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The nanotech versus the biotech revolution: Sources of productivity in incumbent firm research

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Abstract

Does the adaptation of incumbent firms to new methods of inventing follow similar patterns across industries and inventions? We investigate this question in the context of the revolutionary scientific advances enabling biotechnology and nanotechnology, both of which represent inventions of methods of inventing for incumbent firms. We hypothesize that an incumbent firm's ability to exploit these new methods of invention depends initially on access to tacit knowledge on how to employ the new methods. Over time, however, as firms learn and/or the knowledge becomes codified in routine procedures or commercially available equipment, inventive output is more highly dependent on traditional R&D investments. We empirically test these hypotheses on two longitudinal samples over the 21-year time period between 1980 and 2000: 80 incumbent pharmaceutical firms generating 15,607 biotechnology patents, and 249 firms across a diverse set of industries that were granted a total of 3236 nanotechnology patents. We find broad support for our conjectures.

Keywords: Capability development; Research productivity; R&D investments; Alliances and acquisitions; Tacit knowledge

1. Introduction

Research and development (R&D) at atomic, molecular, or macromolecular levels, i.e., nanotechnology, by allowing the manipulation and creation of new organic and inorganic materials, processes, and products, provides enormous technological opportunities in all sectors of the economy. Such scientific breakthroughs present both opportunities and challenges to existing firms, as newly emerging firms face the same opportunities as incumbents without their organizational rigidities (Henderson and Clark, 1990; Hill and Rothaermel, 2003; Reinganum, 1989; Rothaermel and Hill, 2005; Zucker and Darby, 1997). This, of course, underlies the Schumpeterian hypothesis that radical technological change sets in motion a process of creative destruction by which new firms, whose technological identities are aligned with the new technology, can replace incumbent firms' market position (Schumpeter, 1942).

Prior research in biotechnology has challenged this view by showing that while new biotechnology enterprises played a critical role in the biotechnology revolution, their emergence did not displace the major pharmaceutical firms. As discussed by Gans and Stern (2000) as well as in Gans et al. (2002), over half of the top 10 pharmaceutical firms had well established market positions in the seventies, before the biotechnology revolution. They show that a well functioning market for ideas (through licensing, strategic alliances, and acquisitions) allowed a cooperative equilibrium to emerge

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in which biotechnology firms formed alliances with larger pharmaceutical firms rather than competing in the market for downstream products (see also Rothaermel, 2000, 2001). For the new biotechnology firms, alliances with pharmaceutical companies provided complementary assets for commercialization of products; and for the pharmaceutical firms, the new enterprises provided critical expertise in new techniques for discovery as well as manufacturing and process development, bolstering their fledging product pipelines (Galambos and Sturchio, 1998; Henderson et al., 1999; Hoang and Rothaermel, 2005). Similar arguments can be made for R&D sourcing by pharmaceutical firms through acquisitions of research-intensive small biotech firms (Higgins and Rodriguez, 2006). By drawing on the expertise of the new biotech enterprises, incumbent firms were able to adapt to the revolutionary changes in molecular biology of the 1970s rather than becoming victims of a Schumpeterian gale of creative destruction (Gans and Stern, 2000; Hill and Rothaermel, 2003; Rothaermel and Hill, 2005).

Existing firms across a wide variety of industries have faced similar challenges with the dramatic avenues for scientific discovery in nanotechnology enabled by the invention of the scanning tunneling microscope (STM) in IBM's Zürich laboratory in the early 1980s. Although the sources of the enabling inventions in nanotechnology and biotechnology differ, with the latter coming from university labs, both were revolutionary in that they were entirely *new methods of inventing* (Darby and Zucker, in press; Griliches, 1957), and thus posing substantial threats to incumbent firms.

The question we therefore address is whether the emergence of nanotechnology created a "gale of creative destruction" or whether incumbent firms have weathered the storm with similar strategies to those of incumbents in the biotech revolution? This question is of paramount importance as nanotechnology potentially affects many more sectors than did the biotechnology revolution. While biotechnology allowed the creation of new organic materials, nanotech allows the creation of new materials, both organic and inorganic. Despite the surge of papers predicting great economic and social value of nanotechnology, there has been little systematic empirical research on these issues (Roco and Bainbridge, 2001). Notable exceptions are Lemley (2005) and Sampat (2005) which examine patent quality, and Darby and Zucker (in press) which examine patenting, coauthoring patterns, and entry of new nanotechnology enterprises. The dearth of rigorous academic research on economic and social issues pertaining to nanotechnology motivated the special issue in which this article is included.

We examine whether the evolution of existing or incumbent firm adjustment to nanotechnology is following similar patterns to those in biotechnology. To empirically test if nanotechnology is following biotechnology in leveraging R&D alliances and R&D acquisitions, we use samples of 80 incumbent pharmaceutical firms attempting to patent in biotechnology and 249 incumbent firms across different industries that have been assigned at least one nanotechnology patent by the U.S. Patent and Trademark Office (PTO) since 1980.

2. Revolutionary inventions: new *methods* of inventing

Because the scientific discoveries underlying both nanotechnology and biotechnology represent inventions of methods of inventing (Darby and Zucker, in press), one might expect to observe similar development patterns in the strategies of incumbent firms when attempting to build an innovative presence in the new technologies. Indeed, Darby and Zucker's analysis of nanotech publishing, patenting, and the entry of nanotech start-ups near academic centers of excellence shows similar patterns to those in their earlier work on the biotechnology revolution (Darby and Zucker, in press; Zucker et al., 1998). The argument is that new methods of inventing create intellectual human capital that is naturally excludable. The inventors possess tacit knowledge that while often critical to further development is not easily transferred to others. This knowledge may well involve memory of avenues for development that were tried and failed, as well as those that look promising. This natural excludability provides a window of opportunity for inventors to earn above normal profits if they choose to form new enterprises to develop their discovery. Moreover, in the more than two decades since both the biotech and nanotech enabling inventions, universities have adopted liberal policies regarding faculty entrepreneurship which have facilitated the formation of new enterprises around university inventions (Thursby et al., 2001). Such firms are typically more nimble than larger, established firms and hence better suited to develop revolutionary inventions (Holmstrom, 1989).

More importantly for our purposes, the significance of tacit knowledge for further development means that, even if inventions developed are patented (as was the case with both recombinant DNA and the STM), other firms have a disadvantage in exploiting new methods of inventing. Thus, the ability of incumbent firms to adopt these new methods depends on close collabora-

tion with inventors. While some existing pharmaceutical firms have hired scientific stars (as measured by their number of journal publications and citation impact) (Rothaermel and Hess, in press), inventors of new technologies are frequently university faculty, and tend to start their own enterprises when attempting to commercialize these inventions, while remaining at universities (Audretsch and Stephan, 1996; Zucker et al., 1998), rather than taking employment at incumbent firms. Taken together, this leads to the following hypothesis regarding incumbent adoption of revolutionary inventions:

H1. When technological change associated with a revolutionary invention is embodied in human capital, incumbent firm ability to exploit the invention will depend on their alliances and/or acquisition of firms with direct access to this human capital.

Over time, as a result of further development on the part of original inventors as well as other scientists and collaborating incumbent firms, knowledge related to these methods becomes more routine and codified in commercially available documents or instrumentation. In the case of both biotechnology and nanotechnology, firms eventually developed instrumentation that enabled other firms to more easily and economically employ the new methods of invention. With codification, natural excludability diminishes, which leads to our second hypothesis:

H2. When technological change associated with a revolutionary invention is embodied in physical capital, incumbent firm ability to exploit the invention depends on the firm's expenditure on the capital.

It is important to realize that these hypotheses are not mutually exclusive. As noted by Darby and Zucker (in press), the use of commercially available instrumentation for many novel applications may well be more productive through (if not require) collaboration with scientists involved in the original invention. If this is the case, we would expect to find firms attempting to exploit revolutionary inventions forming alliances or consummating acquisitions, as well as making substantial changes in equipment purchases.

Nonetheless, these two hypotheses together suggest key potential differences between the biotechnology and nanotechnology revolutions. In particular, as others have argued in the case of biotechnology (Galambos and Sturchio, 1998; Henderson et al., 1999), the transition from random screening to guided drug discovery was difficult and lengthy. The time before instrumentation for automatic gene sequencing, an enabling technology in biotechnology, was commercially available was almost two decades (Zucker et al., 1998). By contrast, the enabling technology in nanotechnology was the STM, and by 1989 the atomic force microscope (AFM) was commercially available (Darby and Zucker, in press). According to our hypotheses, this would suggest that incumbent firms in biotechnology would rely on alliances and acquisitions much longer than would incumbent firms in nanotechnology.

2.1. Biotechnology

The scientific discoveries underlying biotechnology, which allow for the manipulation of the inner structure of microorganisms like DNA, were accomplished in the mid-1970s. A research team led by Stanley Cohen (then a professor at Stanford) and Herbert Boyer (then a professor at the University of California, San Francisco) published their scientific breakthrough on recombinant DNA [rDNA] (Cohen et al., 1973). In 1975, cell fusion techniques for producing highly purified proteins (*monoclonal antibodies*) were developed by Cesar Milstein and Georges Kohler, who later shared the Nobel Prize for Medicine for this groundbreaking research. In 1976, the first fully-dedicated biotechnology company, Genentech, was founded by Herbert Boyer and venture capitalist Robert Swanson.

The year 1980 experienced several watershed events that mark the beginning of commercialized biotechnology (Stuart et al., 1999): (1) the highly successful initial public offering of Genentech, the first public biotechnology company, which set a record for the fastest increase in stock price at IPO; (2) the passage of the Bayh–Dole legislation, which made university patenting of inventions resulting from federally funded research the rule rather than the exception; (3) the decision that new life forms can be patented[2]; (4) the patent protecting the Cohen–Boyer method of recombinant DNA was granted and assigned to Stanford University (U.S. Patent 4,237,224), which in turn licensed it freely at a nominal fee.

While Leroy Hood developed protein sequencing instruments in the 1970s, and published an article describing automatic sequencing in 1980, it was not until 1990 that the first patent was filed for an automatic DNA sequencer (National Academy Press, 1997). Nonetheless, once Applied Biosystems (ABI) acquired

[2] *Diamond v. Chakrabarty* 447 U.S. 303 (1980).

the exclusive license, this instrumentation was commercially available, and thus diffused rapidly, with thousands of DNA and protein sequencers sold worldwide.

2.2. Nanotechnology

Nanotechnology is seen as a scientific field with great technological opportunity and economic potential, with the hopes are especially high for breakthroughs and advances in medicine, manufacturing, high-performance materials, information technology, and energy and environmental technologies. While a commonly agreed upon definition of nanotechnology has yet to emerge in the literature, we follow the National Nanotechnology Initiative's (NNI) definition[3]:

> "Nanotechnology is the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications. The diameter of DNA, our genetic material, is in the 2.5 nanometer range, while red blood cells are approximately 2.5 micrometers. Encompassing nanoscale science, engineering and technology, nanotechnology involves imaging, measuring, modeling, and manipulating matter at this length scale.
> At the nanoscale, the physical, chemical, and biological properties of materials differ in fundamental and valuable ways from the properties of individual atoms and molecules or bulk matter. Nanotechnology R&D is directed toward understanding and creating improved materials, devices, and systems that exploit these new properties."

The scientific and technological breakthroughs driving the adoption and diffusion of nanotechnology were accomplished in the 1980s. The development of the scanning probe microscopy is generally considered one of the key enabling technological breakthroughs that put nanotechnology at the front lines of physical science research (Jacoby, 2000). In 1981, Gerd Karl Binnig of Germany and Heinrich Rohrer of Switzerland invented the scanning tunneling microscope (STM) at IBM's Zürich Laboratory. The STM provided the first images of individual atoms on the surfaces of materials. For their invention of the STM, Binnig and Rohrer received the Nobel Prize in Physics in 1986. While taking a leave from IBM in 1985 to conduct research at Stanford University together with his IBM colleague Christoph Gerber and Calvin Quate, they developed the atomic force microscope. The AFM was commercially available in 1989 and provided a significant advancement over the STM because it enabled researchers to conduct microscopic examinations of materials that did not conduct electricity.

[3] NNI is a U.S. federal R&D program established to coordinate the multi-agency efforts in nanoscale science, engineering, and technology. See http://www.nano.gov/html/facts/whatIsNano.html.

3. Empirical model

There is a long tradition, stemming from Evenson and Kislev (1975), Griliches (1979, 1984), of estimating firm inventive output in terms of a knowledge production function such as:

$$Y = f(\mathbf{K}, \mathbf{V}; \mathbf{z}) \quad (1)$$

where Y is a measure of research output, $\mathbf{K}$ is a vector representing the various sources of intellectual human capital, $\mathbf{V}$ is a vector of all other R&D inputs used by the firm, and $\mathbf{z}$ is a vector of parameters. To emphasize the fact that both $\mathbf{K}$ and $\mathbf{V}$ are functions of enabling technological inventions, we can write Y as:

$$Y = f(\mathbf{K}(tech),\ \mathbf{V}(tech); \mathbf{z}) \quad (2)$$

where *tech* denotes that the technical change of interest embodied in both human and physical capital. From our prior discussion, it is clear that $\mathbf{K}$ can represent the firm's internal capability or knowledge base or the type of tacit knowledge discussed by Darby and Zucker (in press) that is accessed by alliances or acquisition of new enterprises. As well, $\mathbf{V}$ represents own employees as well as physical capital used for R&D, either purchased or rented external equipment. Examples of the latter would include fees for use of STM, AFM, or other equipment, such as electron beam writers, from the universities that are part of the U.S. National Nanotechnology Infrastructure Network (NNIN) which provides non-university firms access to various types of capital-intensive equipment. Thus, as in Cohen and Levinthal (1989) and Adams (1990), firms build not only on their own inputs, but also on those they acquire from the outside—either through spillovers or explicit market transactions such acquisitions of R&D firms or through licenses.

In the empirical analysis, we use the number of (biotech and nanotech) patent applications granted by application date as our measure of inventive output. Between 1980 and 2003, the 80 incumbent pharmaceutical firms were granted a total of 15,607 biotechnology patents; and the 249 firms patenting in nanotechnology were granted a total of 3236 nanotechnology patents. Fig. 1 plots the time trends for the total number of biotech patents granted versus the total number of nanotech patents granted, using a logarithmic scale. It is

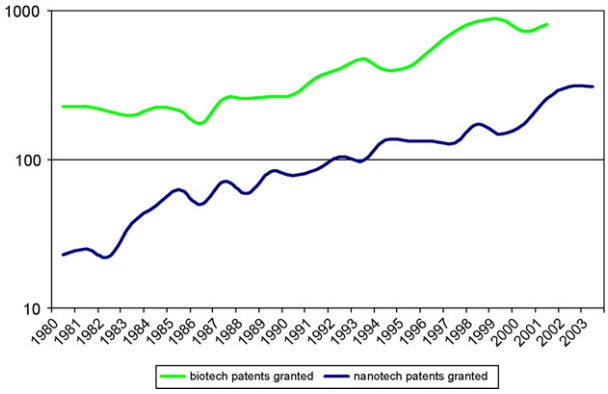

Fig. 1. Annual number of biotech patents and nanotech patents granted (logarithmic scale).

interesting to note that the shape and slope of the functions seem to approximate one another, perhaps with the nanotech patenting trend being somewhat steeper. Moreover, if we lag the nanotech patenting time series by 4 years, it correlates at $r = 0.95$ with the biotechnology patenting time series. This could be the basis for the speculation that nanotech patenting might follow a similar trend as, if not an even a more accelerated one than biotechnology patenting.

While it is natural to think of patents as a useful measure of inventive output, they are clearly only one possible measure. They are less indicative of the value to a firm of inventive output than are market-related measures. Certainly in the case of nanotechnology, however, it can be argued that using market-based measures of research productivity is premature given the early stage of nanotechnology product development.

4. Research methodology

4.1. Sample

We drew two longitudinal samples of incumbent firms to assess the effects of R&D expenditure on traditional inputs, internal knowledge capital, and intellectual capital acquired outside the boundaries of the firm on patenting in biotech and nanotech, respectively. As noted above, one sample contains 80 incumbent pharmaceutical companies attempting to adapt to biotechnology, while the second sample contains 249 incumbent firms across a different set of industries that have been assigned at least one nanotech-related patent by the U.S. PTO since 1980. Moreover, all firms in the nanotech sample are public enterprises. This additional filter was necessary in obtaining financial data. Thus, the nanotech sample is defined by incumbent firms that are public and that are assigned at least one nanotech-related patent. Taken together, the sample firms are large incumbent firms that are attempting to patent in new technology. Indicative of their large size is that the average incumbent firm active in biotechnology had average annual (inflation-adjusted) revenues of over U.S.$ 13 billion, while the average incumbent firm in nanotech had average annual (inflation-adjusted) revenues of over U.S.$ 10 billion.

4.1.1. Biotechnology

To assess incumbent firms' patenting behavior in biotech we drew a sample of global pharmaceutical companies. Incumbent pharmaceutical firms are the firms that were in existence prior to the emergence of biotechnology. These companies are generally large enterprises with a focus on proprietary drug discovery and development like Ajinomoto (Japan), Hoffmann-La Roche (Switzerland), or Pfizer (U.S.). The scientific breakthroughs in biotechnology described above represent a radical process innovation for incumbent pharmaceutical firms in the way new drugs are discovered and developed (Stuart et al., 1999; Rothaermel, 2000). In addition, incumbent pharmaceutical firms face tremendous pressures to innovate, as illustrated by the following trends (Higgins and Rodriguez, 2006): total R&D expenditures have grown from U.S.$ 6.8 billion in 1990 to U.S.$ 21.3 billion in 2000 (17% of sales); new drug development costs have increased from U.S.$ 231 million to U.S.$ 802 million between 1990 and 2000, and average sales per patented drug has fallen from U.S.$ 457 million in 1990 to U.S.$ 337 million in 2001.[4]

The pharmaceutical companies in this study focus on human *in vivo* therapeutics. This segment of the biotechnology industry comprises incumbent pharmaceutical companies that engage in research, development, and commercialization of biotechnology therapeutics that are placed inside the human body (*in vivo*), as opposed to *in vitro* therapeutics, which are used outside the human body. While biotechnology affects many different industries, the industry focus on biotechnology *in vivo* human therapeutics is reflective of its economic importance and potential, its regulatory environment, and consumer market. Focusing on human therapeutics enabled us to create a homogenous sample, while at the same time controlling for industry idiosyncrasies.

While the pharmaceutical industry has long been one of the most R&D intensive ones, the commercialization of biotechnology is also characterized by

[4] All data in constant 1999 U.S. dollars.

substantial acquisitions of biotechnology firms and alliances between pharmaceutical companies, biotechnology firms, and research universities as well as non-profit research organizations like the National Institutes of Health. In their study of the pharmaceutical industry, Higgins and Rodriguez (2006) find evidence for the importance of sourcing R&D through acquisitions of biotechnology firms. Hagedoorn (2002) shows that the level of interfirm cooperation is highest in the biotech-pharmaceutical industry among all high-tech sectors. These facts – the emergence of biotechnology as a radical process innovation for incumbent pharmaceutical firms, high levels of R&D intensity, significant technology sourcing through acquisitions and alliances, and that three decades have elapsed since the path-breaking scientific breakthroughs were first accomplished – make the pharmaceutical industry an ideal setting in which to test the knowledge production function explicated above.

To draw this sample, we relied on numerous sources documenting the global pharmaceutical biotechnology industry (in alphabetical order): *BioScan* (*annual volumes*), *Burrill & Company Life Sciences Annual Industry Reports*, *Compustat*, *Datastream* (*Thomson Financial*), *Ernst & Young's Annual Biotech Industry Reports*, *FIS Mergent*, *Osiris*, *Recombinant Capital*, *Scrip's Yearbooks on the Global Pharmaceutical Industry*, *SIC listings*, among others. We identified all pharmaceutical companies active as of 1980 and followed them through 2003. While the sample frame spans a 24-year time period, to overcome a right censoring introduced through a, on the average, 3-year time lag between patent application date and patent grant date (Darby and Zucker, in press), we ended the time series underlying this study in 2000. The sample frame for the biotech sample, therefore, consists of 1680 firm-year observations (80 firms × 21 years).

To overcome a survivor bias, we tracked each firm's life history in a detailed "family tree" linking all firms in existence at the end of our study period back to their various ancestors in 1980. This enabled us to explicitly control for horizontal mergers by pharmaceutical firms in the sample. For example, Pharmacia merged with Upjohn in 1995. Here, we tracked each firm individually until 1995, after which we merged the data for both firms, and created a dummy variable (1 = horizontal merger), indicating that these two firms had become one firm from 1995 onwards.

It is important to note that the pharmaceutical industry is characterized by significant concentration where a few dozen firms dominate the market for proprietary drugs. While tracking detailed pharmaceutical sales is difficult, because firms generally do not report sales differentiated by industrial sector, the sample firms capture the vast majority of all pharmaceutical sales worldwide. In particular, we were able to track the detailed pharmaceutical sales of 35 non-diversified companies in the sample. These 35 focused pharmaceutical companies represent only 44% of the sample, but accounted for 69% of the total sales for pharmaceuticals at the end of our study period (IMS Health, 2003). We are fairly confident that the remaining 45 firms account for a minimum 20% of pharmaceutical sales, given the oligopolistic structure of this industry. These data suggest that the sample drawn is indeed representative of the global pharmaceutical industry.

4.1.2. Nanotechnology

Since nanotechnology affects many different processes and products across a fairly diverse set of industries, we were in need of a different approach to identify a sample of incumbent firms. The only feasible option was, at this early point in nanotechnology commercialization, to include all public firms that were assigned at least one patent in nanotechnology by the U.S. Patent and Trademark Office since 1980 (see also Sampat, 2005). This search process yielded a sample of 249 incumbent firms, with a sampling frame of 5229 firm-year observations (249 firms × 21 years). To overcome a potential survivor bias, we applied the same procedure for horizontal mergers within the nanotech sample as described above when discussing the biotech sample.[5] Similarly, we obtained patent data until the end of 2003, but to overcome a right truncation effect, we ended the study period in 2000.

4.2. Data

We used the following sources to construct the two longitudinal panel datasets: We obtained firm's R&D expenditures (as well as all other financial data) from *Compustat* and *Datastream*. Alliance data for the biotechnology industry were drawn from *BioScan* and *Recombinant Capital*. *BioScan*, which is published by American Health Consultants, is a publicly available industry directory that provides data about the worldwide biotechnology industry. The sources for the *BioScan* data are mainly company questionnaires, but also include news releases, annual reports, SEC and FDA filings, journals, and investment reports, among others. *Recombinant Capital* is a life science industry consulting firm

[5] A total of 17 firms were active simultaneously in biotech and nanotech patenting.

that provides detailed descriptions of alliances in the pharmaceutical biotechnology industry. The sources of *Recombinant Capital* alliance data are comprised of SEC and FDA filings, press releases, industry conferences, and industry contacts, among others. *BioScan* and *Recombinant Capital* appear to be the two most comprehensive publicly available data sources documenting alliance activity in the biotechnology industry. Both sources are fairly consistent and accurate in reporting alliances (their inter-source reliability was greater than 0.90). Alliance data for the nanotech sample was drawn from the *SDC Platinum* database, published by *Thomson Financial*. We also used this source to track R&D acquisitions by both the incumbent firms in the biotech and nanotech samples.

Patent data were obtained from the U.S. Patent and Trademark Office (PTO), an agency of the U.S. Department of Commerce, as well as from the NBER patent database (for a description of the NBER database see Hall et al., 2001) and *Delphion* research corporation. The latter two data sources are directly based on U.S. PTO data, but allow for some more efficient searches using specific computer algorithms. We obtained detailed annual data on the complete population of all biotechnology patents assigned to the global pharmaceutical companies in the sample. The U.S. PTO compiled these data based on the complete set of *biotechnology* patents.[6] Since there are no defined nanotech patent classes as of this writing, nanotech patents were obtained through following the procedure outlined in Huang et al. (2003). This technique was also applied by Sampat (2005). Huang et al. (2003) identified a set of unique keywords pertaining to nanotechnology to define nanotech-related patents.[7] We searched the universe of patents and identified nanotech patents as the patents that contained any of the nanotechnology keywords.

[6] The dataset contains all biotechnology patents as identified by the U.S. PTO in the following patent classes: 424 [Drug, bio-affecting and body treating compositions (different sub-classes)], 435 [Chemistry: Molecular biology and microbiology], 436 [Chemistry: Analytical and immunological testing], 514 [Drug, bio-affecting and body treating compositions (different sub-classes)], 530 [Chemistry: Natural resins or derivatives; peptides or proteins; lignins or reaction products thereof], 536 [Organic compounds], 800 [Multicellular living organisms and unmodified parts thereof and related processes], 930 [Peptide or protein sequence], PLT [plants].

[7] The keywords are: atomic force microscopy, atomistic simulation, biomotor, molecular device, molecular electronics, molecular modeling, molecular motor, molecular sensor, molecular simulation, nano%, quantum computing, quantum dot%, quantum effect%, scanning tunneling microscop%, self assembl%, selfassembl%.

4.3. Measures

4.3.1. Dependent variable

Patents represent inventions in a specific technological field because they are only granted for processes or products that are novel, non-obvious and industrially useful as judged by an individual possessing proficient knowledge in the relevant technical area (Acs and Audretsch, 1989). Patent applications granted and recorded by application year is our proxy for research output (Y), and thus is the dependent variable of this study. In particular, the dependent variable is the number of patent applications granted to a firm.

We record the patent application date rather than the granting date to more accurately proxy the time of invention. It is important to note here that the U.S. PTO only records application dates when patents are granted. Thus, all patents recorded by application date are patents that were also granted. Patent data were collected until the end of 2003 to overcome right censoring. Moreover, the patent application date is a fairly good time proxy for when the invention occurred. Darby and Zucker (in press) estimate that the time lag between the date of a completed invention and the patent application date is no more than 2–3 months.

The reliability of patent count data has been established empirically, because prior research has shown that patent count data are highly correlated with citation-weighted patent measures, thus proxying the same underlying theoretical construct (Hagedoorn and Cloodt, 2003; Stuart, 2000). For example, the bivariate correlation between patent counts and citation-weighted patents has been shown to be above 0.77 ($p < 0.001$) in the pharmaceutical industry (Hagedoorn and Cloodt, 2003), and above 0.80 ($p < 0.001$) in the semiconductor industry (Stuart, 2000), indicating some generalizability of this assertion.

To assess incumbent firms' patenting performance in biotechnology, we used the annual number of biotechnology patent applications granted to the firm as the dependent variable (Y_b = research output in biotech). Likewise, to assess incumbent firms' patenting performance in nanotechnology, we used the annual number of nanotechnology patent applications granted to the firm as the dependent variable (Y_n = research output in nanotech).

4.3.2. Independent variables

4.3.2.1. Lagged patents. Lagged patents (*biotech* and *nanotech*, respectively) is one proxy for the intellectual human capital internal to the firm. We lagged total patents by one time period, and included it as right-hand

side variable. This allows us to control for a potential specification bias that can arise from unobserved heterogeneity (Jacobson, 1990).

4.3.2.2. R&D acquisitions. One way the firm can gain access to external intellectual human capital is through R&D acquisitions. We proxied this by annual counts of the firm's R&D acquisitions. These are (vertical) acquisitions of small research-intensive (nanotech or biotech) firms that are based on the new technology, rather than horizontal mergers among sample firms, which we explicitly control for. R&D acquisitions can be reasonably seen as an attempt to internalize tacit knowledge (Higgins and Rodriguez, 2006). Over the study period, we tracked a total of 1671 acquisitions. These split into 770 nanotech acquisitions (46%) of new nanotech firms and 901 biotech acquisitions (54%) of new biotech firms.

4.3.2.3. R&D alliances. A second way the firm can gain access to external intellectual human capital is through R&D alliances. We proxied this by annual counts of the firm's R&D alliances. We tracked a total of 4353 R&D alliances, and analyzed the content of each alliance. These alliances split into 590 nanotech R&D alliances (14%) and 3763 biotech R&D alliances (86%).

4.3.2.4. R&D expenditures. We proxied incumbent firms' investments in all other R&D inputs by their R&D expenditures. We preferred to use R&D expenditures, in combination with an explicit control for firm revenues, over creating a R&D intensity measure (R&D expenditures/Revenues), because it allows for a more straightforward interpretation of the results, which is more difficult in ratios.

To purify the R&D data from expenditures devoted to purchase external technology through acquisitions, for example, we adjusted the gross R&D expenditures as reported by the firms through subtracting their in-process R&D expenditures. In process R&D expenditures are defined by *Compustat* as the "the portion of R&D considered to be 'purchased' and written off immediately upon acquisition if the R&D items are deemed not to have an alternative use. This item includes purchased technology [through acquisitions]." While this enhances the accuracy of the measure, it is not perfect, because it does still contain expenditures for R&D licenses. Since the in-process R&D expenditures for R&D acquisitions did not amount, on average, to more than 1.5% (nanotech sample) and to no more than 2.6% (biotech sample) of total R&D expenditures, we expect the expenditures for R&D licenses to be even smaller, and thus should not introduce a systematic bias in our estimates. Nonetheless, we are unable to account for the R&D expenditures devoted to licenses, because firms do not record them separately. In addition, all financial data used in our analysis are inflation-adjusted in constant 2003 U.S. dollars.

4.3.2.5. Time indicator. Since the study period from 1980 to 2000 covers 21 years of observation, it is likely that the effect of different knowledge sources may change over time.[8] This is relevant for our analysis in part because biotech and nanotech are at different stages in their respective development, with biotechnology approximately a decade ahead of nanotechnology due to the earlier invention of the enabling technologies.

To empirically assess this possibility, we created a time indicator (δ_t) to test for a structural break in the univariate time series of biotech and nanotech patenting (Vogelsang, 1997; Rothaermel, 2001). We split the time series in half, taking 1990 as the midpoint, which is justified by the fact that key advances in commercially available instrumentation in both biotech and nanotech occurred immediately prior to this date, as explicated above. This variable takes on the value of 0 before 1990, and 1 afterwards. The null hypothesis states that $\delta_t = 0$, meaning biotech and nanotech patenting, respectively, Y_b and Y_n, are governed by a deterministically trending process without an observable shift in the deterministic time trend. The research hypothesis states that $\delta_t \neq 0$, implying that patenting performance is trend stationary, with a time break in the deterministic trend function. We included the time indicator (δ_t) as a direct effect as well as a moderator of the key variables of interest (R&D acquisitions, R&D alliances, and R&D expenditures).

4.3.3. Control variables

4.3.3.1. Standard Industry Classification (SIC) codes. To control for industry effects, we included indicator variables for the most frequent four-digit Standard Industry Classification codes. In the biotechnology sample, the primary SIC code was 2834 (pharmaceutical preparations) for 57% of the sample. In total, the 80 firms in the biotech sample were spread over 13 different primary SIC codes.[9]

[8] We thank an anonymous reviewer for emphasizing this possibility.

[9] The distribution of SIC codes is as follows: SIC 2834 (pharmaceutical preparations) 51 firms; SIC 2800 (chemicals and allied products) 6 firms; SIC 2820 plastic materials, synthetic resin/rubber, cellulose (no glass) 2 firms; SIC 2821 (plastic materials, synthetic resins and non-vulcan elastomers) 2 firms; and 1 firm each in the following SIC codes: SIC 2060 (sugar and confectionery products); SIC 2090 (miscellaneous food preparations and kindred products); SIC 2200 (textile mill products); SIC 2221 (broadwoven fabric mills, man made fiber

In the nanotech sample, the primary SIC code was 2834 (pharmaceutical preparations) for 7% of the sample, SIC 2911 (petroleum refining) for 4% of the sample, and SIC 3674 (semiconductors and related devices) for 6% of the sample. These were the most frequent SIC codes in the nanotech sample; firms with the primary SIC code in industries other than the three mentioned were so few that we were unable to include them in the regression analysis due to the lack of variance for these less frequent SIC codes. In total the 249 nanotech firms spread over 114 different primary SIC codes.[10]

4.3.3.2. Firm merged. As detailed above when discussing the sample construction, we explicitly controlled for horizontal mergers among the sample firms through the inclusion of an indicator variable (1 = firm merged).

4.3.3.3. Revenues. We controlled for the firms' annual revenues (constant 2003 U.S. dollars in MM). As indicated above, this control variable is especially pertinent because we include R&D expenditures as one of the key independent variables.

and silk); SIC 2840 (soap, detergents, cleaning preparations, perfumes, cosmetics); 2844 (perfumes, cosmetics and other toilet preparations); SIC 2870 (agricultural chemicals); SIC 2911 (petroleum refining); SIC 5090 (wholesale-miscellaneous durable goods); and for 10 firms a primary SIC code was not specified.

[10] The distribution of SIC codes is as follows: SIC 2834 (pharmaceutical preparations) 17 firms; SIC 3674 (semiconductors and related products) 16 firms; SIC 2911 (petroleum refining) 9 firms; SIC 3826 (laboratory analytical instruments) 7 firms; SIC 2810 (industrial inorganic chemicals) 6 firms; SIC 3841 (surgical and medical instruments and apparatus) 6 firms; SIC 3845 (electromedical and electrotherapeutic apparatus) 6 firms; SIC 2821 (plastic materials, synthetic resins and non-vulcan elastomers 5 firms; SIC 3572 (computer storage devices) 5 firms; SIC 3812 (search, detection, navigation, guidance, aeronautical systems) 5 firms; SIC 2670 (converted paper and paperboard products (no containers/boxes) 4 firms; SIC 2844 (perfumes, cosmetics and other toilet preparations) 4 firms; SIC 2860 (industrial organic chemicals) 4 firms; SIC 3559 (special industry machinery) 4 firms; SIC 3577 (computer peripheral equipment) 4 firms; SIC 3640 (electric lighting and wiring equipment) 4 firms; SIC 3690 (miscellaneous electrical machinery, equipment and supplies) 4 firms; SIC 3714 (motor vehicle parts and accessories) 4 firms; SIC 2800 (chemicals and allied products) 3 firms; SIC 2835 (in vitro and in vivo diagnostic substances) 3 firms; SIC 2836 (biological products, no diagnostic substances) 3 firms; SIC 2840 (soap, detergents, cleaning preparations, perfumes, cosmetics) 3 firms; SIC 2890 (miscellaneous chemical products) 3 firms; SIC 3570 (computer and office equipment) 3 firms; SIC 3570 (electronic computers) 3 firms; SIC 3663 (radio and TV broadcasting and communications equipment) 3 firms; SIC 3728 (aircraft parts and auxiliary equipment) 3 firms; SIC 3861 (photographic equipment and supplies) 3 firms; SIC 8731 (services-commercial physical and biological research) 3 firms; SIC 2000 (food and kindred products) 2 firms; SIC 2111 (cigarettes) 2 firms; SIC 2621 (paper mills) 2 firms; SICC 2820 (plastic material, synthetic resin/rubber, cellulose, no glass) 2 firms; SIC 3290 (abrasive, asbestos and miscellaneous non-metallic mineral products) 2 firms; SIC 3350 (rolling drawing and extruding of non-ferrous metals) 2 firms; SIC 3523 (farm machinery and equipment) 2 firms; SIC 3540 (metalworking machinery and equipment) 2 firms; SIC 3612 (power, distribution and specialty transformers) 2 firms; SIC 3661 (telephone and telegraph apparatus) 2 firms; SIC 3670 (electronic components and accessories) 2 firms; SIC 3679 (electronic components) 2 firms; SIC (motor vehicles and passenger car bodies) 2 firms; SIC 3828 (instruments for measuring and testing of electricity and electric signals) 2 firms; SIC 3842 (orthopedic, prosthetic and surgical appliances and supplies) 2 firms; SIC 9997 (industrial conglomerates) 2 firms; and 1 firm each in the following SIC codes: SIC 1311 (crude petroleum and natural gas); SIC 1600 (heavy construction other than building construction – contractors); SIC 2040 (grain mill products); SIC 2070 (fats and oils); SIC 2080 (beverages); SIC 2082 (malt beverages); SIC 2400 (lumber and wood products, no furniture); SIC 2531 (public building and related furniture); SIC 2600 (papers and allied products); SIC 2631 (paperboard mills); SIC 2750 (commercial printing); SIC 2761 (manifold business forms); SIC 2842 (specialty cleaning, polishing and sanitation preparations); SIC 2851 (paints, varnishes, lacquers, enamels and allied products); SIC 2870 (agricultural chemicals); SIC 2891 (adhesives and sealants); SIC 3011 (tires and inner tubes); SIC 3021 (rubber and plastic footwear); SIC 3089 (plastic products); SIC 3100 (leather and leather products); SIC 3211 (flat glass); SIC 3220 (glass and glassware, pressed or blown); SIC 3221 (glass containers); SIC 3231 (glass products, made of purchased glass); SIC 3250 (structural clay products); SIC 3312 (steel works, blast furnaces and rolling mills, [Coke Ovens]); SIC 3411 (metal cans); SIC 3420 (cutlery, handtools and general hardware); SIC 3452 (bolts, nuts, screws, rivets and washers); SIC 3510 (engines and turbines); SIC 3531 (construction machinery and equipment); SIC 3533 (oil and gas field machinery and equipment); SIC 3555 (printing trades machinery and equipment); SIC 3561 (pumps and pumping equipment); SIC 3562 (ball and roller bearings); SIC 3564 (industrial and commercial fans and blowers and air purifying equipment); SIC 3576 (computer communications equipment); SIC 3578 (calculating and accounting machines [no electronic computers]); SIC 3579 (office machines); SIC 3580 (refrigeration and service industry machinery); SIC 3585 (air-conditioning and warm air heating equipment and commercial and industrial refrigeration equipment); SIC 3613 (switchgear and switchboard apparatus); SIC 3620 (electrical industrial apparatus); SIC 3621 (motors and generators); SIC 3651 (household audio and video equipment); SIC 3669 (communications equipment); SIC 3672 (printed circuit boards); SIC 3678 (electronic connectors); SIC 3695 (magnetic and optical recording media); SIC 3720 (aircraft and parts); SIC 3721 (aircraft); SIC 3724 (aircraft engines and engine parts); SIC 3730 (ship and boat building and repairing); SIC 3760 (guided missiles and space vehicles and parts); SIC 3822 (auto controls for regulating residential and commercial environments); SIC 3823 (industrial instruments for measurement, display, and control); SIC 3843 (dental equipment and supplies); SIC 3851 (ophthalmic goods); SIC 3949 (sporting and athletic goods); SIC 3950 (pens, pencils and other artists' materials); SIC 4813 (telephone communications [no radiotelephone]); SIC 5040 (wholesale-professional and commercial equipment and supplies); SIC 5160 (wholesale-chemicals and allied products); SIC 7011 (hotels and motels); SIC 7200 (services-personal services); SIC 7370 (services-computer programming, data processing, etc.); SIC 7373 (services-computer integrated systems design); SIC 8711 (services-engineering services).

4.3.3.4. Total assets. We controlled for the firms' size through the inclusion of their total assets (constant 2003 U.S. dollars in MM).

4.3.3.5. Firm nationality. We attempted to control for institutional and cultural difference by coding for the nationality of each pharma firm based on the location of its headquarters. One indicator variable takes on the value of 1 if the firm is headquarted in the U.S. (*U.S. Firm*), the other indicator variable takes on the value of 1 if the firm is headquartered in Europe (*European Firm*), with an Asian location as the reference category. It is noteworthy that the two samples vary quite significantly with respect to their degree of internationalization. The biotech sample is much more globalized: 26% of the firms are U.S. based, 39% of the firms are European, and 35% are Asian. The nanotech sample is primarily a U.S. sample with 94% of the firms, while only 3% of the firms are either European or Asian. The latter is not surprising, since we sampled on firms that were granted at least one nanotech patent by the U.S. PTO. While the biotech sample is global in nature, the nanotech sample is predominantly a U.S. one. This may be less of a concern, however, since the majority of research in nanotech (54%), as proxied by high impact scientific articles, takes place in the U.S., while the European countries contribute about 19% to nanotech research (Darby and Zucker, in press).

4.4. Estimation procedures

The underlying datasets are longitudinal panels, following the same set of firms over time. The advantages of panel data include allowing the researcher to control for the initial values of the dependent variable, recognize time lags, enhance statistical power through the investigation of a larger sample size, and reducing the threat of collinearity among independent variables, which in turn improve the econometric estimates (Hsiao, 2003).

The dependent variable of this study, firm patenting, is a non-negative, integer count variable. Non-negative, integer count variables violate one of the main assumptions of the classical linear regression model, as this dependent variable cannot be normally distributed. For such data, count models provide an econometric improvement over the classical linear (OLS) regression models. The Poisson estimation is the simplest but most restricted count data model, because it assumes equity between the conditional mean and variance. Social science data, however, generally exhibit a greater variance than mean, and are thus characterized by over-dispersion. The over-dispersion in the patenting variables are highlighted by the fact that the coefficient of variation (standard deviation/mean) ranges between 2.1 (for biotech patenting) and 4.7 (for nanotech patenting), implying that the patenting rates differ by 210–470% from the averages across the two different samples.

The negative binomial estimation is an extension of the Poisson model and allows for the variance to differ from the mean and hence can handle over-dispersion. In addition, negative binomial regression accounts for an omitted variable bias, while simultaneously estimating heterogeneity (Cameron and Trivedi, 1986; Hausman et al., 1984). We conducted a test for over-dispersion that revealed that a negative binomial estimation provides a significantly better fit for the data than the more restrictive Poisson model (Gourieroux et al., 1984). A negative binomial regression analysis also represents a more conservative estimation procedure. We applied the following random-effects negative binomial model:

$$\Pr(n_{it} = Y) = \int_0^\infty \frac{1}{n_{it}} e^{-\lambda_{it}} \lambda_{it}^{n_{it}} f(\lambda_{it})\, d\lambda_{it} \quad (3)$$

where

$$\lambda_{it} = e^{\beta_0 + \beta_1 K_{Y_{it-1}} + \beta_2 K_{\mathrm{acq}_{it}} + \beta_3 K_{\mathrm{all}_{it}} + \beta_4 R_{it} + \beta_{it} Z_{it} + \varepsilon_{it}} \quad (4)$$

thus

$$\log \lambda_{it} = \beta_0 + \beta_1 K_{Y_{it-1}} + \beta_2 K_{\mathrm{acq}_{it}} + \beta_3 K_{\mathrm{all}_{it}} + \beta_4 R_{it} + \beta_{it} Z_{it} + \varepsilon_{it} \quad (5)$$

where n_{it} is a non-negative integer count variable capturing each incumbent firm's i annual patenting in year t, Y, and thus $\Pr(n_{it} = Y)$ indicates the probability that incumbent firm i receives n patents applied for in year t. The independent variables denote the following constructs:

- $K_{Y_{it-1}}$ denotes prior knowledge stock in terms of patents lagged by 1 year;
- $K_{\mathrm{acq}_{it}}$ is a count number of R&D acquisitions consummated in each year;
- $K_{\mathrm{all}_{it}}$ is a count number of R&D alliances entered in each year;
- R_{it} represents annual R&D expenditures net of in-process R&D devoted to acquisitions;
- Z_{it} is a vector of control variables.

The application of a random-effects negative binomial estimation addresses concerns of heterogeneity, and enables us to include covariates that tend to be time invariant, such as the firm's primary SIC code and national origin (Hsiao, 2003).[11] Further, to interpret the

[11] The results are robust to fixed effects estimation.

results in a meaningful manner and to reduce potential collinearity, we standardized all independent variables before entering them into the various regression models (Cohen et al., 2003). This procedure allows us to compare beta coefficients directly, and thus improves the robustness of the analysis without degrading the quality of the data. To overcome a potential simultaneity bias we lagged the key independent variables (R&D acquisitions, R&D alliances, R&D expenditures) and other time variant control variables (firm revenues and total assets) by 1 year. Prior research provides evidence for the notion that lagging R&D expenditures by one time period appears to be the appropriate specification of a time lag when estimating patenting (Hall et al., 1986).

Recall that our estimation technique is a negative binomial regression, and thus a non-linear, exponential estimation technique as explicated in Eq. (3) above. Therefore, to interpret the reported beta coefficients in a meaningful manner, one needs to exponentiate the respective beta value [$\exp(\beta)$ or e^{β}] to obtain the incidence rate ratio (IRR), holding all other variables constant (see Long, 1997: 228–229; for a recent application see Ichino and Maggi, 2000).[12] To enhance the interpretability of the results, we display incident rate ratios instead of beta values. An IRR of greater than 1 increases the probability that firm i will be assigned the expected number of (biotech or nanotech) patents, whereas an IRR of less than one is reflective of a reduced probability.

Since the time series under investigation is a lengthy one of 21 years, it is likely that the relative importance of different inputs (e.g., intellectual human capital and physical capital) changes over time. Given the dates of the Hood patent and the year the AFM became commercially available, we used, as discussed above, the year 1990 as a time indicator to empirically assess whether such changes of relative impact factors took place. To do so, we estimated a fully specified model including a time indicator in addition to interactions of the time indicator with R&D acquisitions, R&D alliances, and R&D expenses over the entire study period (1980–2000) for both the biotech and nanotech samples. This estimation procedure allows us to compare different stages in the development of biotechnology and nanotechnology in the sense that the scientific discoveries underlying biotech preceded nanotech by about a decade.

[12] A negative beta value translates into an incidence rate ratio of less than 1, while a positive beta value translates into an incidence rate ratio of greater than 1.

5. Results

Table 1 presents descriptive statistics as well as comparative mean t-tests for the variables in this study across both samples. What the data in this table reveal is that, while incumbent firms in both samples face new methods of inventing with biotechnology and nanotechnology, respectively, the firms in both samples differ significantly along the dimensions considered in this study. On average, the incumbent pharma firms produce a larger number of biotechnology patents (8.87) than the incumbents that patent in nanotechnology (0.54), which appears to be a function of different stages in the technology life cycle. During the 1980–1990 decade, the average number of biotech patents generated per year was 3.97, while the average number of biotech patents generated per year in the second decade (1990–2000) was 10.97, a statistically significant increase of about 275% ($p < 0.001$). Similarly, the average number of nanotech patents generated per year during the 1980–1990 decade was 0.25, while the average number of nanotech patents generated in the second decade (1990–2000) was 0.68, a statistically significant increase of 272% ($p < 0.001$).

About 57% of the incumbent firms patenting in biotechnology are in pharmaceutical preparations (SIC 2834) as their primary industry, while only 7% of the sample firms patenting in nanotech are in SIC 2834. Seven percent of the sample firms in the pharma sample underwent a horizontal merger, while only 2% of the incumbents in nanotech merged horizontally. The incumbent firms patenting in biotechnology have greater revenues, greater assets, and spend more on R&D than incumbents patenting in nanotechnology. As mentioned above, the biotech sample is international (39% EU, 26% US, 45% Asian, mostly Japanese), while nanotech sample is, through the way it was drawn, primarily U.S. (94%). Finally, the incumbent firms patenting in biotechnology use a higher number of R&D acquisitions (0.51) and R&D alliances (2.32) than the incumbent firms patenting in nanotech (0.13 and 0.12, respectively).

Table 2 depicts the regression results for biotech sample. Model 1 tests for the effect of time during the entire study period (1980–2000). The results show that the direct effect for the time indicator (year 1990) is statistically significant ($p < 0.001$). In addition, the interaction between R&D alliances and the time indicator as well as the interaction between R&D expenditures and the time indicator are each positive and statistically significant ($p < 0.05$ and $p < 0.001$, respectively). Taken together, these results imply that the effect of different mechanisms to source new knowledge on biotech patenting

Table 1
Comparison of biotech and nanotech samples

	Patents	SIC 2834	Firm merged	Revenues ($MM)	Assets ($MM)[a]	EU	US	R&D acquisitions	R&D alliances	R&D expenditures ($MM)[a]
Biotech										
Mean	8.87	0.57	0.07	13,293.26	13,782.03	0.39	0.26	0.51	2.32	711.33
S.D.	18.81	0.49	0.26	21,851.39	17,291.54	0.49	0.44	1.65	6.16	899.92
Min	0	0	0	3.13	7.93	0	0	0	0	0.01
Max	204	1	1	209,980.30	179,263.70	1	1	30	120	7,131.00
Nanotech										
Mean	0.54	0.07	0.02	10,027.77	11,764.32	0.03	0.94	0.13	0.12	452.79
S.D.	2.53	0.25	0.13	21,740.45	36,437.74	0.18	0.25	0.60	0.67	1,060.42
Min	0.00	0	0	0	1.11	0	0	0	0	0
Max	57.00	1	1	199,659.60	647,486.00	1	1	17	19	10,437.22
Mean difference										
t-Stat.	18.52	42.88	8.54	4.82	2.72	31.30	−63.92	9.52	14.37	8.45
Sig. level	0.001	0.001	0.001	0.001	0.01	0.001	0.001	0.001	0.001	0.001
	Bio patents > Nano patents	SIC 2834 Bio > SIC 2834 Nano	Merged bio > Nano merged	Revenues bio > Revenues nano	Assets bio > Assets nano	EU bio > EU nano	US bio < US nano	Bio Acq > Nano acq	Bio All > Nano all	R&D Exp bio > R&D Exp nano

[a] Constant 2003 US dollars.

Table 2
Regression results—biotech sample

	Model 1 (biotech patents, 1980–2000)	
	IRR	S.E.
SIC 2834	1.0868	0.0921
Firm merged	1.2953****	0.0546
EU firm	0.6365****	0.0768
US firm	0.9088	0.0981
Total assets	0.6998****	0.0662
Revenues	1.2875****	0.0919
Lagged biotech patents	1.0129****	0.0014
Time indicator	2.2183****	0.2311
R&D acquisitions	0.9807	0.0325
R&D alliances	0.9734	0.0328
R&D expenditures	0.9738	0.0777
R&D acquisitions × time indicator	0.9905	0.0263
R&D alliances × time indicator	1.0648**	0.0326
R&D expenditures × time indicator	1.2560****	0.0881
Chi square	454.88***	
Log likelihood	−2098.94	

	Model 2 (biotech patents, 1980–1990)		Model 3 (biotech patents, 1990–2000)	
	IRR	S.E.	IRR	S.E.
SIC 2834	1.0655	0.2362	1.0411	0.0986
Firm merged	1.0116	0.1283	1.3547****	0.0627
EU firm	0.8413	0.3050	0.6147****	0.0756
US firm	0.7456	0.2329	0.8513*	0.0959
Total assets	0.7035*	0.1760	1.1134	0.2075
Revenues	1.0518	0.0744	0.7804	0.1907
Lagged biotech patents	1.0433****	0.0042	1.0123****	0.0016
R&D acquisitions	1.0169	0.0569	0.9794	0.0390
R&D alliances	1.0965**	0.0478	0.9801	0.0344
R&D expenditures	1.4116	0.4438	1.1915**	0.0907
Chi square	145.02****		160.69****	
Log likelihood	−589.59		−1598.52	

* $p < 0.10$.
** $p < 0.05$.
*** $p < 0.01$.
**** $p < 0.001$.

has changed significantly over the 21-year time period, endorsing a time split of the sample in 1990.

This was done in Model 2 (1980–1990) and Model 3 (1990–2000). These models allow us to illuminate more precisely how the effects of the different knowledge mechanisms have changed over time. In both models, describing the earlier decade (1980–1990) and the later period (1990–2000), the lagged number of biotechnology patents is, as expected, positive and significant, with a factor change of 4.33 and 1.23%, respectively. This provides a baseline estimation on which we can assess the effects of the other knowledge sourcing mechanisms in a conservative fashion, above and beyond the given biotechnology patent stock held by each firm.

In the earlier decade (1980–1990), an incumbent pharmaceutical firm's R&D alliances were a statistically significant predictor of biotechnology patenting ($p < 0.05$), with a factor change of 9.65%. This implies that each time the number of R&D alliances a pharmaceutical firm entered with providers of the new biotechnology increases by one standard deviation, the expected number of biotechnology patents granted to the incumbent firm increases by 9.65%. Noteworthy is that that neither an incumbent firm's R&D acquisitions of new biotechnology ventures nor its R&D expenditures were significant in predicting biotechnology patenting in the early period (1980–1990).

These results change, however, in the later period (1990–2000). Here, we find that R&D alliances are no longer significant in predicting biotechnology patenting. Rather, an incumbent pharmaceutical firm's R&D expenditures are now a significant predictor of biotechnology patenting ($p < 0.05$), with a factor change of 19.15%. This implies that each time an incumbent pharmaceutical firm increases its R&D expenditures by one standard deviation, the expected number of biotechnology patents increases by almost 20%. An incumbent firm's R&D acquisitions remain, as in the early period, not significant in predicting biotechnology patenting by incumbent pharmaceutical companies.

The results for the control variables also change over the two decades. In the early time period (1980–1990), firm size, proxied by total assets, was a relative liability in generating biotechnology patents when compared to smaller firms. In the later time period (1990–2000), we find that firms that merged horizontally during this time period, increased their number of expected biotechnology patents by 35%, on average. It is also interesting to note that both the U.S. (−15%) and the European firms

Table 3
Regression results—nanotech sample

	Model 4 (nanotech patents, 1980–2000)	
	IRR	S.E.
SIC 2834	0.9262	0.2635
SIC 2911	0.7805	0.3322
SIC 3674	0.7501	0.1685
Firm merged	0.9931	0.0263
EU firm	0.9529	0.0985
US firm	1.0828	0.0985
Total assets	0.9610	0.0504
Revenues	1.2779**	0.1414
Lagged nanotech patents	1.0703****	0.0066
Time indicator	1.9657****	0.1561
R&D acquisitions	0.9928	0.0188
R&D alliances	1.0110	0.0120
R&D expenditures	1.0002****	0.0001
R&D acquisitions × time indicator	1.0787****	0.0193
R&D alliances × time indicator	1.0048	0.0142
R&D expenditures × time indicator	0.8281****	0.0292
Chi square	569.92****	
Log likelihood	−2583.97	

	Model 5 (nanotech patents, 1980–1990)		Model 6 (nanotech patents, 1990–2000)	
	IRR	S.E.	IRR	S.E.
SIC 2834	0.6096	0.2402	1.1533	0.4076
SIC 2911	1.0069	0.6230	1.2982	0.6982
SIC 3674	0.6399	0.2643	0.9010	0.2326
Firm merged	0.9638	0.0412	0.9895	0.0334
EU firm	0.9167	0.1589	0.9523	0.1128
US firm	1.1787	0.1584	1.0485	0.1117
Total assets	0.9402	0.0823	1.2574***	0.1078
Revenues	1.2649*	0.1995	0.9904	0.1715
Lagged nanotech patents	1.0918***	0.0354	1.0740****	0.0075
R&D acquisitions	0.9149**	0.0441	1.0156	0.0191
R&D alliances	1.0978	0.1065	1.0093	0.0116
R&D expenditures	1.0003***	0.0001	1.0001*	0.0001
Chi square	76.26****		259.63****	
Log likelihood	−1022.82		−1724.66	

* $p < 0.10$.
** $p < 0.05$.
*** $p < 0.01$.
**** $p < 0.001$.

(−39%) pharmaceutical firms are laggards in biotechnology patenting when compared to their Japanese counterparts. This could possibly be explained by the relatively late entry of the Japanese into the pharmaceutical industry (Thomas, 2003), implying a lower level of inertia in regards to patenting in biotechnology.

Table 3 depicts the regression results for nanotech sample. Model 4 tests for the effect of time during the entire study period (1980–2000). The results show that the direct effect for the time indicator (year 1990) is statistically significant ($p < 0.001$). In addition, the interaction between R&D acquisitions and the time indicator as well as the interaction between R&D expenditures and the time indicator are each positive and statistically significant (both at $p < 0.001$). Taken together, these results imply that the effect of different mechanisms to source new knowledge on nanotech patenting has changed significantly over the 21-year time period, endorsing a time split of the sample in 1990.

Model 5 depicts nanotech patenting between 1980 and 1990, while Model 6 shows the results for predicting nanotech patenting during the 1990–2000 time period. Parallel to the biotech sample, in Model 5 describing the early decade (1980–1990), and in Model 6 depicting the later period (1990–2000), the coefficient of the lagged number of nanotechnology patents is positive and significant, with a factor change of 9.18 and 7.40%, respectively.

In the earlier decade (1980–1990), an incumbent pharmaceutical firm's R&D expenditures were a significant positive predictor of biotechnology patenting ($p < 0.01$), but with a relatively small factor change of 0.03%. Moreover, R&D acquisitions are found to exert a statistically significant negative effect on nanotechnology patenting ($p < 0.05$), with a factor change of −8.51%. This implies that any time the number of R&D acquisitions is increased by one standard deviation, the expected number of nanotech patents is reduced by approximately 8.5%. In contrast to the significant effect of R&D alliances on biotechnology patenting, the results in Model 5 reveal that R&D alliances are not statistically significant in predicting nanotech patenting.

As in the earlier period, R&D expenditures remain a significant predictor of nanotechnology patenting in the later period (1990–2000), albeit only marginally at $p < 0.10$. Moreover, the factor change remains rather small with 0.01%. Noteworthy is also that neither R&D alliances nor R&D acquisitions are a statistically significant predictor of nanotech patenting by incumbent firms in this later time period.

The results of the control variables reveal that firms with greater revenues in the earlier period (1980–1990) tend to generate more nanotech patents, with an impact factor of about 26.5%. In the later period (1990–2000), incumbent firms that are larger in terms of total assets tend to obtain more nanotechnology patents. The factor change for total assets is about 26%.

6. Conclusion

We examined herein the extent to which the nanotechnology and biotechnology revolutions to date exhibit similar evolutionary patterns. Our focus has been on incumbent firm adjustment rather than newly emerging firms, and we framed the question in the context of two hypotheses that stem from the Zucker et al. (1998) explanation of natural excludability associated with revolutionary inventions. In particular, we hypothesized that an incumbent firm's ability to exploit new methods of invention depends initially on access to tacit knowledge about how to employ the new methods, but over time, as firms learn and/or the knowledge becomes codified (in routine procedures or commercially available equipment) inventive output is more highly dependent on traditional R&D investments.

Thus, while one might expect similar evolutionary patterns because both biotechnology and nanotechnology represent new methods of inventing, the period of natural excludability might well have been longer in biotechnology than nanotechnology. Roughly 20 years elapsed between initial enabling discoveries in biotechnology and the first patent on an automatic DNA sequencer. By contrast, it was only a decade after the STM that the AFM was commercially available. We argued that given this difference, biotechnology patenting might rely on external intellectual capital over a longer time period than would nanotech patenting. When testing this hypothesis on a sample of pharmaceutical firms attempting to innovate within biotechnology, we find that patenting in biotechnology is explained not only by a firm's knowledge stock in terms of past biotech patenting, but also through knowledge gained from outside the boundaries of the firm, especially R&D alliances. This finding lends partial support for Hypothesis 1, in which we suggested that when technological change associated with a revolutionary invention is embodied in human capital, incumbent firm ability to exploit the invention will depend on their alliances and/or acquisition of firms with direct access to this human capital.

Notable in predicting biotechnology patenting was the difference in results in the early and later periods considered. In the early period in biotech (1980–1990), R&D alliances are significant, but not in the later period

(1990–2000), where R&D expenditures become significant. Biotech was first focused on (external) R&D alliances, and now on internal R&D expenditures, since automatic gene sequencing is available. By contrast, in nanotech, R&D expenditures are significant in both periods, but the magnitude of effect is very small. In the early period (1980–1990), R&D acquisitions actually reduce the expected number of patents. This may well reflect the critical role of equipment such STM and AFM early on. These findings lend support for Hypothesis 2, in which we posited that when technological change associated with a revolutionary invention is embodied in physical capital, incumbent firm ability to exploit the invention depends on the firm's R&D expenditure.

We need to caution, however, that the differential finding between biotechnology and nanotechnology may be a reflection of the different degrees of maturity in the two technology life cycles. This may also explain the differences in the incumbent firms active in biotech and nanotech patenting revealed above. These firm differences may well be endogenous to the respective stage of each technology in their respective life cycle. While nanotech appears to be catching up fast with biotech, it is nonetheless a younger technological breakthrough, thus external knowledge stocks might become more important in future stages of development and maturity. While firms have been actively patenting during the last two decades, the properties of materials at the nanoscale are only beginning to be understood. Further, enabling inventions beyond the STM and AFM, such as quantum dots and carbon nanotubes, which were not patented until the mid-1990s, may well initiate new evolutionary patterns.

Should future research, however, find that the results presented herein are not materially influenced by the maturity of the underlying technology, one can speculate that knowledge is just more distributed in biotech (Powell et al., 2005), and that nanotech is more based on large-scale internal efforts (capital-intensive instrumentation, etc.) that the large firms that make up our sample can more easily afford through greater R&D expenditures than resource-constraint technology start-ups.

It should also be noted that our results depend to some extent on the key phrases that we used to construct our nanotechnology sample following Huang et al. (2003). As new discoveries open up new avenues for research, appropriate key phrases may change, and new algorithms for identification of firms are emerging with efforts such as Nanobank (http://www.nanobank.org).

Also, while our coarse-grained measure of R&D alliances did indeed show differential effects on research productivity in biotech versus nanotech, future research should track patent citations or faculty involvement to capture knowledge flows from universities more accurately (Bozeman and Mangematin, 2004; Bozeman and Corley, 2004; Catherine et al., 2004; Rothaermel and Thursby, 2005a,b). Due to the early stage of both biotech and nanotech, we relied on simple patent counts, which tend to correlate highly with patent quality (Hagedoorn and Cloodt, 2003). Nonetheless, future research should consider proxying research productivity by the underlying quality of the patents (Henderson and Cockburn, 1996). Finally, prior research has shown how large pharmaceutical firms have attempted to build new capabilities in biotechnology through the recruitment of employees with new skills and tacit knowledge based on biotechnology (Lacetera et al., 2004; Rothaermel and Hess, in press; Zucker and Darby, 1997). Thus, future research could attempt to further investigate the recruitment of intellectual human capital as opposed to access by alliances or acquisition.

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