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Knowledge Diversity in the Emerging Global Bio-Nano Sector

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ASTRACT

As scientists are able to understand and manipulate ever smaller scales of matter, research in the fields of biotechnology and nanotechnology has converged to enable such radical innovations as lab-on-a-chip devices, targeted drug delivery, and other forms of minimally invasive therapy and diagnostics. This paper provides a descriptive overview of the emerging bio-nano sector, identifying what types of firms are entering, from what knowledge base, where they are located, and their strategic choices in terms of technological diversity and R&D strategy. The firms engaged in bio-nano research and development span the range from start-up firm to multinational pharmaceutical, biotech, chemical, and electronics firms: two thirds of bio-nano firms are relatively young and relatively small. The United States dominates this sector, with more than half of all bio-nano firms located in the USA. Even within this sector which epitomizes the convergence of technology, there is a broad range of technological diversity, with the most diverse firms overall coming from a base in electronics, the most diverse start-up firms coming from a base in nanomaterials, and the most narrowly focused firms coming from a biotechnology/pharmaceutical base. We find that hybridization has been the dominant knowledge diversity strategy, with 93% of the bio-nano firms with nano-patents holding multi-class patents.

INTRODUCTION

Despite the early stage of research and development, the convergence of biotechnology and nanotechnology has generated high expectations among national governments and venture capital firms. Biotechnology is an established industry and highly research intensive: biotechnology and pharmaceutical firms perform approximately 20% of all corporate R&D, spending nearly $100 billion on research globally in 2006 (UK Department of Innovation, Universities and Skills, 2007). Nanotechnology is a nascent industry, but one that is also highly research intensive and considered commercially promising enough that national governments spent nearly $12 billion on nanotechnology R&D in 2008 (Plunkett Research, 2008). Of the approximately 2,500 companies globally involved in nanotechnology research (Lux Research, 2008), we find that 10% of these firms are conducting bio-nano research – that is, research in both biotechnology and nanotechnology. As scientists are able to understand and manipulate ever smaller scales of matter, research in the fields of biotechnology and nanotechnology has converged to enable such radical innovations as lab-on-a-chip devices, targeted drug delivery, and other forms of minimally invasive therapy and diagnostics.

This bio-nano research has begun to be commercialized, both by incumbent firms and by start-up ventures. Since 2005, nanotechnology venture capital funding has exceeded $500 million annually in the US (Plunkett Research, 2008). Bio-nano has been creating disproportionate value creation in these start-up ventures, with Jacob Grose of Lux Research stating that “Healthcare and life sciences companies have accounted for a staggering $1.68 billion of the $2.57 billion total valuation of nanotechnology start-ups at IPO” (Nanotechnology Now, 2008). By 2015, bio-nano revenues are forecast to be in the range of $5 billion (Global Industry Analysts, Inc., 2010). Why is there so much excitement about the marriage of nanotechnology and biotechnology? We believe that this is the case because the convergence of two technologies generates a multitude of opportunities for radical innovation.

In this paper, we describe our global sample of bio-nano firms as at 2005 and 2008. This is the first known firm level exploration of all of the firms which have capabilities in both biotechnology and nanotechnology. We describe the size, age, location, and technology capabilities of the firms with strengths in both the biomedical sector and the emerging field of nanotechnology. We also describe their development of nano-patents over time, and classify these patents to establish the dominant areas of technological knowledge they are bringing to this nascent bio-nano field. Further, we develop a range of diversity measures to track their technological knowledge diversity, which allows us to investigate technology convergence at the firm level.

Very little has been published in academic journals about the emerging bio-nano industry. Comparisons between the biotechnology and nanotechnology industries have been made, including the manner in which incumbent firms innovate in new fields (Rothaermel and Thursby, 2007) and the role technical and scientific service firms play in the nanotechnology and the biotechnology industries in Italy (Chiaroni et al., 2008). Specific biomaterial fields have also been studied at the firm level (Lysaght and Hazlehurst, 2004). However, there has only been one paper to our knowledge describing the emerging bio-nano sector: a case study approach focusing on the knowledge acquisition and integration characteristics of 10 research projects in bio-nano-technology (Rafols, 2007). There is a need for an overview of this nascent sector, demonstrating how firms are entering, from what knowledge base, with what level of dual competency, and with what strategies. This paper addresses that gap, and, in considering the firm as a unit of analysis, and commercialization metrics as dependent variables, attempts to reveal the commercialization practices of an emerging field.

We also add to the recent discussion about emerging industries and technological knowledge diversity. Suzuki and Kodama (2004) analyze the technological diversity over time of two large Japanese firms in the electronics and chemical industries, and propose that technological diversity aids innovation and firm performance over the long term. Huang and Chen (2010) investigate knowledge diversity of a large sample of firms in the IT sector and argue that there is an inverse U relationship between knowledge diversity and innovation performance. Avenel et al. (2007) studied the knowledge diversity strategies by which firms enter the multidisciplinary nanotechnology sector. They argue that convergence at the firm level can be achieved through either a strategy of “juxtaposition” where a firm has several independent research groups research various technological fields, or one of “hybridization” where a firm has forged truly interdisciplinary research groups. We seek here to depict the technological knowledge diversity strategies employed by firms entering the inherently interdisciplinary bio-nanotechnology sector.

METHODOLOGY

The data collection sources and methodology are first described, followed by metrics utilized to measure the technological capabilities of sample firms and then metrics used to investigate knowledge diversity in bio-nano firms.

Data Collection

Through the use of DMS's databases "IndustryAnalyzer" and "NewsAnalyzer"[1], we have identified the global sample of firms with capabilities in both biotechnology and nanotechnology at two points in time, 2005 and 2008. As the two DMS databases we used are for firms with biomedical capabilities, we searched this database for firms with the following search string: "nanomaterials, fullerenes, nanotubes, buckyballs, nanotechnology, or nanoparticles." This enabled us to capture a total of 247 firms with products, services, or research activities in both the relatively established biomedical sector and the emerging nanotechnology field. From these databases, we were also able to collect data on each firm's location, technological capabilities and business models. We examined the 2005 cohort and 2008 cohort of bio-nano firms to draw conclusions about firm entry and exit during this time interval.

We gathered data on the 8,255 US "nano" patents issued by these bio-nano firms up to and including patents issued in 2008. Using the US Patent and Trademark Office website[2], we searched each firm's patents along with the word (or terms beginning with) "nano" for example, "Bayer AND nano".[3] We then searched the resulting patents for false positives, and re-ran the search to exclude these.[4]

When testing for relationships between knowledge diversity and performance, we chose a 2003 issue date as our cutoff, as we wanted a lag of at least 3 years between the diverse knowledge being present in the firm (when the patent was filed) and the output metrics measured. We use this data to calculate knowledge diversity metrics and to classify the technological capabilities of the sample firm. Next we gathered data on firm size and growth. For the global bio-nano sample obtained, we compiled revenue and employee data from 2004-2006 through the use of the financial databases MINT Global, Zephyr and Mergent Online, as well as Lexis Nexis searches, Standard and Poor's corporate register, internet searches and direct contact with some companies. When we discovered the vast range of size among the bio-nano firms in our sample, we realized that revenue, revenue growth, employment and employment growth were not suitable as success metrics, but, rather, as descriptive variables to depict the

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[1] http://www.industryanalyzer.com/

[2] http://www.uspto.gov/

[3] We chose to limit the analysis to patents which mentioned the word nano to make the analysis manageable. This filter does not appear to obscure the firms' capabilities, as the firm generally files its patents in the area of its strongest capabilities. Many of the firms in the sample patented exclusively in bio and chemistry fields, even when we are examining patents that mention "nano"

[4] We filtered out false positives that referenced only sodium nitrate or sodium nitrite and not extended forms of "nano", while keeping those that referenced either of these chemicals and extended forms of nano, such as "nanom", to re-capture the nanomaterials patents: ((AN/"Bayer" AND nano$) ANDNOT (("NANO.sub.3" OR "NANO.sub.2") ANDNOT (((nanom$ OR nanop$) OR nanot$) OR nanos$)))

types of firms entering this emerging sector. Firm size is also used to differentiate between the knowledge diversity strategies of small and large bio-nano firms.

Technological Capability Metrics

We classify the technological capabilities of the firms based on a categorization of their nano-patent portfolio by patent class. Every patent is classified into one primary patent class, and may include several secondary patent classes, each representing the technological domain the patent is related to (e.g., class 977 represents nanotechnology knowledge). Each primary or secondary classification is also accompanied by a sub-class, which was not used here (e.g., 977's sub-class 734 represents fullerene knowledge). First we classified all of the patent classes into five general categories: biology (B), chemistry (C), electronics/physics (P), nanotechnology (N), and other (O).[5] Then we calculated the proportion of (primary and secondary) patent classes used to classify the entire bio-nano patent portfolio of each firm according to these categories. Each firm received a ratio of:

$$\frac{\text{sum of only biology and chemistry patent classes}}{\text{sum of all biology,chemistry,electronics/physics,and nanotechnology patent classes}} \qquad (1)$$

Technological Knowledge Diversity metrics

The independent variable that we investigated the most thoroughly was knowledge diversity. We created several measures to investigate the knowledge diversity in this bio-nano sample of firms. As a first level examination, we counted the number of nano-patents in each firm's portfolio which were either single-class or multi-class.[6] In almost half of the nano-patents (40-50%, depending on timeframe), the same class as mentioned in the primary class was repeated in additional secondary classes, resulting in a single-class patent. Thus, we were able to measure how many firms hold a mix of single-class and multi-class patents, and how many firms exclusively hold single-class or exclusively multi-class patents. This count of single- and multi-class patents gives us a first level indication of whether a firm is combining diverse knowledge in their R&D.

To look more closely at knowledge diversity, and create finer gradations of knowledge diversity, we employed an additional type of diversity metrics. To measure the breadth of the nano-patent portfolio of each firm, we created counts of how many different primary patents classes were mentioned in the portfolio (*Breadth of primary classes*) and also how many different primary and secondary patent classes were mentioned in the portfolio (*Breadth of all classes*). The larger the breadth of (primary and secondary) patent classes mentioned, the higher the diversity of the patent portfolio. We also created a simple count of the *maximum classes per patent*, to examine the most diverse patent in a firm's patent portfolio. Next we normalized the breadth measures by the number of patents held in each firm's portfolio, resulting in a count of *the average classes per patent*, allowing for the same class to be mentioned multiple times, as well as a count of the *average unique classes per patent*. *Average unique classes per patent* is

[5] The categorization we developed is available upon request to the corresponding author. This classification was done independently by three of the authors with acceptable levels of replicability, and we mutually agreed on the remaining classes. Each author has at least one technical degree in either biology, materials engineering, or mechanical engineering.

[6] A multi-class patent is one in which the primary and secondary classes mentioned in the patent span more than one class.

also the metric that Avenel et al. (2007) use to test hybridization in their nanotechnology sample. In this paper, we report only on the diversity metrics necessary to demonstrate the technological knowledge diversity of these firms involved in bio-nano research.

RESULTS AND DISCUSSION

Bio-nano research and commercialization is not yet widespread but it is growing. In 2005, there were 165 bio-nano firms globally. By 2008, this number had increased to 221. There were 82 new entries into the bio-nano field during this time and 26 exits. To enter the sector, a firm either was founded with bio-nano capabilities or an established firm developed bio-nano capabilities. About three quarters of these firms are relatively young, and the remaining quarter of the sample are incumbent firms extending their capabilities into either biotechnology or nanotechnology.

As shown in **Figure 1**, the bio-nano firms in our sample have produced a rapidly increasing amount of nano-patents over the past 3 decades, ranging from 80 nano-patents issued per year in 1980, to 113 nano-patents per year in 1990, to 355 nano-patents per year in 2000, to over 750 nano-patents per year in 2008. For the bio-nano firms in our sample, 92 firms had nano-patents issued as of 2003. The firms' nano-patent portfolios range from a minimum of zero patents to a maximum of 793 patents, with the median number of firm nano-patents being 6. This emerging sector was analysed to reveal the defining characteristics of firms in this emerging sector: namely, their size, age, location, technological capabilities, technological diversity, business models, and clinical focus. The success of these firms was measured and correlated to some of their strategic choices.

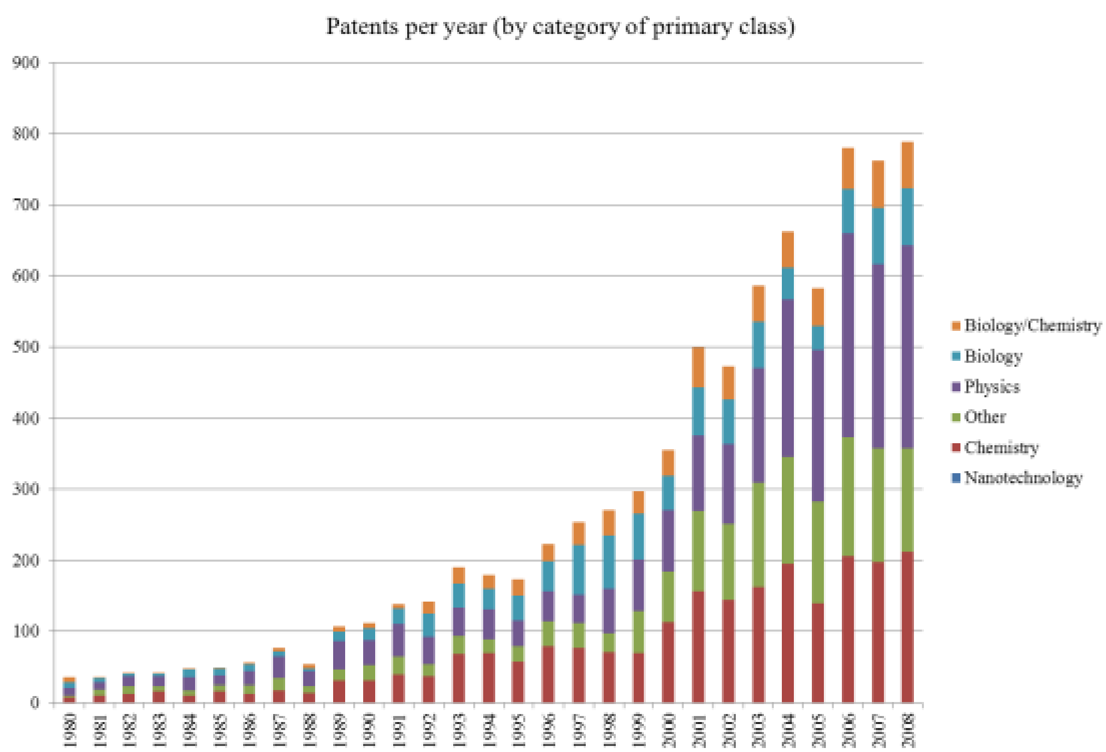

Figure 1: Nano-patents over time in our bio-nano sample, categorized by primary class

Size, Age and Location

The sample includes pure play bio-nano startups all the way through to multinational chemical and pharmaceutical companies such as Merck and Dow and multinational electronics firms such as IBM and Hewlett-Packard. These firms span the spectrum in size from 1 employee to 470,000 employees, and from $0 to $92 billion in annual revenues. Despite this vast range, bio-nano firms are pre-dominantly young, with nearly three quarters of the sample firms formed within the past 2 decades. Bio-nano firms are also predominantly small: the median annual revenue generated by firms in the sample is only $5 million, with the smallest quartile earning between $0 and $0.8 million, the largest quartile earning between $270 million and $92 billion, and two thirds of the sample firms earning less than $25 million in annual revenues.[7] The median firm size in the sample is approximately 70 employees, with the smallest quartile of the firms between 1 and 15 employees, and the largest quartile between approximately 1,800 and 470,000 employees. The range of firms involved in bio-nano research is extremely diverse.

Bio-nano firms range in age (as at 2008) from just formed to the long history of a firm formed 340 years previously. These firms are predominantly new, with the youngest quartile from 2 to 8 years of age, and the median age of the bio-nano firms being 12 years. The established incumbent firms are limited to the oldest quartile, which ranges from 22 to 340 years of age.

The US was the dominant country for bio-nano firms throughout the study period, with 97 US firms identified with bio-nano capabilities as of 2005 and 129 US firms as of 2008, remaining relatively constant at 59 % and 58% of the sample respectively. In fact, the state of California alone has more bio-nano firms (28 in 2008) than any other country in the world: thus several US States are analyzed as separate regions. Germany is next at 21 firms, with bio-nano firms spread across 19 countries in total. **Table 1** summarizes the location of global bio nano firms by region and the changes from 2005 to 2008. Although the proportion of bio-nano firms remained relatively constant by region, within regions the UK had the greatest increase in bio-nano firms over the interval of observation, moving from 6 to 11 firms. Asian firms are surprisingly underrepresented, although there has been a strong increase from 5 bio-nano firms to 9 bio-nano firms in Asia over the 3 year interval studied.

	US	Europe	Austral-Asia	ROW	Total
Number of Firms in 2005	**97**	**41**	**14**	**13**	**165**
Number of Firms in 2008	**129**	**57**	**19**	**16**	**221**

Table 1: Location of bio-nano firms: Sample overview 2005 and 2008

Technological Capabilities

We classified the technological capabilities of the firms in our sample based on a categorization of their bio-nano patent portfolio. **Figures 2a** and **2b** provide an overview of the sample in a manner that captures the size of the firms in terms of revenues, the size of their nano-patent portfolios, and their technological capabilities in terms of their proportion of biology and

[7] These numbers exclude the firms which did not report revenues. For 68 of the firms, no 2006 revenue data were available. Of the remaining 179 firms that reported revenues, 3 firms reported zero revenues, exactly half reported revenues of less than $5 million, and 68 firms (38% of 178) reported more than $25 million in revenues.

chemistry as per Equation 1. The horizontal axis of **Figures 2a** and **2b** ranges from 0% to 100%, with 0% representing an absence of biology or chemistry patents in the firm's portfolio, and 100% representing solely biology or chemistry patents in the firm's portfolio. The bubble size represents the number of bio-nano patents per firm.

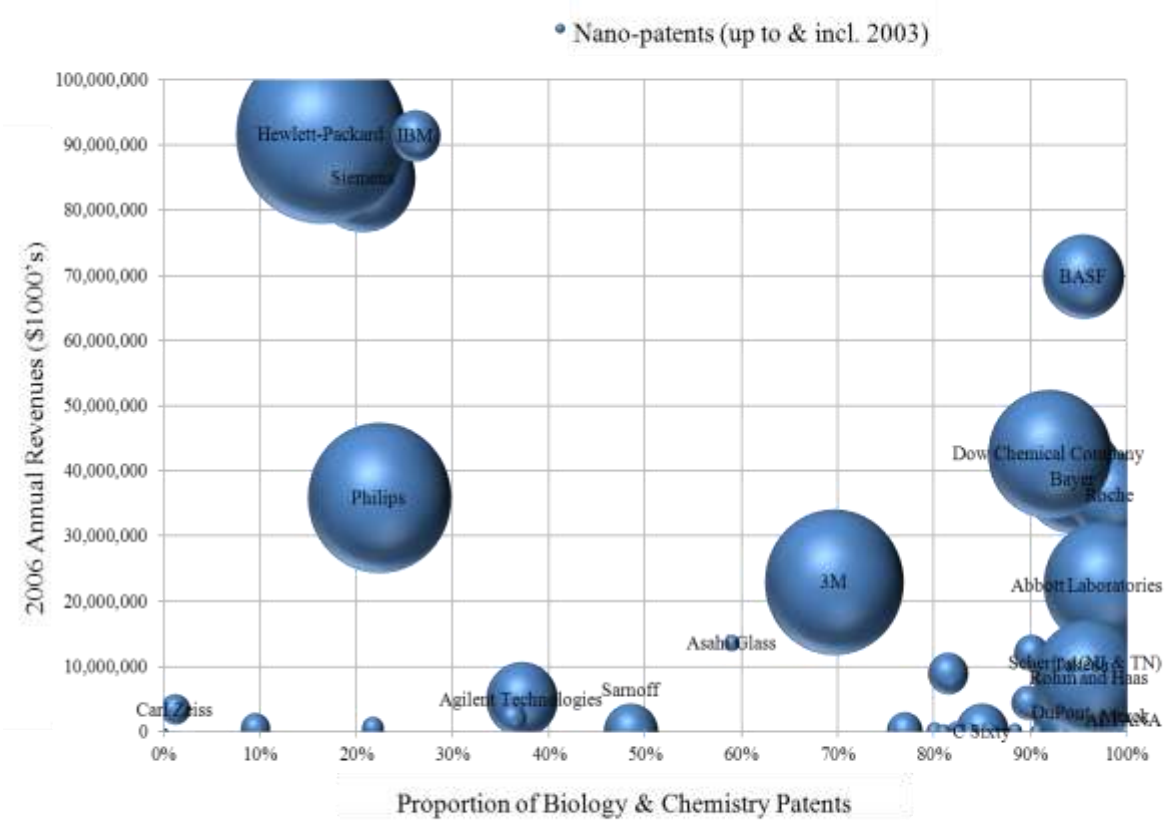

Figure 2a: Size and technological capabilities of all sample firms with nano-patents

Figure 2a depicts the entire sample, and demonstrates the broad range of firms entering this emerging field, ranging from no revenue up to multinational firms with nearly $100 billion in annual revenues. It is evident that the majority of the firms have their dominant capabilities in biology and chemistry fields. In striking contrast, 4 multinationals (Hewlett-Packard, IBM, Philips and Siemens) are approaching nanotechnology research from the physics and nanotechnology fields. Notable dual competency firms include Agilent Tech., Sarnoff, Asahi Glass and 3M.

Figure 2b focuses on the smaller firms in this field, depicting only firms with annual revenues less than $25 million. Many of the small firms in this sector have virtually all of their capabilities (as measured by proportion of patents by categorization) in the fields of biology and chemistry.[8] Additionally, all but 4 of the small firms had more than 80% of their capabilities in

[8] To be in the sample, however, the firms have been identified as having capabilities in both bio and nano fields, and the patents considered all contain the word "nano" within the text of the patent. Additionally, to be plotted on Figure 2a or 2b, the firms must have at least 1 nano-patent.

biology or chemistry. Thus, most of the small firms in this sector are coming into this sector from a biology base, so much so that many had not patented any of their knowledge in the nanotechnology, physics, or electronic fields as of 2003. Only one of the small bio-nano firms in the sample is truly a dual capability firm, with patents relatively equally filed in both nanotechnology/physics and biology/chemistry fields. This firm is Luna Innovation, which has a division, "Luna Nanoworks" dedicated to "developing pharmaceuticals empowered by carbon nanomaterials."[9]

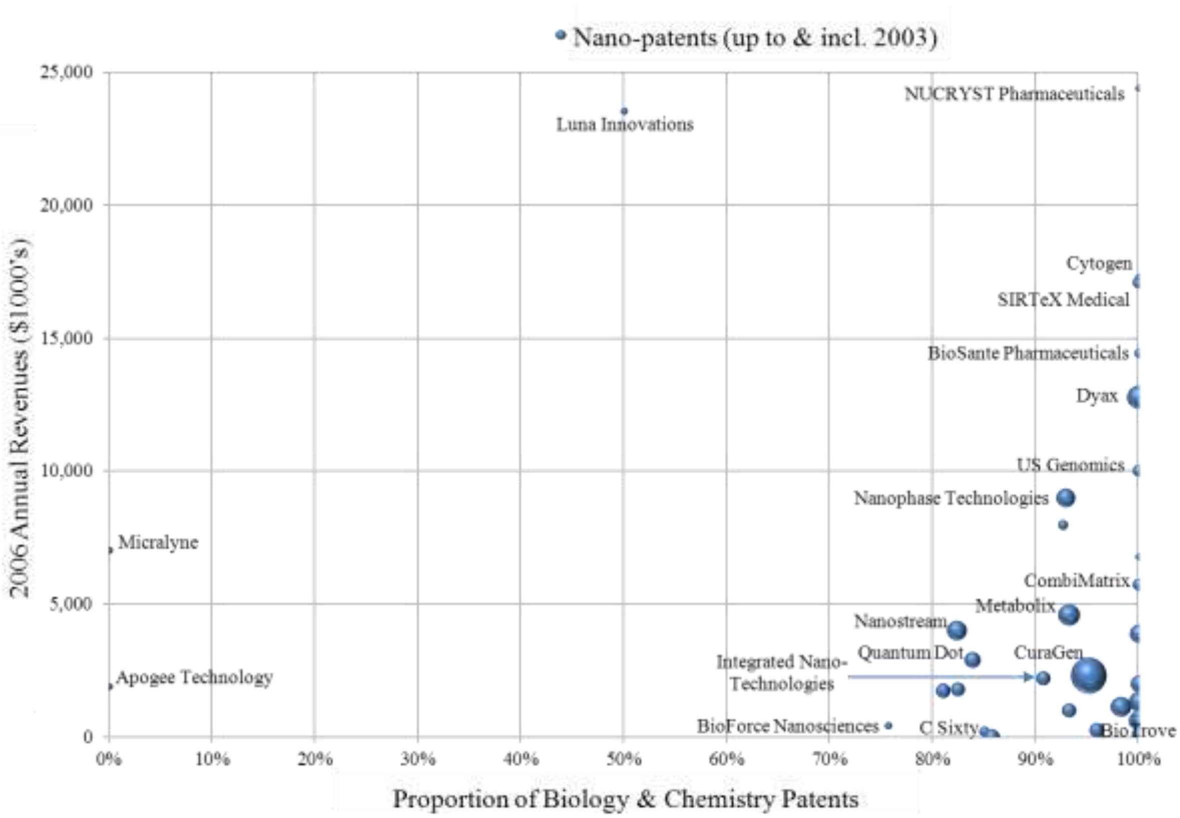

Figure 2b: Size and technological capabilities of smaller sample firms with nano-patents

Technological Knowledge Diversity

From the nano-patent portfolios of our bio-nano firms, we first examine how many of their patents were classified in a single class versus multiple classes. These counts can be used as an indicator of the R&D strategies of juxtaposition vs. hybridization proposed by Avenel et al. (2007). Thus we differentiate "juxtaposition" R&D strategies from "hybridization" strategies, with multi-class patents as evidence of multi-disciplinary R&D teams working together (hybridization) and single class patents evidence of more narrow and traditionally focused teams working independently (juxtaposition). We tracked the evolution of the sample firms' preference for single- vs. multi-class patenting activity for 2003, 2006 and 2008.

[9] http://www.lunananoworks.com/index.asp (accessed June 14, 2010)

Hybridization is the dominant knowledge diversity strategy, although juxtaposition is also employed in some cases by over half of the sample. Of the 94 bio-nano firms holding nano-patents issued during or before 2003, 62 firms (66%) hold single-class nano-patents: of that number, 7 firms (7%) hold exclusively single-class nano-patents. In contrast, there are 87 firms (93%) holding multi-class nano-patents, including 32 firms (34%) which hold exclusively multi-class nano-patents. Large firms (revenues over $500 million) hold a higher proportion of single class patents than smaller firms: 38% of their patents are single class versus 23% for smaller firms.

Over the period of time from 2003 until 2008, hybridization continued to be the norm for these bio-nano firms, but the tendency to hold exclusively multi-class nano-patents declined. Of the 138 bio-nano firms holding nano-patents issued during or before 2008, 126 firms (91%) held multi-class nano-patents, including 32 firms (23%) which held exclusively multi-class nano-patents. In contrast, 106 firms (77%) held single-class nano-patents: of that number, 12 firms (9%) held only single-class nano-patents. This represents an 11% increase in the percentage of firms holding single-class nano-patents (juxtaposition strategy). There is also a slight increase in the percentage of firms holding exclusively single-class patents (7% to 9%). This could indicate a deliberate shift in R&D strategy over time towards more reliance on juxtaposition.

Next we employed additional diversity metrics calculated from the patent classifications of nano-patents issued from these bio-nano firms. These metrics are meant to reveal the varying degrees of knowledge diversity applied within the bio-nano firms. We expected to find a significant amount of diversity in our sample firms, given that they are in an emerging field which spans at least 2 previously unrelated areas of knowledge. This was generally the case, as depicted in **figures 3a and 3b**. We were also able to observe the range of firm approaches at the patent and patent portfolio levels, and note the existence of firms which appear to be extremely narrow in their patentable knowledge base.

In terms of patent counts, the number of different primary classes held in each firm's nano-patent portfolio ranged from a single class up to 78 primary patent classes, with a median of 3 primary patent classes represented in a firm's nano-patent portfolio. The *breadth of all patent classes* held (different primary *and* secondary classes) held in each firm's patent portfolio ranged from a single class up to 113 patent classes, with a median of 7 patent classes. **Figure 3a** depicts this diversity metric for the entire sample, along with firm revenues and the size of each firm's nano-patent portfolio, while **Figure 3b** focuses in on the start-up bio-nano firms. It is evident from **Figures 3a** and **3b** that these measures are strongly correlated to the size of a firm's nano-patent portfolio. **Figure 3a** visually highlights the extremely diverse patent portfolios of multinational firms with a base in electronics (and some of those with a base in chemicals) and the narrow focus of Proctor and Gamble. **Figure 3b** indicates that start-up nano-materials and nano-manufacturing firms are the most diverse, and that the most narrowly focused start-up firms have a base in biotechnology and pharmaceuticals.

The count of unique classes per patent ranged from 1 through 8, with a median of 4, and the patent with the maximum unique classes issued was by C-Sixty. The average count of all primary and secondary classes per patent in a firm's portfolio ranged from 2 through 21, with a median of 6. Our hybridization metric (the average unique classes per patent in a firm's portfolio) ranged from 1 through 6, with a median of 2, again demonstrating the wide range in patent diversity in the sample. Hybridization was highest in the smallest firms (< $5million in revenue) and lowest in the largest firms (> 500 million in revenue).

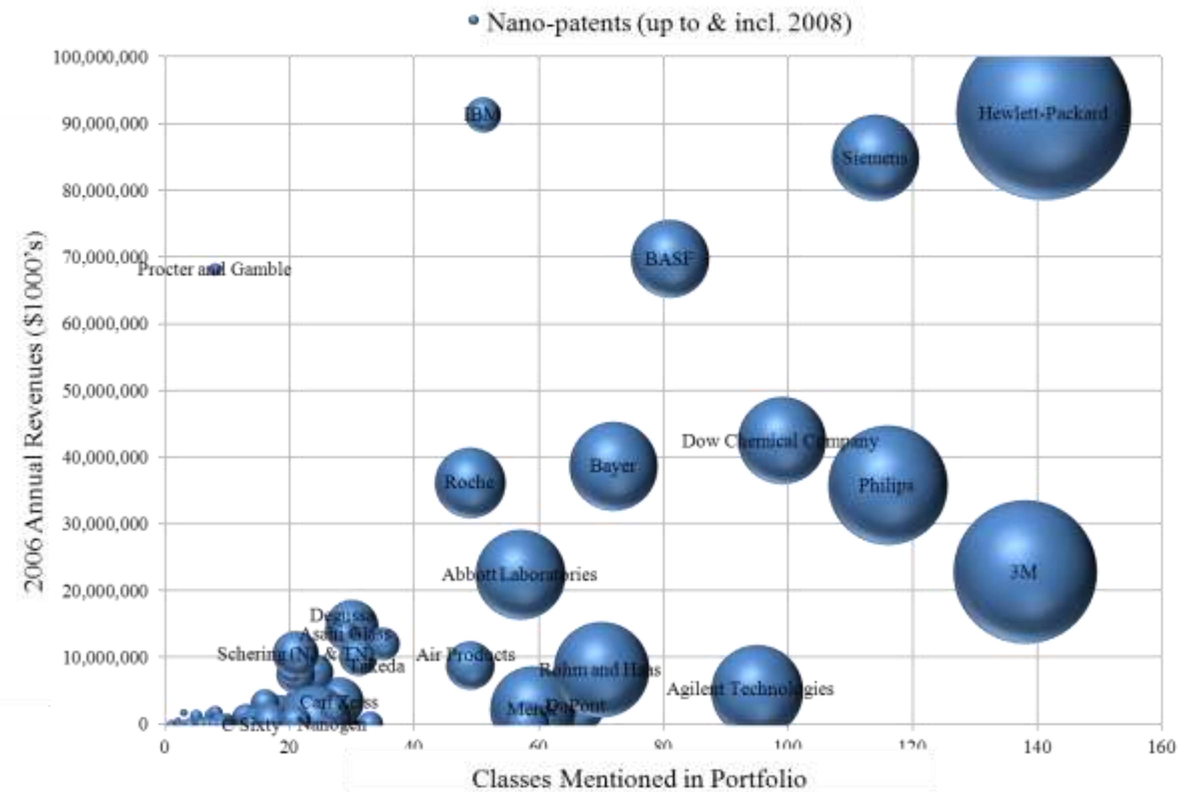

Figure 3a: Diversity of firm nano-patent portfolios: All classes held

CONCLUSION

This paper describes the types of firms entering the emerging field of bio-nanotechnology. This description of all bio-nano firms globally includes rich data on firm size, location, technological capabilities and knowledge diversity. This paper also adds to the discussion of technological knowledge diversity in emerging technology sectors and of the R&D strategies employed in a sector which embodies technological convergence.

Our search methodology identified 247 bio-nano firms globally, with 221 bio-nano firms remaining active in 2008. Whereas these firms are spread across 19 countries, the USA dominates the emerging field, with 58% of all bio-nano firms based there. There has been rapid growth in knowledge and pre-commercialization ability in this sector, with an eightfold increase in nano-patents by our identified global sample of bio-nano firms since the 1980s, and a doubling since 2000. More than half of the bio-nano sector is made up of start-up firms, with the median age of firm being 12 years, the median number of employees being 70, and the median revenue being $5 million, as at 2006. Two thirds of the sample firms are relatively small, with annual revenues of $25 million or less. Large multinational pharmaceutical, chemical, and electronics firms also play a significant role in the sector, with a dominant position in nano patents, and take different approaches into the bio-nano sector.

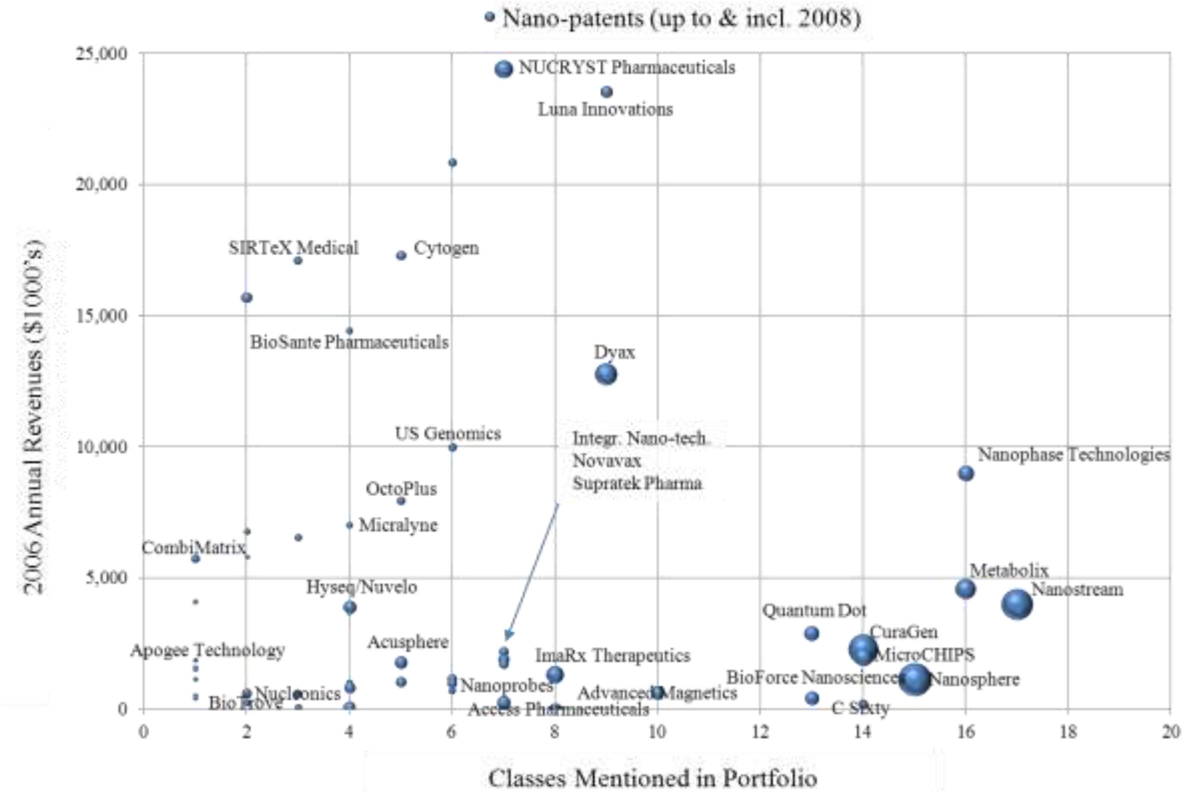

Figure 3b: Diversity of start-up firm nano-patent portfolios: All classes held

Our sample and analysis show that the bio-nano sector is emerging predominantly from firms with biology and chemistry capabilities, which have ventured into nanotechnology. This trend is particularly notable with start-up firms: most of the smaller firms in the sample patent heavily, and many exclusively, in biological and chemical fields. There are also four electronics multinationals which have predominantly physics, electronics, and nanotechnology capabilities: Hewlett-Packard, IBM, Philips and Siemens.

The firms have a great range in knowledge diversity, even within this sector of technological convergence. Of the 92 firms which had issued nano-patents as of 2003, 60 firms issued at least one single-class patent (not diverse) and 85 firms issued at least one multi-class patent. Only seven firms held solely single-class patents (and five of those seven firms held only a single nano-patent) and a considerable 32 firms held solely multi-class patents, albeit with small patent portfolios. The least technologically diverse (i.e., more focused) firms with more than one patent were Proctor and Gamble and the biotechnology venture, CombiMatrix. The most technologically diverse firm overall was Hewlett-Packard. The start-up firm, C-Sixty, held the most diverse multi-class patent spanning 8 classes.

Thus hybridization has been the dominant knowledge diversity strategy, with 93% of the bio-nano firms with nano-patents holding multi-class patents and 35% of the bio-nano firms holding exclusively multi-class patents as of 2003. Over the period of time from 2003 until 2008, hybridization continued to be the norm for these bio-nano firms, but the tendency to issue exclusively multi-class patents declined. Large firms held a larger percentage of single class patents than small firms, and large firms referenced fewer unique classes per patent than smaller firms.

The bio-nano firms with the greatest knowledge diversity overall are multinational electronics and chemical firms. Large multinational firms in general have a strikingly higher portfolio diversity than smaller firms and are more likely to achieve that diversity through a juxtaposition strategy. Of the start-up bio-nano firms, we find that the most diverse are those with a base in nanomaterials and the most narrowly focused are coming from a base of biotechnology and pharmaceuticals. These diversity metrics are valuable in showing a range of approaches to competing in an emerging sector at the convergence of two fields of knowledge.

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