwined (when scientific ideas represent not only new insights but also new technical solutions), the same idea is often inscribed in both a patent and a paper (publication), thus forming a patent–paper pair. These two “documents” form a natural experiment because they transcribe the same idea and yet the texts are distinct—a paper describes experimental results, while a patent defines utility and makes claims on inventiveness. Such pairs are, therefore, paradoxical: they make a contribution to distinctive institutions and trajectories and yet they represent inscriptions of one underlying idea. Pairs also constitute an instant when science and technology overlap. Thus, they exemplify the intertwined and co-evolutionary nature of scientific and technical ideas and communities. Using the pair methodology overcomes the difficulties typically associated with comparing networks—the fact that the starting ideas are rarely similar and that the focal authors and inventors rarely contribute to both science and technology. To my knowledge, this pair methodology has only been used in one previous study (Ducor, 2000).

Pairs can be found through a careful analysis of the content of both texts. In my methodology, a pair forms the basis for a traditional quantitative, bibliometric analyses of innovation, spillovers and networks (Jaffe, 1998; Podolny and Stuart, 1995). By measuring first generation citations to the “focal” patent and paper, I trace the networks of scientific and technical progress and build on previous work that defines the trail of progress in terms of citations (Scotchmer, 1991).

While the citation networks of patents and papers can be thought of as functionally equivalent, they arise

<sup>6</sup> 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.

through distinctive mechanisms and are driven by different forces. In the analysis of technical change, citations from one patent to another have been used to represent progress and building on earlier ideas (while recognizing that the mechanisms through which this progress actually takes place are uncertain and intermediated by patent examiners) (Flemming and Sorenson, 2000). Likewise, references to scientific papers in patents are also widely used as a proxy for spillovers from science to technology (“science linkage”) standing on the shoulders of public research to evolve and develop technical ideas.<sup>7</sup> Extending citation measures into the scientific literature, citations are used to measure importance and impact and provide some mapping of the accumulation of scientific progress. Taken together, the citation networks from the patent–paper pair provide a basis for the comparison of networks of scientific and technical progress and their overlap.

A single pair provides scope for a full exploration of the two citation networks. For each citation in the network, I gather four variables: (i) inventor(s) or author(s); (ii) assignee(s) or affiliation(s);<sup>8</sup> (iii) year of citation; and (iv) number of citations to that paper or patent (from the Web of Science or US Patent Office (USPTO) database). I analyze the set of individuals for affiliations, whether they have co-authored or -invented with the focal individuals and whether they are graduate students at the focal institutions (through the Michigan Dissertation Abstracts database). For inventors, I gathered data on the total number of patents (from the USPTO) granted and the number of papers authored (according to the Web of Science). To overcome the limitations of purely quantitative research, this analysis is complemented with qualitative work. There are two critical advantages to combining bibliometric and rich qualitative data: first, there may be key interactions between the networks not captured by bibliometric metrics—indeed one of the goals of this study is to explore whether and to

what extent this is the case; second, I am exploring questions of process—the processes through which two networks influence one another is probably only accessible through qualitative analysis. The qualitative method chosen includes interviews, observation and archival research. Interviews are with key authors and inventors who appear in the two networks. My methodology was to request in person interviews. Each interview lasted between 1 and 3 h. The focus of discussion was the interactions between the scientific and technical networks and asked individuals about their:

- direct activity in the scientific and the technical community—the extent to which they were engaged in publishing, patenting and licensing;
- typical interactions with the technical and/or scientific community;
- specific institutions with which they had interacted;
- views on the link between scientific and technical communities.

Interviews were supplemented with observations of laboratory group meetings of key university-based scientists. Archival research included a detailed content analysis of the papers and patents and for the patents, the links between assignee firms, scientists and any licenses to the focal or other patents.

#### 4. Field study: tissue engineering in cartilage

The field study reported here is in a biomedical setting, an arena where scientific and technical progress overlap and patent–paper pairs arise. Moreover, given increased funding for medical science and expectations for dramatic innovations, issues of co-evolution are particularly pertinent. In this paper, I explore the overlapping networks generated in the co-evolution of a single patent–paper pair in tissue engineering. The pair describes the attachment of cartilage cells to a polymer scaffold in order to tissue engineer replacement human cartilage. In this section, I outline the broad empirical study, the scientific and technical foundations of the innovation and the choice of the pair. The study provides insights into the varied and complex inter-relationships that characterize progress in tissue engineering. It also highlights the limitations of traditional bibliometric measures of interaction

<sup>7</sup> 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 Olivastro (1992).

<sup>8</sup> 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.

and points to the rich and often multiplex nature of interactions.

#### 4.1. Empirical study

Tissue engineering is recognized to be one of the most promising arenas for scientific and medical advance in the 21st century (Nathan et al., 2001). It combines insights from biotechnology, cell biology and polymer chemistry. This analysis, therefore, broadens our insights into biomedical commercialization beyond biotechnology into domains that will become critical in health care and aims to be complementary to but not repetitive of much of the scholarship on spillovers in biotechnology.

I began by gathering data from a range of literature sources including: (1) review articles from prestigious scientific and medical journals; (2) the 'Handbook on Tissue Engineering'; (3) press coverage through Lexus–Nexus; and (4) conferences on tissue engineering. In addition, I conducted preliminary patent searches. I supplemented this with interviews of leading academic figures in the area, many of whom are within the Harvard-Massachusetts Institute of Technology Community and therefore, readily accessible to me. The interviews took the form of semi-structured conversations, which follow two lines of inquiry: the nature of the scientific challenges in tissue engineering and the technical applications of tissue engineering.

After a few months of fieldwork, I elected to narrow my focus to cartilage tissue. While tissue engineering holds much promise for the pancreas, blood vessels, liver and spinal cord, cartilage (together with skin) is the application with at least one commercial application<sup>9</sup> and a considerable market—there are over one million surgical procedures in the US involving cartilage replacement (Langer and Vacanti, 1993). Having gathered information on the scientific and technical origins of cartilage (see Section 4.2), I found a patent–paper pair and carried out a systematic analysis (see Section 4.3).

<sup>9</sup> In August 1997, Genzyme Tissue Repair was granted product approval for their Carticel SM Service, the trade name for autologous cultured chondrocytes. This product is used in the repair of cartilaginous defects of the femoral condyle caused by acute or repetitive trauma (FDA, 1997).

#### 4.2. Scientific and technical background

Tissue engineering has emerged as a new field with active scientific and technical communities;<sup>10</sup> it encompasses diverse disciplines; and has a wide range of applications (Niklason and Langer, 2001). A recent article described it as combining “the principles of engineering and the life sciences... toward the generation of logical substitutes aimed at the creation, preservation or restoration [of organs]” (Vacanti and Mikos, 1999). Research is focused on understanding the way in which cells are assembled into tissues during development. At its simplest, tissue engineering combines the three components of tissues—cells, extracellular matrix and growth factors—to understand and achieve new tissue formation (Vacanti and Langer, 1999). Interviewees highlighted two distinctive paths representing the intellectual foundations of tissue engineering: one scientific and other technical.

The scientific foundations lie in basic questions: how do cells organize, develop and function at the level of living systems rather than individual cells (Lanza et al., 2000)? This endeavor rests in part upon the foundations of molecular biology but represents a shift away from its core concerns (Morange, 1998) towards an interest in the higher level architecture of cells. For example, in cartilage research a key is to elucidate the relationship between the chemical structure and mechanical function of the matrix (collagen and polyglycans) and cells (chondrocytes), questioning exactly how a material's chemistry can lead to the unique mechanical properties found in scaffold-like architectures.<sup>11</sup>

The technological foundations are distinctive. They are constructed around the need to find real solutions for organ failure—a significant challenge because the body has lent complex and refined properties to natural tissues that are hard to imitate. Current developments can be constituted as combinations of scaffolds, cells and factors to meet specific needs. But interviewees suggested that the historical origins of this technology

<sup>10</sup> The emergence of the field is of course itself a complex and highly contested process, but one that will not be explored here. It does, however, provide a setting for interesting future work in this direction.

<sup>11</sup> This approach is exemplified by Professor Alan Grodzinsky, from the Massachusetts Institute of Technology, interviewed 13 April 2001 (Buschmann et al., 1995).

lie in three distinctive periods in the development and use of biomaterials: metals, polymers and cells. The emergence of the practical, technological and commercial construction of tissue engineering (cells) came with the idea of fabricating living replacement parts in the laboratory from biological rather than man-made components. In cartilage, advanced polymer engineering techniques are used to create scaffolds that are combined with chondrocytes and growth factors in such a way as to mimic human cartilage. Tissue engineering is pioneered by traditional polymer and chemical engineers on the one hand and cell scientists and biotechnologists on the other. The marketplace reflects these diverse and dynamic origins.

#### 4.3. Patent–paper pair

To find a patent–paper pair for more detailed analysis, I explored the USPTO database using key words: chondrocytes (234 patents), cartilage (921 patents) and tissue scaffold (128 patents). In this set of patents, the most prolific inventors were Dr. J. Vacanti<sup>12</sup> and Professor R. Langer<sup>13</sup>. My preliminary interviews also identified Langer and Vacanti as key individuals in tissue engineering. In a search of their joint research publications, I found 53 joint papers and matched these with 11 co-invented patents. I chose the earliest pair for analysis.<sup>14</sup>

The patent is one of the earliest for tissue engineering. The patent and paper were published (granted) in 1991. Basic citation statistics are presented in Table 1.<sup>15</sup> It is cited 76 times, which is high by most comparative measures. It is the first co-patented research between Vacanti and Langer and was jointly assigned to their two institutions. It included a third co-inventor, Dr. Charles Vacanti. Later that year, the three scientists, together with Dr. B. Schloo published a “paired” paper in the *Journal of Plastic and Reconstructive Surgery* outlining experiments for in vivo cartilage “engineering” (Vacanti et al., 1991).

<sup>12</sup> Formerly affiliated to Children’s Hospital, now Professor of Surgery at Massachusetts General Hospital.

<sup>13</sup> Professor of Chemical Engineering, Massachusetts Institute of Technology.

<sup>14</sup> Patent no. 5,041,138, “neomorphogenesis of cartilage in vivo from cell culture”, granted August 1991.

<sup>15</sup> All citation data are current as of June 2001—citation numbers may have increased since that date.

Table 1  
Basic data on the focal patent and paper

	Focal patent	Focal paper
Date published	21 August 1991	1 November 1991
Number of citations in patents	76	5
Number of citations in papers	0	158

Table 2  
Citations to patents and papers

	Number of references (citations)	Average age of references (time from publication of references to patent–paper pair publication)
Paper	18 References cited	12 Years
Patent	13 Patents; 4 scientific papers	6 Years for patents; 9 years for scientific papers

The scientific paper builds on prior scientific work—it cites 18 scientific references (Table 2). In contrast the patent cites only four non-patent references—none of which are cited in the paper, suggesting that at the time of the patent there was limited current literature to draw on and that the citation process is distinctive. Nonetheless, the pair forms the starting point to analyze the scientific and technical networks that build on ideas at the intersection of scientific and technical insights.

## 5. Empirical findings

In the course of my empirical study on the overlapping networks of science and technology in cartilage tissue engineering, I explored three questions: (1) what are the basic bibliometric characteristics of the two citations networks and what drives this; (2) what is the bibliometric evidence for overlap between the two networks; and lastly (3) what are the characteristics of the ties that characterize overlap, co-evolution and -mingling at the individual and institutional level? I present my findings below, but in summary they elucidate two points. In the first place, the bibliometric data suggest that the scientific and technical networks in tissue engineering are distinctive with limited overlap: contrary to previous analysis in the biotechnology and

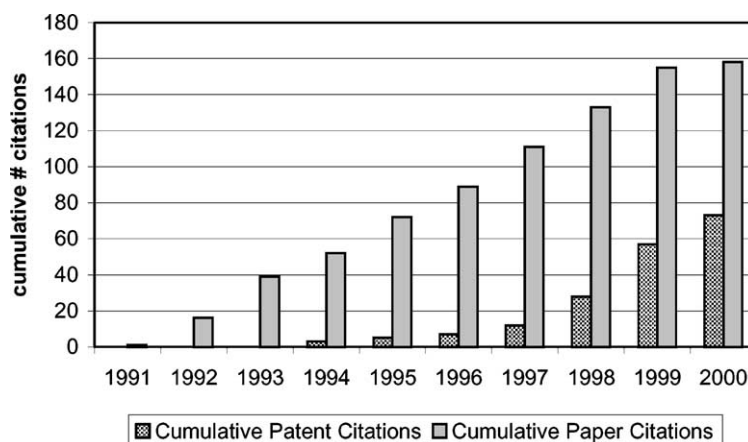


Fig. 1. Cumulative patent and paper citations form the trajectory of progress.

pharmaceutical industries there are few industry-based individuals who publish or co-author. In the second place, extensive interviews suggest that in fact dense ties link the two networks taking the form of consulting, Scientific Advisory Board membership, licensing, sponsored research and firm founding. In particular, academic scientists actively pursue publication and patenting and other links, both individual and institutional, to the firms engaged in technical advance, thus actively shaping co-evolution.

### 5.1. Basic bibliometric analysis

The scientific network is extensive—it includes 158 papers. In contrast there are only 76 citations to the patent—high for a patent.<sup>16</sup> The two networks show quite distinctive temporal patterns: the scientific network develops soon after the paper is published with a peak in citations in 1994 and a steady flow in later years; the patent citation network has a much greater lag—the maximum year for citations is 1999 (Fig. 1). When I analyzed the institutional affiliations for the papers there were 73 institutional affiliations (for first and last authors only)<sup>17</sup> and among them only two

firms, the others are academic—only three papers were authored or co-authored by individuals in firms. The technical network is quite different. The overall size of the institutional network is smaller (32 institutions) and includes a mix of industry and academic institutions: 21 firms; 6 academic institutions and 3 hospitals (in addition to the 2 focal institutions).

Many individuals contribute to the scientific network. Over 450 authors in total and 190 first and last authors contributed to the network (Table 3). Vacanti and Langer, the focal scientists, made a significant contribution to scientific progress through the papers they co-authored that build on their foundational research. They authored 50 of the 158 papers (32%) and this is only a fraction of their individual research output for the period. This suggests that for this case, scientific progress relies on detailed and cumulative knowledge building by key individuals building on their own work but drawing on the literature and findings of others. The patent network is smaller and less cumulative—it includes only 99 inventors. The

Table 3  
Size of the patent and paper networks

	Number of inventors/authors	Number of assignee/affiliation institutions
Patent citation network	99	32
Paper citation network	190 (First and last authors; >450 in total)	73 (First and last authors)

<sup>16</sup> It should be noted that the vast majority of patents receive no citations and that there is a very skewed distribution of citations.

<sup>17</sup> 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.



Table 4  
Ties to the focal authors/inventors in the patent and paper network

	Number of patents/papers by focal individuals	Co-inventing and -publishing activities of the focal individuals generates	Of remaining patents/publications: number by co-inventors	Of remaining patents/publications: number by co-authors (who are not co-inventors)	Patents/publications whose inventor/author has no direct tie to focal individuals (%)
Patent network	12	11 Co-inventors	5/64	0/64	78
Paper network	50	79 Co-authors	8/108	15/108	54

contribution of Vacanti and Langer to technical progress is more limited. They invented 16% of the patents compared to 32% of the papers. This reflects in part a lower degree of inventorship than authorship activity by the focal authors/inventors and underscores their role primarily in the scholarly scientific community rather than in the commercial technical community. But perhaps more pertinent than their absolute contribution to either domain are the networks that they create in building upon their early scientific and technical breakthroughs.

The scientific network seems to be characterized by collaboration. Only nine of the papers are single authored. Of the remaining papers, 64% are collaborations within the same institution and 36% are collaborations between at least two institutions. Langer and Vacanti, in their 50 papers have created a co-authorship network of 79 different co-authors, some co-authoring multiple papers. Many co-authors then go on to participate in the network when they write with others, suggesting that co-authorship is part of a closely related process of building the trajectory (Table 4). I found that co-authorship (and the collaboration that precedes it) is often built on the need for complementary expertise. My interviews and observation of laboratory meetings underscored the awareness of scientists of the need to combine different arenas of expertise for successful scientific progress. 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 critical of the relative lack of sophistication of the group’s approach. One group member then pointed out: “the molecular biologists. . . do have valuable techniques to

pinpoint exactly what tissue has been made.” Collaboration creates ties across different research groups and often institutions. However, the ties were often built on personal relationships: The Langer–Vacanti collaboration of 15 years was built on a shared post-doctoral research experience and brought together Vacanti’s surgical understanding of new organs with Langer’s expertise in creating polymer scaffolds for therapeutic applications. Personal (academic) ties seemed to overcome geography: in one group meeting, a professor suggested that his group collaborate with a professor at a West Coast institution. He said, “he was working in the Griffith lab before going out to the West Coast.”<sup>18</sup>

In the technological network Langer and Vacanti co-invent with only 11 additional co-inventors. These co-inventors had all published at least six co-authored papers with the focal individuals, suggesting that while a high status individual, such as Langer creates a broad network of co-authors to build scientific progress, his co-inventorship network is limited to a few scientific collaborators. Several of these co-inventors went on to patent alone and to cite the focal patent (and the focal paper). Despite the key scientists creating a smaller network of co-inventors, the technical network is still characterized by collaboration—only nine of the patents have single inventors. However, there is much more limited diversity of collaboration and very limited cross-institutional patenting.

The basic bibliometric results suggest that the scientific and technical networks are quite distinct along multiple dimensions: size, individuals, institutions and the nature of collaboration. The role of the focal

<sup>18</sup> Professor Linda Griffith was a post-doctoral student with Professor Langer (a focal individual) who now has an independent laboratory at MIT.

individuals is also quite different in each network and yet they contribute to both not only by design (in the patent–paper pair) but also in the evolution of both scientific and technical progress. My archival research also found that in addition to their role as inventors/authors they are engaged in the founding of firms to commercialize intellectual property. This suggests that at a minimum the focal individuals shape co-evolution in a number of ways. In [Section 5.2](#), I explore the bibliometric measures of overlap and use the insights gained from interviews and archival research to deepen our understanding of the modes and process of overlap and co-evolution by focal scientists and others.

### 5.2. Overlapping networks

The two networks are distinct, but a critical question remains as to whether the two networks co-evolve with overlapping and co-mingled ideas and membership. Traditional measures of co-evolution and spillovers focus on: (i) cross-citation of papers in patents; (ii) publication as well as patenting by firms; and (iii) co-publishing across academic and business institutions. For the tissue engineering networks, taking the first measure—citation of papers in patents—there is surprisingly limited cross-citation. Despite the overlapping content between the patent and paper, there are only five citations to the 1991 paper in any of the patents in the first generation patent network.<sup>19</sup> Vacanti and Langer filed four out of five of these patents and a former graduate student who is also a co-author and -inventor filed the other patent. Nonetheless, interviews enforce the notion that scientific and technical ideas are certainly exchanged by those who engage in both patenting and publication within the cartilage setting.

Therefore, turning to the second traditional measure of the intersection of these two networks, specifically firms engaged in publishing and patenting, there is only one patenting firm—Advanced Tissue Sciences (ATS)—that has published papers in this network ([Table 5](#)). This is unexpected since the more recent em-

Table 5

Institutional overlap for patenting and publishing activities—number of institutions in each category

	Papers only	Patents only	Patents and papers
Scientific/academic institutions	62	3	8 (2 Focal)
Business/technical institutions	1	20	1

pirical 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, eight academic/hospital institutions participate in both the scientific and technical networks. At an individual level, only one person with an industry affiliation both patents and publishes and he was previously an academic at Columbia University before moving to ATS. The other individuals active at the intersection of the two networks are academic scientists. Langer and Vacanti continue to participate in both networks. There are 14 other science-based individuals who participate in both networks, of whom 8 publish and patent in collaboration with Langer and Vacanti (for some but not all of their patents and papers). Turning to the third measure of overlap and spillovers, co-authorship across institutional boundaries, the tissue engineering network defined here shows limited activity. Of the three papers authored by firms, two include industry–academic collaboration.

In aggregate, these results run counter to our expectations regarding significant publication activity on the part of firms in new leading-edge arenas of technology in which the scientific and technical progress is closely linked and mutually reinforcing ([Liebeskind et al., 1996](#)). However, our interviews and more detailed bibliometric analysis point to a much greater overlap and activity in the intersection of the two networks than traditional bibliometrics suggest. These activities can be usefully organized into two categories: first, the roles of individuals in both networks shaping co-evolution which extends the notion of individuals publishing and patenting; and second, cross-boundary ties between scientific and technical institutions which extends and includes the notion of ties through co-authorship.

<sup>19</sup> This individual finding runs counted to the accepted notion expressed by [Flemming 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.

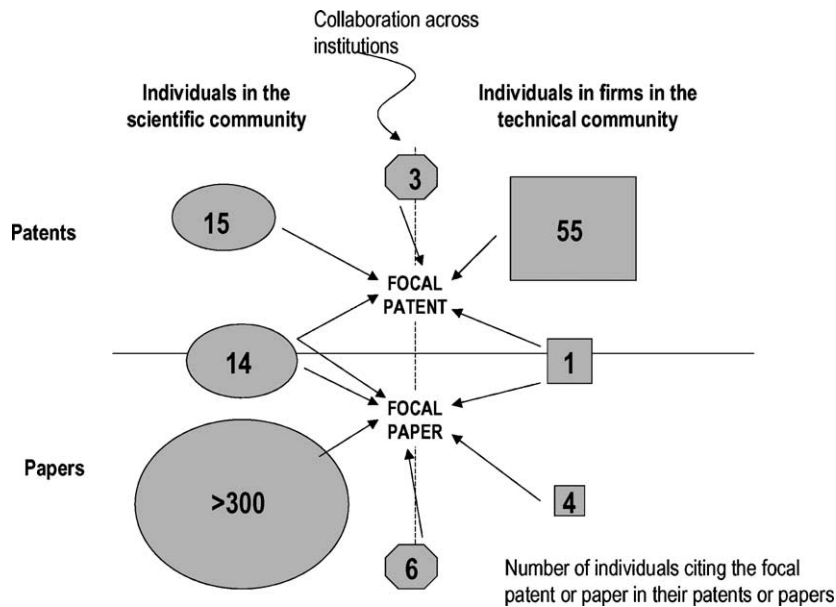


Fig. 2. Individual overlap of scientific and technological networks. Note that the number of individuals in the patenting network does not sum to 99 because some cannot be assigned to either academic or industry institutions.

### 5.2.1. Individuals contributing to scientific and technical networks

While bibliometrics reveals few industry-based individuals engaging in scientific and technical networks, more detailed analysis suggests that some do participate in both. Some like the former academic mentioned above do so by shifting institutional settings. More informal participation in both networks also arises through conference participation by those from industry settings. Conference participation routinely brings the scientific and technical communities together particularly in the context of medical applications: at the recent Advances in Orthopedic Tissue Engineering Conference in January 2000, 6 of the 18 speakers were from industry. The scientists present were among the most central figures in the field. Even though presentations do not constitute publications per se, they allow industry-based individuals to participate in the scientific community and vice versa.

More commonplace than those in the technical network participating in the scientific community, in tissue engineering is the role of scientists not only in publishing but also patenting. Emphasizing the growing role of academics in the generation of intellectual

property, 40% of the patents were obtained by individuals in universities or hospitals (Fig. 2). Scientists (not only the focal individuals) are, therefore, involved in co-evolution. Interviews point to a range of motivations. The link to medicine provided an important rationale for patenting: one scientist described patenting as “necessary evil” to get research into clinical trials. When speaking of Langer, MIT’s Technology Licensing Director 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 work.”<sup>20</sup> Participation in technical evolution can also be financially rewarding.

An extension of patenting as a means of shaping co-evolution for medical, technical or commercial goals is the role of academic scientists as consultants and members of the Scientific Advisory Boards of firms who shape technical progress. All of the scientists I interviewed had acted as consultants in one form or another for tissue engineering firms. In some instances, their work related to the design of clinical

<sup>20</sup> MIT Enterprise Forum Inc., satellite broadcast on 21 May 1998.

trials and advice on taking tissue engineered constructs through FDA approval. This made use of their expertise and experience on FDA Review Boards. Consulting also took the form of access to particular animal models and experimental systems, however, this was more often linked to inter-institutional arrangements that included sponsored research rather than academics participating alone in both the scientific and technical worlds. The closest ties I found in interviews were through membership of the Scientific Advisory Boards that provide scientific advice and send a signal of scientific legitimacy to investors. Limited empirical evidence is suggestive of their role as a signal of future success (Audretsch and Stephan, 1996). Thus, through a series of different modes—conferences, patenting, consulting and Advisory Board membership, scientists become active participants not only in the scientific community but also the technical one. These modes seem likely to be taken up by the graduate students of those already active at the intersection of the two communities. Likewise, through career experience, conferences and the ties that working with academic consultants bring those in the technical network participate in the scientific community.

### 5.2.2. *Inter-related and overlapping institutions*

Scientists most closely engaged in the co-evolution of science and technology had ties beyond patents and consulting. They shaped co-evolution by founding firms to take their patented ideas forward to commercialization. Indeed the “natural history” of the focal Patent no. 5,041,138 is a story of firm founding and acquisition. However, this activity, whilst it takes place at the initiative of an individual scientist, is distinctive from the activities I explored above because it leads to complex inter-institutional relationships as well as individual ones. Likewise sponsored research, co-invention and licensing also tie the scientific and technical communities through institutional arrangements.

My interviews and archival research suggest that soon after the patent–paper pair was published (granted) its inventors created a new firm called ‘Neomorphics’. The firm was granted some rights to the patent from the co-assignees. For a short period, the scientists were closely engaged in the firm and scientific ideas were exchanged between the laboratories and

the firm. In 1992, Neomorphics was acquired by ATS (founded in 1986) with the sale including rights to the 1991 focal patent and related patent portfolio. The relationship between ATS and the scientific community is complex. For a period after the acquisition, Langer and Vacanti continued to be closely involved with the business. Thus, ATS is tied to scientific progress not only through its founder, Dr. Gail Naughton<sup>21</sup>, a former scientist and other scientists who have shifted from academia, but also through ties to the founders of an acquired firm. Furthermore, others shift from the scientific to the technical network: one of Langer’s technicians moved to ATS; Dr. Ishaug, an author of ATS papers, moved to the firm after completing her doctorate in the laboratory of one of Vacanti and Langer’s close collaborators, Professor Mikos. Of the two ATS papers in the network, one is co-authored with Dr. Daniel Grande, Director of the Orthopedic Research Laboratory, North Shore Hospital who is also active in both scientific and technical communities with co-publishing and -patenting relationships with ATS and other de novo firms.

ATS is not unusual in its dense and overlapping ties to the tissue engineering scientific community. Osteobiologics, another firm in the patent (but not paper) network has close ties to the scientific network, but not through the obvious bibliometric measures. The firm is a Texas-based start-up co-founded by Dr. Barbara Boyan. As Professor and Director of Orthopedic Research at University of Texas, she remains affiliated to an academic institution but also patents. Of her patents, some are assigned solely to Osteobiologics and others to the University of Texas (some of which are then licensed to the firm). Boyan highlights another mode of co-evolution of science and technology—co-inventorship between members of the scientific and technical communities. This is a process that to my knowledge has been overlooked in the literature on spillovers. There are two mechanisms through which this takes place: The first is co-inventorship with joint assignment; the second is co-authorship with the academic inventor assigning their work not to their academic institution but solely to the firm. Dr. Grande

<sup>21</sup> Gail Naughton received her Ph.D. in biology and was a member of the Faculty of the School of Nursing of Hunter College in New York City.

again exemplifies an example of co-inventorship and -assignment.<sup>22</sup>

## 6. Discussion

This paper explores the co-evolution of science and technology in an emerging area of biomedical science. While the questions of the link between science and technology are old and important, there have been limited attempts to explore in detail the processes through which the networks of science and those of technology are linked. Traditional approaches to exploring co-evolution and spillovers have focused on a few, limited modes of overlap and interaction across institutional boundaries. The approach I have taken is to study co-evolution using a novel quantitative and qualitative methodology of identifying and analyzing a patent–paper pair and its networks. This should inform our understanding of the interactions between scientific communities who shape scientific progress and technical communities who are developing applications and commercializing them.

For biomedical science that encompasses cartilage tissue engineering, I have shown that scientific and technical progress arises in two distinctive networks—one predominantly the community of science and the other more mixed between the institutions of science and technology. Furthermore, there are few traces of the traditional measures of spillovers and co-evolution, e.g. cross-citation and co-publication. I find instead that these two communities are co-mingled through a range of ties centered on key scientists who: (1) engage in the practices of both scientific and technical communities—patenting, consulting, Advisory Board membership (as do their graduates); (2) build inter-institutional ties across boundaries through sponsored research, licensing and firm founding; and (3) continue to participate in both scientific and technical progress after an initial idea. This result suggests that we ought

to re-conceptualize the overlap of the networks as complex, multi-faceted and active—we might think of co-publication and cross-citation as the tip of the iceberg. Co-evolution most likely arises through a rich set of mechanisms that have only just started to be uncovered. In particular, spillovers seem to arise through active participation of academic scientists in co-evolution and technical progress rather than positive externalities from a passive scientific community to the commercial setting. This has at least two implications, one managerial and the other of policy relevance.

While the empirical study is limited to one particular setting, its lessons are far reaching for biomedical science and potentially beyond to other science-based firms and industries. As we have seen for tissue engineering the processes that underlie the co-evolution of science and technology are complex and seem to require considerable overlap between two, traditionally distinctive communities. With respect to firms, therefore, I propose that the shape and nature of overlap will have a strong influence on the innovation process: those firms that manage the balance of science and technology both externally and internally will derive significant advantage over their competition. In particular, this will mean developing new strategies that incorporate the academic scientists as important actors in the commercialization process. The capture of spillovers, particularly from academic centers active in patenting as well as publishing, may require that firms develop licensing as well as publishing strategies. However, the question of what roles and inter-institutional arrangements are the most effective remains unexplored. This suggests that future research efforts be focused on the entire spectrum of ties that firms have to the scientific community and the influence of such ties on commercial success. In particular, attention should be paid to a firm's ties both to relevant technical networks but also scientific networks for those innovations that are built on patent–paper pairs (or strongly science-based ideas). It should also be noted that there might be a temporal dimension to the role of ties, with the two communities showing significant overlap for new scientific domains and gradually diverging over time.<sup>23</sup>

<sup>22</sup> In 1995, he filed a patent co-invented with Lucas that was jointly assigned to his academic institution and MorphoGen Pharmaceuticals, a New York-based start-up company (Patent no. 5,906,934; mesenchymal stem cells for cartilage repair, approved 25 May 1999). Lucas and another co-inventor Henry Young continue to build on the technology with their 1996 patent (Patent no. 5,837,235; pluripotent mesenchymal stem cells and methods of use thereof, approved 27 October 1998) assigned to MorphoGen alone.

<sup>23</sup> 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).

Further, shedding light on the interaction between the academic and industrial “worlds” may generate policy implications for issues, such as the exploitation of biomedical insights, and of topical relevance, conflict of interest in biomedical technology transfer.<sup>24</sup> The possibility of deeply co-mingled scientific and technical institutions raises a number of public policy implications in the tradition of Nelson’s work on the Bayh–Dole Act and university-based technology transfer (Rosenberg and Nelson, 1994). Of particular relevance is the deeper understanding it brings of the role of scientists and academic physicians in commercialization. Certainly this empirical study highlights the very active role played by the focal scientists. In general, it has been assumed that more involvement in the transfer of what is often regarded as somewhat tacit knowledge, is beneficial. However, active participation in both communities, particularly for scientist–physicians may be problematic and lead to real or perceived conflict of interest unless the nature of overlap, co-mingling and ties are clearly elucidated. These issues are high on the agenda of medical research centers in the light of recent problems with clinical trials and have been the subject of extended debate in the *New England Journal of Medicine* (Angell, 2000). This paper makes some contribution to our knowledge of how biomedical innovations are commercialized. Further research is needed: first, to understand the range of pathways through which biomedical innovations are commercialized; second, to explore the performance implications of the role of inventors in commercialization; and third, to explore the influence on success of the role of scientist–physicians in order to create new and effective policies for conflict of interest.

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<sup>24</sup> A series of articles and editorials in the *New England Journal of Medicine* outlines the issues and controversy surrounding the commercialization of ideas developed in leading medical research institutions.

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