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Vertical alliance networks: The case of university–biotechnology–pharmaceutical alliance chains

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Abstract

Many young biotechnology firms act as intermediaries in tripartite alliance chains. They enter upstream partnerships with public sector research institutions, and later form commercialization alliances with established, downstream firms. We examine the alliance activity in a large sample of biotechnology firms and find: (i) firms with multiple in-licensing agreements are more likely to attract revenue-generating alliances with downstream partners; however, (ii) the positive relationship between in-licenses and downstream alliances attenuates as firms mature, and (iii) the diversity and the quality of the academic connections of firms' principals influences their chances of successfully acquiring commercialization rights to scientific discoveries in universities.

Keywords: Strategic alliance; Biotechnology industry; Brokerage; Social networks; Technology transfer

1. Introduction

In the growing literature on inter-corporate partnerships at the nexus of strategic management, organizational theory, and organizational economics, biotechnology has emerged as perhaps the most frequently examined research site. This is unsurprising given the seemingly inexhaustible incidence of alliance formation in the sector (Hagedoorn, 1993). Studies of alliances in the biopharmaceuticals industry have generally pursued one of three broad research objectives. First, the industry has hosted a number of studies that test theories of alliance formation (e.g., Barley et al., 1992; Powell et al., 1996; Walker et al., 1997). Second, researchers have explored the deal-specific and competitive conditions that engender governance choices in alliance agreements, such as the decision to take a partial ownership stake in a partner (e.g., Pisano, 1989, 1991; Robinson and Stuart, 2007). Third, a number of studies have gauged the consequences of collaborative activity for firm-level performance outcomes, including the rate of innovation (Shan et al., 1994), growth (Powell et al., 1996), valuations of early stage companies (Stuart et al., 1999), and the adaptability of established organizations (Rothaermel, 2002).

It is well understood that the majority of alliances in the biotechnology sector are vertical: many collaborations unite the efforts of two organizations that, at least under the parameters of the alliance contract, engage in relatively distinct sets of activities along the value chain in the life sciences. In the types of deals that have garnered the most attention in the academic literature, a biotechnology firm conducts research and development and transfers the output(s) to a pharmaceu-

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tical or life sciences company, which then undertakes additional development and the marketing of any resulting products (see, for example, Pisano, 1989; Reuer et al., 2002; George et al., 2002; Robinson and Stuart, 2007). In the language of Teece (1986), biotechnology firms often have expertise in the development of novel scientific approaches to drug development, while the complementary assets to advance and ultimately commercialize these technologies reside in pharmaceutical firms. Although the actual relationship between partners is more iterative and interactive than this simplistic characterization suggests, biotechnology alliances often entail a vertical division of labor along a value chain, rather than horizontal linkages among firms engaged in similar activities.

Much of the existing literature on strategic alliances implicitly locates biotechnology firms at the upstream pole of the pharmaceutical (or agricultural biotechnology) industry value chains. In other words, biotechnology firms are understood to be originators of technology, which is then eventually brought to the marketplace by strategic alliance partners with extensive marketing organizations and experience in managing the clinical trials process (e.g., Barley et al., 1992; Rothaermel, 2001; Rothaermel and Deeds, 2004; Robinson and Stuart, 2007). This is a fair characterization of many alliances in the industry. However, as a different body of work on the origins and evolution of biotechnology firms has illuminated, many biotech firms maintain close links with universities (see for example, Liebeskind et al., 1996; Audretsch and Stephan, 1996; Powell et al., 1996; Zucker et al., 1998; George et al., 2002; Murray and Stern, in press). Indeed, with just a handful of exceptions, the drugs on the market today with biotechnological origins have emanated from license agreements for scientific discoveries made in universities (Edwards et al., 2003). Given the multiplex relationship between biotechnology firms and universities, the primary question we address here is: how do the extensive, formal interactions between these two types of organizations influence the dynamics of downstream alliance activity in the industry? We also explore a secondary question: to what extent is the propensity to in-source university science a function of the within-academe networks of the founders and scientific advisors of the biotechnology firms? In other words, in this paper we treat biotechnology firms as the unit of analysis and analyze their rates of formation of upstream-oriented alliances with universities and downstream-focused transactions with established firms.

We hypothesize that one of the most significant roles performed by biotechnology companies has been to identify and in-license science created in universities, and then to further develop and ultimately transfer this intellectual property to larger firms that possess the resources to commercialize the technology. Thus, although virtually all biotechnology firms conduct substantial internal research and most add value to the technologies they in-license, these organizations often perform the role of value-added intermediaries in the migration of intellectual property from universities to downstream strategic partners.[1] We draw upon the literature on brokerage and intermediation in technology development to formulate predictions about the dynamics of the tripartite alliance chains that emerge as scientific discoveries progress from universities to biotechnology firms, and then to the established firms located further down the value chain.

Although our analysis will be situated in the biotechnology sector and we will refer to conditions in the industry while formulating the predictions, we believe that the arguments we develop are relevant to other, science-driven high-technology industries, including subfields in microelectronics, advanced materials, and the emerging area of nanotechnology. The more general value of the analysis in the paper is to explore the correlates of an increasingly prevalent business model: young technology firms with close ties to research institutions acting as intermediaries in alliance chains that lead to the development and commercialization of science-based discoveries originating in public sector organizations.

The paper contains three primary findings. First, we show that biotechnology firms with a greater number of in-license agreements with universities are more likely to craft revenue-generating alliances with downstream partners. This is the core relationship we seek to confirm: if young biotechnology firms are technology brokers, firms with many university deals will have more to offer to downstream partners in strategic alliances. However, we also hypothesize – and find – that the positive relationship between upstream and downstream alliances attenuates in biotechnology firm

[1] Following convention, we will refer to technology sourcing alliances between biotechnology firms and universities as "upstream" partnerships, and alliances between biotechnology firms and established life sciences companies as "downstream" deals. Thus, throughout the paper, we will use upstream and downstream to designate the direction of an alliance relative to a biotechnology firm's position in the industry's value chain. Also, we interchangeably use the terms "life sciences" and "pharmaceutical" firm to refer to the downstream partners that collaborate with biotech firms. These firms include, in order of frequency, pharmaceutical companies (e.g., Eli Lilly), mature biotechnology firms (e.g., Amgen), and agrochemicals firms (e.g., Dupont, Monsanto). Finally, throughout the paper, we will use the term "broker" and "intermediary" as synonyms.

age, invested capital, and working capital. We argue that changes in biotechnology firms' strategic scope account for this dwindling effect: as young firms mature, accrue financial means, and develop additional capabilities, they become more likely to extensively develop in-licensed technologies, rather than partner with downstream collaborators at an earlier stage of development. Our final result is from regressions of the determinants of university–biotechnology firm deals. Here, we show that the diversity and quality of the connections of firms' founders and advisors within the academic community influence their chances of successfully acquiring the rights to scientific discoveries in universities.

2. University–firm interactions

In the past few decades, universities have become much more proactive in their commercialization efforts (e.g., Di Gregorio and Shane, 2003; Nelson, 2004; Sampat, 2006). Indeed, many universities conceive of their traditional mission of educating students and advancing understanding to have broadened to include patenting and commercializing research discoveries (Bok, 2003). Using data collected by the Association of University Technology Managers, Thursby and Thursby (2002) reported that the number of patents granted, inventions disclosed by faculty, and formal licensing agreements executed at U.S.-based research universities all increased more than 7% per year throughout the 1990s. Henderson et al. (1998), Mowery et al. (2001) and Sampat (2006) further document trends in universities' patenting activities. Some universities have also spawned startups to commercialize scientific discoveries. Shane and Stuart (2002), for example, analyzed a dataset with more than 130 startup companies founded in full or in part to exploit MIT-owned inventions. While MIT is admittedly an outlier, there has been an across-the-board increase in universities' commercialization efforts.

Specifically in biotechnology, innovation has hinged on the coordinated efforts of three types of organizations: universities, biotechnology firms, and established life sciences firms (Kenney, 1986; Arora and Gambardella, 1990; Liebeskind et al., 1996; Powell et al., 1996; Zucker et al., 2002; George et al., 2002). While the alliance literature has been more focused on partnerships between biotechnology firms and downstream life sciences companies, the extensive connections between universities and biotechnology companies have been featured in the growing literature on university–industry relations. In one of the more influential papers on the subject, Zucker et al. (1998) argued that the dependence of young biotechnology firms on university science ran so deep that the geographic configuration of the early biotechnology industry could be expected to parallel the geographic locations of star life scientists employed in universities.[2]

Biotechnology firms maintain broad and deep, formal and informal relations with universities. We estimate that half of all biotechnology firms have been founded by university scientists, most of whom maintained academic appointments post-founding.[3] The majority of firms recruit prominent scholars in universities and non-profit research institutes to serve as compensated scientific advisors. There are also myriad, non-contractual ties between private sector firms and public sector research organizations, such as coauthorships among researchers that span the public–private divide (e.g., Owen-Smith and Powell, 2001; Zucker et al., 2002; Gittelman, 2003a; Stuart and Ding, 2006). The network woven by these informal relationships is dense, as two recent papers illustrate. Beginning with a bibliometric dataset of individual life scientists in universities, Azoulay et al. (in press) found that 38% of the members of a random sample of 3800 U.S.-based, academic life scientists had, at some point in their careers, coauthored one or more papers with scientists working in the private-sector. Starting with a sample of biotechnology firms, Gittelman and Kogut (2003) found that more than 70% of the scientific papers published by members of firms were coauthored with a scientist in academia.

In addition to part-time employment contracts and informal collaborations that connect individuals in biotechnology firms and scientists in universities, formal, inter-organizational contractual linkages are also prevalent. These formal university–firm linkages include technology licensing deals (exclusive or non-exclusive) in which rights to use specific discoveries or scientific materials are acquired by firms, and sponsored research agreements, in which a for-profit firm provides research funding for university research, often in exchange for the right of first refusal to license scientific discoveries. In the following sections, we develop predictions concerning

[2] Close university–industry interactions are not unique to biotechnology—such connections are present in a variety of industries today, and have existed in many of the technologically advanced industries of other times. For example, in a history of the early synthetic dye industry, Murmann (2003) attributed Germany's dominance of the industry to the strength of the country's academic programs in synthetic organic chemistry, coupled with the dense interactions between leading university scientists and researchers in nascent companies.

[3] Audretsch and Stephan (1996) identified 101 founders of biotechnology firms, of which 50 were university-employed scientists. In the much larger dataset used in this paper, we find approximately the same percentage of academician-founded companies.

the relationship between biotechnology firms' upstream alliances with universities and their downstream transactions with life sciences firms, and about the attributes that we anticipate will affect a biotechnology firm's proclivity to enter into university deals.

3. Intermediaries in tripartite alliance chains

There is a long history of research on the contribution of brokers – both individuals and organizations – to the development and commercialization of technology (see Howells, 2006, for a review). Broadly, brokerage or intermediary relations are connections between two actors that are mediated by a third party (Burt, 1976; Galaskiewicz, 1979; Marsden, 1982; Gould and Fernandez, 1989). The brokerage role is quite varied, and brokers are known to facilitate transactions in a number of distinct ways. For instance, brokers can act as gate keepers, deciding who gets access to the interests they represent; they can serve as go-betweens, informing two potential exchange partners of complementarities in one another's interests, skills or resources; or technology brokers can play a combinatorial role, assisting in the bringing together of previously disparate pieces of knowledge to create a novel technological approach (see e.g., Hagadon and Sutton, 1997; Fleming and Sorenson, 2003; Burt, 2004).

A broker can also serve as a liaison, or an actor that interconnects two distinct types of actors in a channel of resource exchanges (Gould and Fernandez, 1989, p. 93). This conception of brokerage is closest to our use of the term in the context of the biotechnology industry: to the extent that early stage firms in the industry receive intellectual property from universities and subsequently exchange it (often after considerable, additional development) with downstream alliance partners, young firms in the industry perform the role of liaison brokers.[4]

In our view, many biotechnology firms can be viewed precisely in these terms: they serve as value-added intermediaries between universities and downstream alliance partners. Consider, for instance, Millennium Pharmaceuticals, a Boston-based company founded to capitalize on scientific advances in genomics and bioinformatics. Like many other young biotech companies, Millennium has cultivated extensive connections within the academic community. One of the company's founders was a genomics expert at the Whitehead Institute for Biomedical Research (an MIT-based research institute). Millennium also assembled a scientific advisory board (SAB) comprising 13 Ph.D. scientists and 10 M.D.s, all but 1 of whom were researchers at universities (including MIT, Harvard, and Princeton) or non-profit research institutes. Thus, a number of prominent academic scientists maintained affiliations with the company.

Fig. 1, constructed from information in the company's 1996 IPO prospectus (SEC form S-1A, file number 333-02490, 06/05/1996), locates Millennium at the hub of a network of upstream and downstream relationships. At the time of its IPO, Millennium had established downstream, product development alliances with three pharmaceutical firms in five different therapeutic areas (obesity, oncology, diabetes, heart disease, and respiratory ailments). In these alliances, Millennium provided its partners access to receptors it had identified to serve as targets for drug development research. In exchange, Millennium received lump-sum payments, the promise of contingent payments based on future accomplishments, and, if a product were ever brought to market, royalties on product sales. Millennium's downstream alliances demonstrate the vertical nature of biotechnology collaborations: the division of labor specified in these transactions dictated that the company's strategic partners would undertake preclinical studies, clinical development, regulatory approval, and manufacturing and marketing of any products resulting from technologies supplied by Millennium. Thus, Millennium contributed intellectual property, while its partners provided financial capital and access to the complementary assets essential for developing the company's genomics technologies into marketable products.

Notice as well that Millennium had created a number of upstream relationships – some casual and some formal – with universities. In arguing that firms like Millennium act as brokers, we do not mean to suggest that the company is merely a passive or thin intermediary. Indeed, before signing up downstream partners, the company had made significant investments in advancing its technology platform, much of which was developed internally.[5] However, it is equally apparent that the com-

[4] Our data are macroscopic and we do not observe the specific behaviors of the biotechnology firms in any of the myriad transactions in the dataset we explore. For this reason, we must be somewhat agnostic about the specific functions of biotechnology firms in the alliance chains we observe. Based on findings in the literature, it is highly likely that biotechnology firms also often play a combinatorial role and sometimes serve as gatekeepers. Given that we cannot observe specific actions, however, we emphasize that young biotechnology firms are liaisons because they are intermediaries situated between universities and established firms.

[5] In the first 3 years after founding, Millennium invested approximately $75 million in R&D to develop its technology platform.

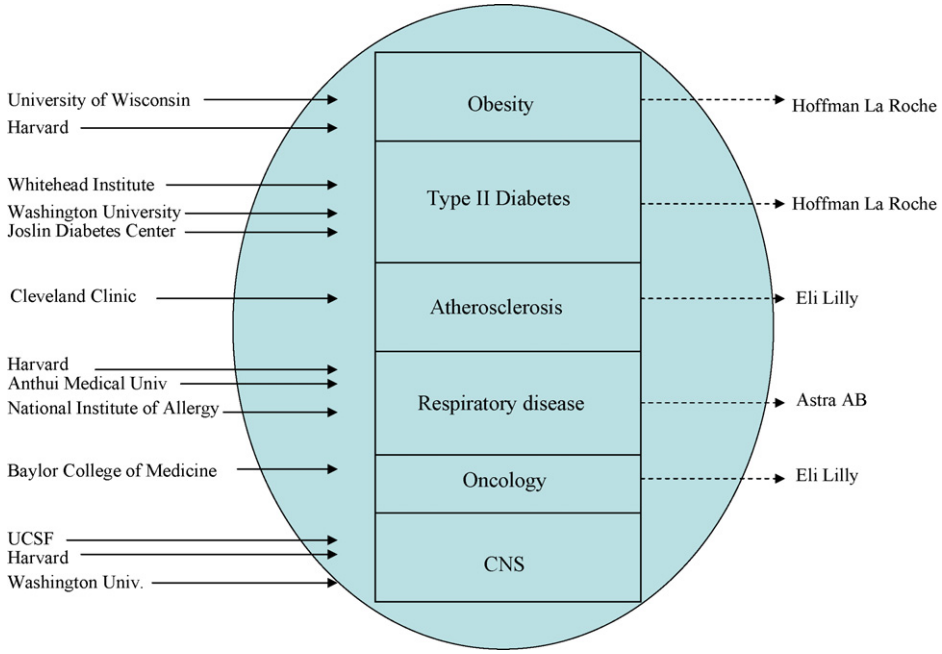

Fig. 1. Millennium pharmaceutical alliance profile at IPO (1996). The shaded oval represents Millennium Pharmaceuticals, with boxes corresponding to research programs in disease areas the company had initiated prior to going public. Solid arrows depict upstream alliances with universities, and dashed arrows depict downstream deals with pharmaceutical firms. All contracts were in place at the time the company filed to offer public shares in 1996.

pany is not the sole developer of the technology it shares with downstream collaborators. In Section 5, we formulate predictions concerning the relationships between upstream and downstream alliance activity at biotechnology firms, as well as the influence of founding team characteristics on the enactment of a technology brokering strategy. Before doing so, we provide as background a brief overview of the major stages in the drug development process. This description of the value chain, or sets of inter-related tasks that occur in the drug development process, represents the activity system in which industry participants make heterogeneous choices about where to focus their labor.

4. The drug development process

The development of novel pharmaceuticals is a complex, multi-year process that often begins with early-stage, exploratory research, and continues through FDA review to the marketing and selling of new medicines. The process begins with the identification of drug targets, which are enzymes, receptors or other proteins that trigger or block biochemical processes within a cell. Once identified, the biological role of these targets in disease initiation or progression is then validated, which entails establishing that a DNA, RNA, or protein molecule directly participates in a disease process and is therefore a suitable target for development of a new therapeutic compound. Validated targets are then screened against (typically hundreds of thousands) molecules, with the aim of pinpointing compounds that trigger or block the disease processes precipitated by the focal targets.

After a compound has been identified and screened, it must pass through a number of additional testing stages. Before it is submitted to the FDA to obtain clearance for human testing, it goes through extensive animal and other forms of pre-clinical testing. Clinical trials then consist of the commonly known three phases. After a drug finally receives FDA approval, firms often make additional investments to establish a pharmaceutical's efficacy relative to other options. Firms also invest substantial sums to market the drug to physicians. According to data from PhRMA, the pharmaceutical industry trade association, the total time involved from the beginning of discovery stage research to marketed drug is 10–15 years.

This is a broad-brushed description of the drug development process that lacks many of the complexities of each stage of the process. It does, however, convey the multi-stage, semi-sequential nature of the development process. Conceiving of basic research related to the biology of disease processes as being at the upstream end of

the industry's value chain and the individual consumer as being at the downstream end, the developmental stages just described can be construed as the major components of the industry's value chain. This industry has been of great interest to organizational researchers because it is populated with a diverse array of actors whose fates are woven together in the fabric of a dense collaborative structure along the industry's value chain (Powell et al., 1996, 2005). Again as a broad generalization, one can consider pharmaceutical firms as engaging in most steps of the value chain, but they typically devote a majority of their investment resources toward financing clinical trials and the sales and marketing of drugs. Whereas the mass of the resources allocated by large, established firms is devoted to downstream activities, upstart biotechnology firms and universities generally devote their resources to work on the upstream segments of the value chain. In our project, we are interested in the alliance federations that connect the actors focusing their efforts (at least within the context of a given development project) at different stages of this value chain. With this overview in mind, we turn to the conceptual development of the empirical relationships we explore.

5. Empirical implications

5.1. Alliance chains

Startup firms are now a prevalent organizational medium for bringing university science to the marketplace. In principle, one can consider any young firm that is founded to commercialize academic science to be engaged in the role of brokering connections between the public and private spheres. Prominent examples include Genentech, Cirrus Logic, and recently, Google.[6] What distinguishes biotechnologies from many other (but, as we discuss in the conclusion, not all) university-originated technologies is that, in the typical case, the process of commercializing biotechnologies is enormously costly. Whereas a young software company might raise sufficient capital to directly market its products to end consumers, early stage biotechnology firms almost uniformly depend on downstream alliance partners to perform many of the activities in the product development process. The substantial financial and capability-based requirements for commercializing biomedical technologies necessitate that early stage companies turn to established, resource-rich organizations to participate in technology commercialization. This factor is paramount in giving rise to the alliance chains we analyze.

A primary benefit of formal alliances with universities is that these deals often transfer rights to research discoveries to participating companies. Because university deals potentially increase their stocks of intellectual property, biotechnology firms with many in-licensing and joint research agreements with universities should have more technology to convey to downstream alliance partners. Insofar as biotechnology firms behave as liaison brokers, an increase in the volume of upstream transactions should positively influence the capacity of these firms to execute downstream partnerships.

In addition, accumulating (if not yet conclusive) evidence suggests that firms which build on basic science enjoy both more productive research and development operations and create more important technologies. In their examination of a large sample of patents across a spectrum of technologies, Fleming and Sorenson (2003) argue that scientific understanding can be construed as a "map" that guides technological search toward fruitful areas or exploration. Specifically with regard to the drug discovery process, Henderson and Cockburn (1994) find that firms which had adopted "science-driven" research and development efforts enjoyed improved productivity. These findings about the volume and quality of technological outputs imply that firms with formal scientific access agreements with universities may have more and better intellectual property to broker to downstream partners. We therefore expect,

Hypothesis 1. The more upstream agreements a biotechnology firm has with universities, the more downstream alliances it will enter with mature life sciences companies.

Obviously, we do not expect the first prediction to run counter to intuition. To be clear, however, Hypothesis 1 is not tautological—neither are downstream alliances necessarily the form of commercialization strategy pursued by a particular company, nor is it a truism that in-licensed technology will augment firms' ability to attract downstream partners. We believe, moreover, that the relationship between the rates of upstream and downstream partnerships will vary over biotechnology firms' lifecycle, and thus that measures of firms' development

[6] These three companies licensed university discoveries, and their formation involved significant participation from university faculty. Stanford and Berkeley jointly held the (now-expired) recombinant DNA patent licensed by Genentech, and co-founder Herbert Boyer was a member of the UC faculty; Cirrus Logic grew out of research at MIT and was founded by Suhas Patil, an MIT faculty member; and Stanford holds the patent on the method for ranking web pages that is licensed to Google.

stage will moderate the relationship set forth in the first prediction.

The strategy literature has documented many of the potential advantages gained from collaborative activity (e.g., Kogut, 1988; Hagedoorn, 1993; Gulati, 1998), but as many have observed, the opportunity costs associated with downstream partnerships are also non-negligible. When a biotechnology firm (or any other company) enters an alliance with a downstream partner, it will cede some proportion – very often, the majority – of the rents to the strategic partner. In fact, in the typical case, the biotechnology firms' downstream partners retain most of the profits generated by any future sales of a product emerging from an alliance. There is evidence that this cost is particularly high for firms in weak negotiating positions: financially strapped biotechnology firms, because they lack bargaining power, often must enter alliances under less attractive terms (Lerner and Merges, 1998).

Because of the many opportunity costs of alliances, a number of biotech firms have pursued a strategy whereby they begin brokering technology, but ultimately perform in house more of the value chain functions, thus lessening their reliance on downstream partners. Returning to the description of the industry's value chain in Section 4, although just a handful of biotechnology companies have become fully integrated across all stages of the drug development process (e.g., Amgen, Genentech, Genzyme, Biogen Idec), many have migrated part of the way down the value chain by investing the surpluses from past alliances and external financing rounds in the development of a broader suite of capabilities. In turn, as biotechnology firms extend their internal scope to incorporate more downstream functions, they become less dependent on downstream alliance partners at the early stages of the drug development process. If this is an accurate characterization of the strategic evolution of a number of firms in the industry, we should observe that,

Hypothesis 2. The magnitude of the positive relationship between the incidences of upstream partnerships with universities and downstream alliances with established firms will attenuate as biotechnology companies mature.[7]

Put differently, we anticipate that the business model of brokering university technology will be most prevalent among young companies, or equivalently, older firms with a broader set of capabilities will be less likely to quickly form downstream partnerships for in-licensed discoveries, choosing instead to directly exploit their technological assets to a greater extent.

5.2. Sourcing upstream deals

Having discussed the interdependence of upstream and downstream alliances, we briefly consider the question of the determinants of in-license agreements between biotechnology firms and universities. Here, our arguments lie at the intersection of an emerging literature on the social networks of entrepreneurs as important determinants of resource mobilization (e.g., Brittain and Freeman, 1986; Shane and Stuart, 2002; Maurer and Ebers, 2006), and the more general literature describing how social networks facilitate access to resources (Granovetter, 1973; Burt, 1992). We assert that the depth and the breadth of the networks of *academic* scientists affiliated with young technology firms influence companies' ability to identify and negotiate access to promising university science. Just as the advantage of a broker lies in the reach of the actor's ties in the community in which he or she intermediates transactions, we anticipate that affiliated scientists that are well positioned in academic circles will be most likely to aid their firms in the process of acquiring rights to university science.

Particularly because universities have become active in promoting technology transfer, however, it is reasonable to question whether connections within the academic community are a prerequisite for identifying promising university technologies? For there to be merit to the argument that affiliated scientists with rich networks are instrumental in formal contracting between biotechnology firms and universities, some factor(s) must preclude interested parties that lack networks in academia from gaining equal access to university science. In fact, if the general argument is correct that biotechnology firms are sometimes created to capitalize on brokering technology between universities and downstream partners, it must be that these upstart firms possess

[7] For this hypothesis to be supported, it is not necessary that biotech firms forward integrate to encompass *all* commercialization functions. One way to imagine the drug development process is as a pyramid. In the early stages of development, researchers often consider a vast array of molecules as potential drug development candidates. At each successive stage of the development process, many of the potential candidates are eliminated. Biotechnology firms that are able to take a molecule down the development pipeline, e.g., to the point at which a lead molecule has been validated and animal tested, are likely to engage in less frequent, but larger transactions. This is because both time and development costs, as well as the value, of a potential molecule increases as the drug candidate successfully passes each of the many hurdles in the development process.

an advantage relative to incumbent firms in creating these linkages in the value chain.[8]

What might such limiting conditions be? We see at least three possibilities. First, an immense amount of research is performed across many universities and research institutes. Consider, for instance, that in recent years the University of California system (including all nine campuses) has, among all organizations, garnered the greatest number of patents in the life sciences. In any given year, there are hundreds of discoveries available for license from the UC system alone. Thus, the large volume of research in this sector creates high search costs for would-be licensors. The difficulty of identifying promising university science may create an opportunity for the formation of brokers to screen and market discoveries emanating from universities.

Second, because many licenses are secured on an exclusive basis, it is often necessary to negotiate access to the most promising scientific research when the research is at an early stage of development, before information about the value of a discovery has disseminated widely. Holding exclusive licenses to university technology is one of the potential sources of competitive advantage of young science-based firms (Rothaermel and Thursby, 2005). Without a connection to the scientists involved in a discovery, interested parties may be too late to obtain direct access from the university. Thus, knowledge of high potential scientific work at the time when it is still in a university lab may be an important determinant of the ability of companies to capitalize on university science.

Third, due to the tacit nature of many state-of-the-art scientific discoveries, participation of the scientist(s) who made a research discovery is often necessary to extract its full value. We think friends and fellow academics are more likely to succeed at enlisting the advice and participation of university inventors in helping private firms advance the technology they have in-licensed. Moreover, in many cases licensable university science pertains to basic discoveries. Insofar as additional development is necessary in an area of scientific specialization that is not well honed in established firms, it is often necessary that a party with the relevant expertise advance the discovery to a more developed state. Thus, because they tend to develop expertise in specific areas of basic scientific research, biotechnology firms are often better equipped to further the advancement of in-licensed technology.

For these reasons, we anticipate that thick networks in the academic community will facilitate the process of searching for and assimilating university-developed scientific discoveries. Thus, we predict,

Hypothesis 3. Biotechnology firms with founders and scientific advisors that are well networked in the academic community will be more likely to enter formal technology-access agreements with universities.

6. Empirical analysis

We have collected information from a number of sources to build a panel dataset that contains firm-year observations on all publicly traded biotechnology companies in the U.S. The dataset includes firms' full alliance histories and financials since the year of their birth, as well as detailed information on the academic scientists affiliated with the companies.

6.1. Data sources

We began by assembling a list of all biotechnology firms. To create a census of firms, we consulted a number of rosters of industry participants, including *Compustat*, *Bioscan*, *Informagen*, *Recombinant Capital*, and *CorpTech*. Next, matching names in this historical census to firms in the Center for Research in Securities Prices (CRSP) database, we identified all biotechnology firms that have issued shares of stock on the U.S. public markets. In this study, we have limited the analysis to publicly traded firms for two reasons: we were only able to acquire information on founders' backgrounds for public firms, and data on alliance activity is most complete for them as well.

We received information on alliances from Recombinant Capital, a biotechnology industry consulting firm and information vendor. The Recombinant Capital Alliance Database contains descriptions of more than 15,000 deals, including agreements between firms and universities. Recombinant Capital scours SEC filings, press releases, industry conferences, and other sources

[8] It is important to clarify that we do not claim that biotechnology firms (and startups more generally) are alone among private-sector companies in possessing formal and informal relationships with universities. The research staffs at pharmaceutical firms, for instance, also are known to associate with university faculty. Cockburn and Henderson (1998) described coauthorships between researchers in pharmaceutical firms, and Gittelman (2003b) found that in France, it is common for established companies (rather than startups) to work directly with university scientists. We merely claim that, in the U.S., members of the research staff at biotechnology firms are likely to be more densely embedded in the academic community than their counterparts at large, established pharmaceutical, chemical, and life sciences companies. This assertion is well supported in the literature, and later we too report supportive evidence.

to identify alliances. Proxy statements are a particularly fruitful source of information about deals because synopses of terms must be reported in filings if a transaction is judged to be "material" to a company's current or future operations. Because of this disclosure requirement, alliance histories are probably most complete for public biotechnology firms.

We analyze a total of 429 U.S.-headquartered biotechnology firms that have issued shares to the public between 1972 and 2002, when we concluded our data collection. We retrieved SEC filings for each of these companies.[9] According to Recombinant Capital, these firms had established a total of 1330 upstream alliances with universities, and a total of 4139 downstream alliances with commercialization partners. The unbalanced panel contains an average of 10.6 observations per firm. Although data availability issues required us to limit the analysis to firms that had filed an IPO prospectus at some point in their lifespans, we were able to collect alliance data and other covariates for all firms in the sample from their birth years. Thus, we have complete (i.e., non-left-censored) alliance event histories for all the firms in the sample we analyze.

From the IPO prospectuses, we coded financial information for firms in the years prior to going public, as well as biographical sketches of company founders and members of scientific advisory boards.[10] After compiling a list of the 1116 Ph.D.-holding academic scientists who were formally affiliated with the firms in our dataset (for ease of exposition, we will refer to the academic founders and SAB members of the companies in our dataset as "affiliated scientists"), we then queried the ISI's *Web of Science* database to collect complete publication histories for each of these individuals. We used the set of scientific papers written by these individuals to construct measures of the company-affiliated scientists' networks in academia, as well as their prominence in the scientific community.

6.2. Covariates

6.2.1. Alliances

All firms in the dataset enter in the year of their incorporation, and we conclude the analysis at the end of 2002. Thus, the dataset is an unbalanced panel with observations on firm-years. After cleaning the data to remove alliances arising for non-strategic reasons (e.g., as settlements to litigation or asset sales caused by financial distress), we constructed current-year and multiple lags of alliance counts, distinguished by agreement and partner type, for each firm-year. The covariate of central interest is a count of the "total number of upstream partnerships" (i.e., deals between biotech firms and universities) for biotech firm i in years $t-1$, $t-2$, $t-3$, or the 3-year window, [$t-1$ to $t-3$]. A second alliance count, which serves as the dependent variable in the tests of hypotheses 1 and 2, is the "total number of downstream partnerships" (i.e., vertical alliances with established firms) created by biotechnology firm(it).[11] Hypotheses 1 and 2 are examined by documenting the relationship between lagged values of the upstream alliance count and the current-period value of the downstream alliance count, and then allowing the relationship to vary with the maturation of the biotechnology firm.

6.2.2. Affiliated scientists' networks

To examine Hypothesis 3, we constructed three measures of the networks of the scientists affiliated with the biotech companies in our data. First, for each company in the dataset, we include a count of the number of academic founders, which we define to be scientists that were research faculty at universities or non-profit research institutes at the time their company was incor-

[9] For companies that filed papers to go public after 1995, IPO prospectuses are conveniently available in the SEC's EDGAR database (http://www.sec.gov/edgar.shtml). We acquired the remaining S-1 forms by traveling to the SEC's main office in Washington, DC, where historical findings can be photocopied. Not every S-1 document provided detailed information about founders and advisors; we were only able to obtain this information for approximately 70% of the companies. The gaps are concentrated in the early period of the industry, when disclosure requirement for securities offerings appear to have been less extensive.

[10] Almost all young biotechnology firms assemble boards of compensated scientific advisors. Board members are often prominent academics who are experts in the scientific fields in which the firm is doing research. In addition to providing guidance on scientific matters, board members lend credibility to young companies (Higgins and Gulati, 2003).

[11] In one-fourth of the downstream collaborations in the dataset, both partners are biotechnology firms. We include these alliances in the data we analyze. Typically, these agreements are established between young and small biotechnology firms and relatively more senior partners. Like deals between biotechnology firms and life science companies, biotech–biotech collaborations routinely entail a vertical division of labor. For instance, in early 2003, the recently public firm Tularik (IPO in 2000) entered into a strategic alliance with Amgen, the biotech firm with the highest market capitalization at the time of this writing. Under the terms of the contract, Tularik is to provide Amgen with drug targets in the area of oncology. The partners will co-develop any drugs resulting from the targets, while Amgen will perform all clinical development and possess worldwide commercialization rights. In the dataset, we would increment Tularik's downstream alliance count for this transaction, but Amgen's downstream alliance count would remain unchanged.

porated. Second, we collected the 129,825 papers written by the 1116 scientists that were affiliated with the firms in our dataset, which we used to compute year-specific counts of the number of unique coauthors accrued by each of the affiliated academic scientists. Following a literature on the information advantages of network reach (Bonacich, 1987), we assume that scientists with high degree scores (counts of relations) in the coauthorship network were most able to gain awareness of potentially commercializable science in universities.

As a third proxy, we computed paper citation counts – the conventional measure of academic prestige – for each academic scientist affiliated with the firms in our dataset. Our assumption in including this measure is that scientists known for their scholarly achievements will, through frequent participation in scientific gatherings and other opportunities that accompany academic prominence, be well networked in scientific circles. From the *Web of Science* database, we collected the cumulative citation counts for each article written by founders or SAB members at the time we downloaded the data (2002). However, the 2002 citation count of a scientist affiliated with a firm founded in the late 1970s could be misleading; a preferable measure would be the cumulative citation counts for an affiliated scientist at the time he or she started or began advising a firm. While it would be very time consuming to produce exact citation counts, we can closely approximate them by distributing each paper's total (2002) citations back through time. We did so assuming that citations arrived according to an exponential distribution with hazard rate (i.e., inverse mean) equal to 0.1.[12] Backward distributing 2002 citation totals yields annually updated citation counts for each article, from which it is straightforward to compute the total number of citations received by each firms' academic affiliates at the time of firm founding. We examine Hypothesis 3 by relating each company's affiliated scientists' coauthorship and citation counts to its upstream alliance formation rate.

6.2.3. Top 10 university

Much of the public dialogue and scholarly work on university–industry relations has emphasized the central role played by a few prominent institutions, such as Stanford and MIT, in generating university-based entrepreneurship. To assess the extent to which the phenomena we study are general or merely result from the partnering strategies of spin-off companies from a small number of elite universities, we create a "Top 10 University" dummy variable. This covariate is defined to be one if a focal firm's *first* university alliance was inked with 1 of the 10 universities who were most actively involved in alliances with biotechnology companies (these 10 institutions are identified in Table 1 below). We coded this variable based on the identity of each firm's first university partner rather than the employers of its affiliated faculty because most firms were connected to faculty from multiple universities.

6.2.4. Size controls

To obtain clean estimates of the effect of upstream alliances, it is important that we carefully account for the size of the firm in the regressions predicting downstream alliance formation. Larger firms presumably have more technology to entice downstream partners, and if the incidence of upstream alliances with universities is correlated with biotechnology firm size, then the results could be misleading if we do not condition on firm size. We therefore included three, time-changing measures of firm size in the regressions. First, we included the log of annual sales revenues of each firm. Second and third, we incorporated two variables to account for the technological size of the firm: annual R&D expenditures, and the stock of patents assigned to the firm up to a given year.

6.2.5. Other controls

All models contain a set of year dummies to account for time-varying factors, such as the availability of financing for biotechnology firms, which may affect the outcomes we examine. Lastly, we included the age of the firm. The age variable is interacted with the upstream alliance count to test Hypothesis 2.

6.3. Estimators

We estimate a set of count models to test the three hypotheses. The dependent variable in the first set of regressions is a count of the number of commercialization alliances biotechnology firm i has created with downstream partners in year t. We use a fixed effect specification to remove the influence of time invariant strategic heterogeneity among firms that may affect the outcome variable.[13] Thus, we present conditional fixed

[12] The bibliometric literature suggests that citations accumulate according to an exponential distribution (Redner, 1998), and this is true of the typical paper in our database. We identified the specific parameter, 0.1, by manually coding 50 randomly selected papers in each of 3 publication years: 1970, 1980, and 1990, and then choosing the parameter that yielded the best fit to the actual time path of citations to these randomly chosen papers.

[13] There is a reasonably broad mix of firms in our sample, so we expect some heterogeneity in firms' alliance strategies. While the majority of

Table 1
Biotechnology firms and universities with the highest alliance counts

Firm name	Number of alliances with universities	University name	Number of alliances with biotech firms
Centocor	25	MIT	65
ImClone Systems	24	Stanford	61
Genetic Therapy	19	University of Texas	50
MedImmune	18	Johns Hopkins	46
Myriad Genetics	17	Harvard	39
Targeted Genetics	17	Mass General Hospital	36
Sugen	15	UC San Francisco	35
Affymetrix	13	Duke University	29
Xoma	13	University of North Carolina	25
A number tied at 12 (e.g., Alexion and Sequenom)	12	UC San Diego	24

The table lists the 10+ biotech firms with the greatest number of alliances with universities (column 1) and 10 universities that have the highest number of alliances with biotech firms (column 3) prior to 2002.

effects negative binomial regressions (Hausman et al., 1984) of the rate of *downstream* alliance formation. Hypothesis 1 anticipates that firms that have a greater number of university deals will be more likely to enter downstream alliances. Hypothesis 2 proposes that the positive association between upstream and downstream alliances will temper as biotechnology firms mature. We examine this prediction by interacting the upstream alliance count with three covariates that capture different dimensions of biotechnology firm maturation: the age of the biotechnology firm; the amount of working capital available to the firm; and the total invested capital in the firm. We expect negative coefficients on each of the interaction effects.

The final set of regressions address the determinants of biotechnology firms' upstream alliances with universities. The dependent variable in these models is the annual count of university alliances established by firm i in year t. Our goal in these regressions is to determine whether affiliated scientists' network characteristics at the time of founding affect the subsequent alliance strategies of biotechnology firms. Obtaining estimates on these initial conditions precludes the inclusion of firm-specific effects (because the covariates of primary interest to us do not vary within firm). To test Hypothesis 3, we therefore report random effects negative binomial estimates.

7. Findings

Before presenting the multivariate results, we describe some of the patterns in the data. Table 1 presents the 10 biotechnology firms and the 10 universities in our dataset that participated in the greatest number of university–biotechnology firm transactions. Among all universities, MIT and Stanford have been the most active in entering contractual agreements with biotechnology companies. As has been documented in the case of academic patenting, it appears that prominent universities are disproportionately involved in licensing. However, of the 2342 upstream alliances in our data, the Top 10 universities reported in Table 1 represent a mere 17.5% of the total transaction volume. Thus, members of a relatively diverse group of universities are actively engaged with biotechnology firms.

Fig. 2 shows, for the full sample, the average number of upstream and downstream alliances biotechnology firms have entered at each year of firm age. In addition, for the upstream alliance propensity, we break out the data by founders' status: we separately report the curve for biotechnology firms with one or more university faculty members as founders and those without any academic founder. As the figure shows, faculty-founded firms are slightly more likely to have a formal university alliance in the early years of their existence, but the difference is not large. Fig. 2 also demonstrates that both the upstream and downstream alliance counts reach peaks prior to the sixth year of a firm's life, and then slowly taper as biotechnology firms mature. Thus, as suggested

the firms in the sample can be broadly classified as human therapeutics companies, the sample contains genomics, proteomics, combinatorial chemistry, gene therapy, and many other types of firms. It is highly likely that these differences in objective will lead to heterogeneities in alliance propensities. The conditional fixed effects estimator allays concerns about time-invariant sources of heterogeneity. For instance, the conditioning will subsume non-time-varying differences in founding conditions, such as whether or not firms were founded by one or more university professors. In addition, although early stage biotechnology firms do often switch therapeutic foci as they evolve, the fixed effects will partially account for inter-firm variation in the focus on specific disease categories.

Table 2
Number and density of alliances among universities, biotechnology firms, and pharmaceutical firms

	Biotech	Pharma	University
(a) Alliances, all years: 1986–2002			
Biotech	4361/0.347	5958/0.475	2234/0.178
Pharma	5958/0.870	777/0.113	108/0.016
University	2234/0.952	108/0.046	N/A
(b) Alliances, early years: 1986–1993, inclusive			
Biotech	429/0.159	1553/0.574	722/0.267
Pharma	1593/0.918	131/0.077	7/0.004
University	722/0.989	7/0.010	N/A
(c) Alliances, recent years: 1994–1996/2003, inclusive			
Biotech	3932/0.397	4406/0.449	1512/0.154
Pharma	4406/0.855	646/0.125	101/0.020
University	1512/0.935	101/0.062	N/A

(a–c) The number and proportion of alliances between actors in category on row with members of category on column. For instance, in the period 1986–1993, 1553 (57.4%) of the 2704 biotechnology firm alliances were with pharmaceutical companies. (The "Pharma" category also includes some non-drug-related companies with a life sciences presence, such as DuPont.) Counts are symmetric but proportions are not because of differences in row sums—the total number of transactions involving the actors on each row.

by Hypothesis 2, the sample averages do indeed suggest the possibility that there are changes in alliance propensities as firms mature.

Table 2(a–c) are simple density tables illustrating the collaborative structure of the life sciences industry. To construct the tables, we report the count and proportion of alliances within and across three types of actors: universities, biotechnology firms, and established pharmaceutical and life sciences companies. Table 2a aggregates the alliances across all time periods; Table 2b and c report the same information but for an early and late period in the evolution of the industry. In making these table, we used all alliances in the Recombinant Capital database (i.e., we do not limit alliance activity to the deals involving the 429 firms in the database we analyze in the regressions).

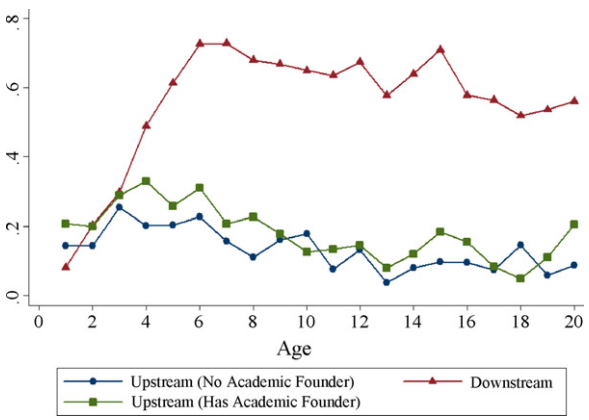

Fig. 2. Biotechnology firms' average number of upstream and downstream alliances formed by year of age and founder status. Plots the average number of upstream and downstream alliances formed by biotechnology firms at a given age. Average number of upstream alliances at a given age is presented separately for firms with and without academic founders. Each data point in the figure is calculated by dividing total number of alliances executed at a given age by number of biotechnology firms of that age.

The patterns in Table 2 are instructive about the roles of the different categories of actors we analyze. The cells in Table 2a indicate the number and proportion of transactions that the organizations in the category on the row completed with the type of actor on the columns. Thus, for example, across all years of the Recombinant Capital dataset, there were 4361 biotechnology–biotechnology collaborations; 5958 alliances between biotechs and established life sciences/pharmaceutical companies; and 2234 formal partnerships between biotechnology firms and universities.

We take a few points from these tables. First, consistent with our portrayal of young biotechnology firms as playing the role of brokers, the level of biotechnology–university engagement greatly exceeds the level of pharmaceutical company–university transactions.[14] In the full alliance dataset, there were a total of 108 university–pharmaceutical deals, versus 2234 university–biotechnology agreements. Across all

[14] The one caveat to this claim is the possibility that there are more missing observations among university–pharmaceutical firm agreements than for university–biotech deals. Although Recombinant Capital attempts to gather the population of all university–company transactions broadly related to the drug and biotechnology sectors, university transactions with large firms may be publicly disclosed less often than are agreements with smaller companies.

years, only 1.6% of the pharmaceutical firm alliance activity is with universities. We take this as prima facie evidence that biotechnology firms have had some kind of comparative advantage with respect to in-sourcing technology from universities.

Second, we can also observe an evolution of the role of biotechnology firms in the collaborative structure of the field. In the pre-1994 time period (2b), biotechnology firm–biotechnology firm partnerships, or agreements that often entail a vertical division of labor between the two partners, were relatively uncommon; just 16% of the overall transactions. In the last decade of the data (2c), this proportion changed dramatically: biotechnology–biotechnology alliances have become typical. They represented 40% of all alliance transactions, and they were almost as frequent as biotechnology–pharmaceutical firm partnerships. We consider this trend to be the aggregate-level manifestation of the maturation of many of the firms in the industry. As some of the industry's early entrants have developed, they have extended their vertical scope to incorporate additional downstream capabilities. In turn, their migration down the value chain has enabled some of the more mature biotechnology firms to participate on the downstream side of the alliance chains in the industry: mature biotechnology firms are frequently on the receiving end of technology in-sourced from their startup counterparts.

Table 3 characterizes the upstream alliances in the data by transaction type, partner type, and deal size. We grouped upstream alliances into four categories: license only, license and collaborative research and/or development, R&D only, and other. Consistent with the most basic claim of the paper, there is clearly a heavy technology access component to the upstream alliances: among the university–biotech firm transactions, 72% contain a license provision and the vast majority of the remaining transactions are either collaborative or sponsored R&D. In addition, university–biotech transactions appear to be relatively homogenous in size; 76% of the agreements involve some form of license fee but no other exchange of resources, and of the 24% of deals that have a funding component, the dollar amounts tend to be relatively small. Among funded alliances, the median deal size is $400,000.

Table 4 provides summary statistics for variables in our models, along with a correlation matrix. Table 5 reports the results from the fixed effects negative binomial regressions of the incidence of downstream alliance formation. In Model 1, there are two statistically significant control variables: the lags of logged annual R&D spending and firm revenues. Net of the conditional fixed effects, firms that increase R&D spending were more likely to subsequently enter downstream alliances. This association may occur because high R&D spending expands the intellectual property portfolio of the firm, thus yielding additional technologies to exchange with downstream partners. After accounting for the level of R&D spending, an increase in lagged revenue decreased a firm's propensity to establish downstream alliances. One possible explanation for the negative effect of revenues conditional on R&D is that firms with high revenues relative to their R&D investment are less in need of the assistance of downstream partners to commercialize

Table 3
University alliances by deal type and partner status

Alliance type	Is alliance funded			Median size of funded alliances
	No	Yes	Total	
(a) With biotech firms				
Licensing only	780	196	976	0.155
Licensing and R&D	425	202	627	0.775
R&D only	404	131	535	0.2
Other	80	17	97	4
Total	1689	546	2235	0.4
(b) With pharmaceutical firms				
Licensing only	20	2	22	NA
Licensing and R&D	31	10	41	9.35
R&D only	27	5	32	25
Other	8	4	12	101
Total	86	21	107	20

Show upstream alliance activity broken down by deal type and whether or not the transaction involved funding net of royalty payments. Median size data is in million dollar for funded alliances only (the median size of all alliances is zero).

Table 4
Descriptive statistics and correlation matrix for regressions of upstream and downstream alliance counts

		Mean	S.D.	Min	Max	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]
[1]	Num. of downstream alliances	0.839	1.422	0	13	1							
[2]	Num. of upstream alliances with univ ($t-1$)	0.215	0.641	0	8	0.197	1						
[3]	Num. of upstream alliances with univ ($t-2$)	0.223	0.667	0	8	0.125	0.311	1					
[4]	Num. of upstream alliances with univ ($t-3$)	0.222	0.639	0	7	0.123	0.266	0.315	1				
[5]	Num. of upstream alliances with univ (3 year window)	0.661	1.420	0	13	0.203	0.717	0.752	0.718	1			
[6]	Age	11.101	5.158	2	34	−0.087	−0.114	−0.123	−0.099	−0.154	1		
[7]	Age^2	149.823	142.850	4	1156	−0.083	−0.094	−0.106	−0.088	−0.132	0.961	1	
[8]	ln(R&D expenses in million dollars) ($t-1$)	1.914	1.130	0	6.78	0.258	0.085	0.105	0.122	0.142	0.178	0.162	1
[9]	ln(revenues in million dollars) ($t-1$)	1.843	1.591	0	8.20	0.097	−0.035	−0.034	−0.036	−0.048	0.440	0.436	0.480
[10]	Working capital (in million dollars) ($t-1$)	36.439	102.474	−87.8	2075	0.072	0.038	0.030	−0.002	0.030	0.180	0.191	0.495
[11]	ln(cumulative invested capital in million dollars) ($t-1$)	4.019	1.876	−3.77	10.03	0.119	−0.004	0.010	0.030	0.016	0.513	0.473	0.705
[12]	Num. of patent applications ($t-1$)	17.378	48.774	0	703	0.080	−0.008	−0.010	−0.028	−0.021	0.300	0.335	0.321
[13]	First university alliance partner is in Top 10	0.157	0.364	0	1	0.047	0.059	0.070	0.104	0.106	−0.065	−0.082	0.121
[14]	Num. of firm founders	1.831	1.272	0	7	0.046	0.004	0.015	0.012	0.014	−0.061	−0.066	0.185
[15]	Num. of academic founders	0.446	0.897	0	4	0.092	0.049	0.068	0.090	0.095	−0.125	−0.131	0.227
[16]	Prestige of (average citation count) of affiliated scientists (in 100)	27.877	38.592	0	273.59	0.219	0.099	0.098	0.109	0.139	−0.090	−0.114	0.377
[17]	Sum of coauthorship count of affiliated scientists (in 100)	3.924	5.562	0	58.5	0.174	0.077	0.080	0.089	0.113	−0.114	−0.128	0.369

		Mean	S.D.	Min	Max	[9]	[10]	[11]	[12]	[13]	[14]	[15]	[16]
[1]	Num. of downstream alliances	0.839	1.422	0	13								
[2]	Num. of upstream alliances with univ ($t-1$)	0.215	0.641	0	8								
[3]	Num. of upstream alliances with univ ($t-2$)	0.223	0.667	0	8								
[4]	Num. of upstream alliances with univ ($t-3$)	0.222	0.639	0	7								
[5]	Num. of upstream alliances with univ (3 year Window)	0.661	1.420	0	13								
[6]	Age	11.101	5.158	2	34								
[7]	Age^2	149.823	142.850	4	1156								
[8]	ln(R&D expenses in million dollars) ($t-1$)	1.914	1.130	0	6.78								
[9]	ln(revenues in million dollars) ($t-1$)	1.843	1.591	0	8.20	1							
[10]	Working capital (in million dollars) ($t-1$)	36.439	102.474	−87.8	2075	0.437	1						
[11]	ln(cumulative invested capital in million dollars) ($t-1$)	4.019	1.876	−3.77	10.03	0.670	0.453	1					
[12]	Num. of patent applications ($t-1$)	17.378	48.774	0	703	0.358	0.400	0.376	1				
[13]	First university alliance partner is in Top 10	0.157	0.364	0	1	−0.013	0.018	0.075	0.001	1			
[14]	Num. of firm founders	1.831	1.272	0	7	0.062	0.086	0.105	−0.008	0.097	1		
[15]	Num. of academic founders	0.446	0.897	0	4	0.013	0.122	0.068	0.001	0.217	0.465	1	
[16]	Prestige of (average citation count) of affiliated scientists (in 100)	27.877	38.592	0	273.59	0.093	0.243	0.200	0.069	0.157	0.215	0.344	1
[17]	Sum of coauthorship count of affiliated scientists (in 100)	3.924	5.562	0	58.5	0.092	0.265	0.176	0.034	0.144	0.282	0.487	0.669

Table 5
Fixed effects negative binomial regressions of rate of downstream alliances

Variables	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7	Model 8
Downstream alliances ($t-1$)								0.047** [0.013]
Age	−0.009 [0.025]	−0.009 [0.025]	0.021 [0.028]	−0.134** [0.034]	−0.147** [0.036]	−0.002 [0.034]	−0.018 [0.039]	−0.010 [0.025]
Age^2	−0.001 [0.001]	−0.001 [0.001]	−0.002** [0.001]	0.002* [0.001]	0.002** [0.0007]	−0.001 [0.001]	−0.001 [0.001]	−0.001 [0.001]
log of R&D expenses ($t-1$)	0.274** [0.038]	0.272** [0.038]	0.255** [0.039]	0.227** [0.045]	0.183** [0.05]	0.279** [0.053]	0.267** [0.056]	0.267** [0.038]
log of revenues ($t-1$)	−0.082** [0.029]	−0.083** [0.029]	−0.076** [0.029]	−0.073* [0.034]	−0.085** [0.035]	−0.081+ [0.043]	−0.067 [0.0401]	−0.099** [0.030]
Num. of patent applications ($t-1$)	−0.001 [0.001]	−0.001 [0.001]	−0.0004 [0.001]	0.001* [0.001]	−0.001 [0.001]	−0.002+ [0.001]	0.001 [0.001]	−0.001 [0.001]
Num. of upstream alliances with univ ($t-1$)	0.095** [0.025]							
Num. of upstream alliances with univ ($t-2$)	0.045† [0.026]							
Num. of upstream alliances with univ ($t-3$)	0.054* [0.027]							
Num. of upstream alliances with univ (3 year window)		0.064** [0.014]	0.195** [0.052]	0.051* [0.021]	0.112** [0.042]	0.071* [0.024]	0.057* [0.019]	0.052** [0.015]
Num. of upstream alliances (3 year window) × age			−0.025** [0.009]					
Num. of upstream alliances (3 year window) × age^2			0.001** [0.0003]					
Working capital ($t-1$)				−0.0002 [0.0002]				
Num. of upstream alliances × working capital ($t-1$)				−0.0002* [0.0001]				
log of cumulative invested capital ($t-1$)					0.052 [0.036]			
Num. of upstream alliances (3 year window) × log of cumulative invested capital ($t-1$)					−0.018* [0.008]			
Constant	0.287 [0.176]	0.285 [0.175]	0.129 [0.184]	0.789** [0.253]	0.805** [0.255]	0.676* [0.241]	−0.215 [0.276]	0.286 [0.176]
log likelihood	−3868.319	−3869.391	−3864.715	−2784.083	−2716.266	−2033.470	−1821.109	−3863.179
Likelihood ratio test	231.996	227.529	233.423	115.856	109.12	105.1	147.4	244.0
Degrees of freedom	25	23	25	25	25	23	23	24

Notes: (1) Number of observations = 4530 and number of firms = 429 in Models 1–3 and Model 8; (2) number of observations = 3168 and number of firms = 368 in Model 4 due to missing observation on working capital; (3) number of observations = 3211 and number of firms = 374 in Model 5 due to missing observations on invested capital; (4) all models include 17 dummy variables indicating years 1986–2002 (<1986 is the base period); (5) all models include firm fixed effects; (6) Model 6 is estimated using biotech firms that have academic founders. Number of observations = 2246 and number of firms = 221. (7) Model 7 is estimated using biotech firms that do not have academic founders. Number of observations = 2285 and number of firms = 208. (8) Standard errors in brackets.

† Significant at 10%.

* Significant at 5%.

** Significant at 1%.

their technology, and thus they enter fewer downstream partnerships.

Of central interest to us in Table 5 is the coefficient on the upstream alliance count. In Model 1, we have included the number of deals executed between the focal biotechnology firm and universities in each of the 3 previous years, $t-1$, $t-2$ and $t-3$. We included three lags to allow for the possibility that it takes time for the focal firm to turn around the intellectual property inputs acquired from universities to downstream alliance partners, both because biotechnology firms typically advance in-licensed technology before entering downstream alliances, and because commercialization alliances are often complex transactions that are painstakingly negotiated. In support of Hypothesis 1, all of the coefficients on the three lags of the upstream alliance count variables are positive and statistically significant. The 0.095 coefficient on the 1-year lag indicates that an additional upstream alliance increases the rate of downstream deal creation by a multiple of 1.1 (=exp[0.095]).[15] As one would expect, the coefficient magnitudes on the second-year lag falls substantially: in Model 1 of Table 5, the parameter estimate on the 1-year lag is nearly twice the magnitude of the coefficient on the 2-year lag. Our results suggest that the influence of university alliances on the downstream alliance rate takes place within the first 3 years after an upstream deal is established; in an unreported regression, we find that the fourth-year lag is statistically indistinguishable from zero.

Models 3–5 in Table 5 examine Hypothesis 2. Model 3 includes an interaction effect between the university alliance count and firm age, which is included as a second order polynomial. For ease of presentation, we have created a single measure of a firm's upstream alliance activity in the interval [$t-1$ to $t-3$], which we use to compute the interaction effects. To illustrate the interdependent relationship between age and upstream alliances as determinants of the downstream alliance rate, Fig. 3 plots the surface implied by the Model 3 coefficient estimates. In support of the assertion in Hypothesis 2, the

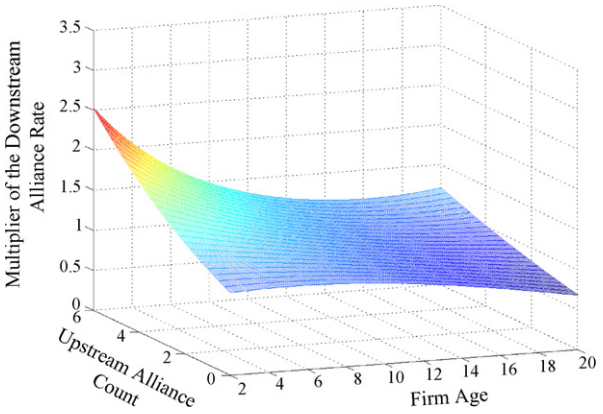

Fig. 3. Effect of age and upstream alliances on downstream alliances. Plots the surface relating the multiplier of the downstream alliance rate to biotechnology firms' upstream alliance count and age. This multiplier surface is generated from the parameter estimates in Model 3 of Table 4. The rate multiplier is given by the estimated equation: $\exp(0.021 \times \text{age} - 0.002 \times \text{age}^2 + 0.195 \times (\text{upstream alliance count}) - 0.025 \times (\text{upstream alliance count}) \times \text{age} + 0.001 \times (\text{upstream alliance count}) \times \text{age}^2$.

effect of the upstream alliance count sharply attenuates with the age of the firm. This is easily observed in Fig. 3 by tracing how the effect of a given level of upstream alliance activity declines with an increase in firm age.[16] The execution of an upstream contract with a university is considerably more likely to be followed by the inking of a downstream alliance contract *when the focal biotechnology firm is young*. We believe these associations exist in the data because more established biotechnology firms are more likely to have the internal resources to advance the technology they have in-licensed, without requiring the assistance of downstream partners until further down the value chain.

Models 4 and 5 in Table 5 offer further support for this conclusion by swapping the firm age interaction for direct measures of the resources under a biotechnology firm's control. Model 4 contains an interaction between the upstream alliance count and a firm's working capital in the previous year. Working capital is the difference between total current assets and current liabilities, and thus is one measure of the amount of capital

[15] Interpreting the strategic significance of an effect is always a matter of judgment. We believe that a rate multiplier of 1.1 for a unit increase in the upstream alliance count is substantial, especially given that, (i) the model includes firm fixed effects, and (ii) upstream alliances in the 2 previous years ($t-2, t-3$) independently affect the downstream alliance formation rate. Because of the fixed effects, the coefficients can be understood to represent changes to firm-specific trends in the downstream alliance rate. In our data, there appear to be a set of firms that are very active in alliances, and another set that is much less so. This primary distinction is absorbed in the conditional fixed effects.

[16] Firm age is included as a polynomial because the fit of the model was significantly improved when we added the quadratic age term. In an unreported regression, we have specified firm age as a spline with cut-points at ages 4, 6, 8, ... years. We then included interaction effects between the upstream alliance count and each of the age pieces. The results of this specification are consistent with the image in Fig. 3: upstream alliances have their greatest effect on the downstream alliance rate for firms that are 4 years and younger. The upstream alliance effect then declines monotonically in firm age.

available to a company for investment. As we had anticipated, the interaction effect is negative: biotech firms that enter upstream alliances but have significant, discretionary investment funds are less likely to follow those transactions with downstream collaborations. This too is consistent with the argument that biotech firms with internal resources are less likely to engage the assistance of downstream partners.

Model 5 includes an interaction term between the upstream alliance count and the total invested capital of the company. Total invested capital is the sum of a corporation's total equity and debt, and thus represents the aggregate capital investment in the firm. In this case as well, the finding parallels the results of the interaction with firm age and with working capital: the effect of university alliances on the downstream alliance rate attenuates as the capitalization of a firm increases. Overall, we conclude that our analysis uncovers evidence of a change in scope as biotechnology companies mature: the model of brokering technology to downstream alliance partners gradually appears to be supplanted by an effort to undertake more of the commercialization work inside the firm.

The next table explores determinants of the formation of upstream partnerships in which biotechnology firms contract with universities to acquire scientific inputs. Table 6 reports random effects negative binomial estimates of biotechnology firms' upstream alliance formation rate, based on observations from the 341 IPO prospectuses with non-missing information on the identities of company founders and scientific advisors. Of the control variables, three have significant effects. Mirroring Fig. 2, there appears to be a negative association between firm age and the incidence of upstream allianc-ing: older biotechnology firms are less likely to establish formal alliances with universities. Thus, not only are more established biotechnology firms less prone to convert upstream alliances into downstream partnerships (Models 2–4, Table 5), they are also less likely to enter into agreements with universities in the first instance.

The baseline model also includes a dummy variable indicating whether a focal firm's first upstream alliance is with 1 of the 10 universities that were most active in the biotechnology partnership network. This "First University Partner is in the Top 10" covariate is positive and statistically significant. Firms whose first transaction was with 1 of these 10 prominent institutions, many of which were founded with the involvement of one or more faculty from these institutions, were substantially more likely to enter subsequent partnerships with universities. Specifically, the coefficient magnitude suggests a multiple of the upstream alliance rate by a factor of 1.49 (=exp[0.40]).

Hypothesis 3 asserts that biotechnology firms with thick networks in the academic community will have greater success at executing university deals to in-license intellectual property. As we had anticipated, Model 1 in Table 6 reveals that biotechnology firms with a greater number of academic founders do in fact contract with universities at a higher rate. Specifically, each addi-

Table 6
Random effects negative binomial regressions of rate of upstream (university–biotech firm) alliances

Variables	Model 1	Model 2	Model 3	Model 4
Age	−0.0616*** [0.0170]	−0.0525** [0.0174]	−0.0569*** [0.0171]	−0.0568*** [0.0172]
log of R&D expenses ($t-1$)	−0.0595 [0.0700]	−0.0338 [0.0708]	−0.0830 [0.0709]	−0.0771 [0.0707]
log of revenues ($t-1$)	−0.0594 [0.0565]	−0.0583 [0.0563]	−0.0663 [0.0565]	−0.0686 [0.0568]
Num. of patent applications ($t-1$)	0.0010 [0.0023]	0.0010 [0.0023]	0.0007 [0.0024]	0.0010 [0.0024]
First university alliance partner is in Top 10	0.4034* [0.1749]	0.3858* [0.1739]	0.3820* [0.1733]	0.3940* [0.1742]
Num. of firm founders	−0.0879 [0.0695]	−0.0964 [0.0694]	−0.0871 [0.0689]	−0.0919 [0.0695]
Num. of academic founders	0.2705*** [0.0821]	0.4350*** [0.1164]	0.2344** [0.0830]	0.2066* [0.0879]
Num. of academic founders × age		−0.0240* [0.0122]		
Prestige of affiliated scientists (in hundred)			0.0041* [0.0019]	
Coauthorship count for affiliated scientists (in hundred)				0.0304+ [0.0155]
Constant	−0.2599 [0.3344]	−0.3710 [0.3409]	−0.3386 [0.3352]	−0.2970 [0.3343]
log likelihood	−1674.518	−1672.550	−1672.236	−1672.596
Likelihood ratio test	93.72	99.03	98.73	96.89
Degrees of freedom	24	25	25	25

Notes: number of observations = 3267; number of firms = 341; all models include 17 dummy variables indicating years 1986–2002 (<1986 is the base period); all models include firm random effects; standard errors in brackets; *Significant at 5%; **Significant at 1%; ***Significant at 0.1%.

tional academic founder multiplies the annual, baseline, upstream alliance formation rate by a factor of 1.35 (=exp[0.298]). The positive effect of academic founders on upstream alliance formation, however, decreases with firm age (Model 2, Table 6). Model 3 adds to the baseline the prestige (academic journal article citations) of the average affiliated scientist. Once again, the parameter estimate is positive and statistically significant, showing that firms with more prominent affiliated scientists participate in more university alliances. Model 4 includes the final proxy for the networks of affiliated scientists – the sum of the scientific coauthors accrued by each firm's affiliated scientists – which is also a positive, statistically significant predictor of the upstream alliance entry rate. Collectively, the results in Table 6 confirm the prediction that the connections of a biotechnology firm in the academic community are strong determinants of the firm's propensity to enter formal, technology access contracts with universities.

7.1. Extensions and robustness checks

One potential concern with our interpretation of the findings is the role of faculty-founded firms in generating the results we observe. If a university–biotech tie is created when a new firm is founded by a faculty member and the professor's work is formally licensed to his/her new company, should we consider the upstart firm to be acting as a broker? This is both a conceptual and an empirical question. Our view is that even if this were the modal case in the data – that is, if the majority of the university–biotechnology deals were between a founder's firm and his/her university employer – the fact remains that the startup firm still operates as an intermediary in a vertical alliance chain. However, others may find less interest in the relationships we observe between the incidences of upstream and downstream partnerships if the startup firm and the university are coupled at the birth of the company.

Concern about this issue of interpretation is significantly lessened by our use of a conditional fixed effects estimator. In particular, if the upstream alliance incidence in Table 4 merely served as a proxy for whether or not a firm originated from a university, it would have an inconsequential effect in the regressions. This is because all non-time-varying attributes of the firm, including whether or not members of its founding team are university faculty, will be subsumed in the conditioning on the firm-specific event count.

Still, the possibility remains that faculty-founded firms engage in upstream alliance strategies to differing effect than do firms founded by non-academics. To explore this issue, we include two additional regressions in Table 5–those reported in Models 6 and 7. These two regressions are estimated on two mutually exclusive sub-samples: one with all firms with academic founders and the second with all non-faculty founded firms. This is equivalent to a fully interactive regression—by estimating separate regressions, we allow all coefficients to differ between these two groups of companies. We find that the upstream/university alliance count significantly affects the downstream alliance formation rate for *both* groups of companies. Perhaps not surprisingly, faculty founded firms seem to get more mileage out of their university deals—the parameter on the upstream alliance count is larger for these organizations, although not significantly so (0.071 versus 0.057). Put differently, we find that both faculty-founded and non-faculty founded firms perform the role of intermediary.[17]

A second issue is that many of the empirical specifications in prior studies of the rate of alliance formation include some form of the lagged dependent variable (i.e., a measure of the extent of the firm's previous alliance activity) as an occurrence dependence term (e.g., Gulati, 1995; Walker et al., 1997; Stuart, 1998; Ahuja, 2000). The rationale for doing this is that the previous event count may absorb the effects of at least some unobserved, firm-specific factors that are not otherwise accounted for in the regressions. Because we estimate conditional fixed effects count models, the estimates are free of firm-specific and time-invariant sources of heterogeneity. However, for consistency with previous studies, Model 8 in Table 4 includes the lagged count of commercialization alliances established by the firm. While the lagged downstream alliance count is statistically significant as we would expect, the estimated effect of the upstream alliance count remains positive and statistically significant.

Finally, our assumption that the categories of actors in our data engage in activities at different stages of the industry's value chain merits additional investigation. We have assumed that the primary foci of the efforts of universities, biotechnology firms, and pharmaceutical partners are at different vertical stages of the value chain, and that these divided labors are then coordinated

[17] We have also investigated the *pattern* of university alliance formation across the two sub-samples. Specifically, conditional on having at least two formal upstream agreements, faculty founded firms have a statistically indistinguishable number of *unique* university partners. In other words, faculty-founded firms with multiple university agreements typically craft deals with multiple universities; they show no greater tendency to license technology from the same university than do non-faculty founded firms.

Table 7
The distribution of stages of research at the time of alliance formation

	University with all biotech firms			University with public biotech firms only			University with pharmaceutical firms		
	Freq.	Percent	Cum.	Freq.	Percent	Cum.	Freq.	Percent	Cum.
Discovery	858	64.17	64.17	540	60.2	60.20	45	70.31	70.31
Formulation	45	3.37	67.54	29	3.23	63.43	1	1.56	71.87
Lead molecule	299	22.36	89.90	238	26.53	89.96	12	18.75	92.62
Preclinical	67	5.01	94.91	42	4.68	94.64	3	4.69	95.31
Phase I	32	2.39	97.30	24	2.68	97.32	1	1.56	96.87
Phase I/II	1	0.07	97.37	1	0.11	97.43	0	0	96.87
Phase II	22	1.65	99.02	15	1.67	99.11	1	1.56	98.43
Phase III	10	0.75	99.77	6	0.67	99.78	0	0	98.43
Approved	3	0.22	100	2	0.22	100	1	1.56	100
Total	1337	100		897	100		64	100	

Notes:

(1) Distribution of stages for upstream alliances formed between universities and all biotech firms are in the left pane, between universities and public biotech firms in the middle pane, and between universities and pharmaceutical firms in the right pane.
(2) Approximately 35% of the alliance deals in the data have missing information regarding the stage of work at the time the collaboration was established. All deals in which the alliance stage was unreported are excluded from this table.

through chains of alliances. However, because we treat the biotechnology firm as the unit of analysis and model the rate of alliance formation at the firm level, we cannot explore the influence of the actual stage of upstream alliances in a regression framework.

We have already observed suggestive evidence of the collaborative role structure in the industry in Table 2a–c. In particular, the distribution of collaborative activity clearly suggests that biotechnology firms are intermediaries; they actively partner with universities and pharmaceutical firms, whereas interactions between universities and pharmaceutical firms are less frequent. While space constraints limit us from presenting a full fledged analysis, Table 7 is illustrative of the role of universities in upstream alliances. In this table, we report the stage of research of all transactions involving universities, broken out by partner type—all biotechnology firms, publicly owned biotech firms, and pharmaceutical partners. The striking result in this table is that the stage of the agreement is constant across all three groups of partners: universities are overwhelming involved in pre-clinical agreements, and the modal university deal is at the discovery stage, regardless of partner type. Complementary analyses of the activities of biotechnology–biotechnology and biotechnology–pharmaceutical alliances do evince a pattern of movement down the value chain relative to the stage at which university partnering is concentrated.

8. Conclusion

It has long been observed that middlemen are pivotal agents in facilitating the optimal deployment of resources in the economy. Like intermediaries in other industrial settings, biotechnology firms, we have shown, occupy the middle wrung in vertical, tripartite alliance chains in the life sciences industry. In much the same way as a commodity broker exploits his or her network to facilitate exchanges, biotechnology firms capitalize on their thick networks in the academic community to assist in the development and transfer of university-originated science to established firms with in-house commercialization capabilities.

Taking the perspective of biotechnology firms, the empirical analyses we have presented document a cycle of determinants and consequences of alliance activity in this technological sector. Starting upstream and working our way down, we have found that biotech firms with prominent and well-networked academic founders and scientific advisors are more likely to enter formal alliances with universities. Next, we have found that biotechnology firms with more upstream, university contracts are more frequent participants in downstream, commercialization alliances. Putting together the results of the two tables of regression output, we observe that biotechnology firms with strong academic connections (but, not necessarily academic founders) are ideally

suited to capitalize on the business model of brokering university technology.

We would be remiss if, before concluding, we did not acknowledge some of the shortcomings of this paper. The brokerage argument we have developed implicitly assumes that all parties involved – universities, biotechnology companies, and established pharmaceutical firms – benefit from the tripartite alliance chains we observe. Based on the existing literature, it is well documented that biotechnology firms with more research alliances with established partners enjoy better financial performance (e.g., Powell et al., 1996). In unreported analyses (available from the authors upon request), we have found that biotechnology firms with many upstream and downstream alliances grow at fast rates and that private biotechnology firms with strong alliance history go public rapidly. However, with the data available to us, we were not able to empirically gauge the returns to allianc-ing experienced by the entities that biotechnology firms are situated between: established life sciences firms and universities.

A second shortcoming of the paper is that the many data requirements necessary to explore our hypotheses required that we limit the analysis to biotechnology firms that have filed IPO prospectuses. Although we were able to assemble and analyze the full life histories of most of these firms, the fact remains that firms that failed before going public or that were still private as of the time we assembled the data are excluded from the analysis. Because firms that file to go public are, on balance, more successful than the typical private firm, this data limitation likely imparts a bias of unknown direction. Some caution in interpretation of the results is therefore warranted.

Third, our paper suffers from a common limitation of studies that use archival alliance databases. Specifically, we are unable to determine the duration of the alliances in the data, and while we do have some information about types and magnitudes of alliances that we have examined in a series of unreported analyses, the difference we observe are based on the terms conveyed upon the announcement of an alliance, rather than the actual content of the transactions between firms. Of course, the fact that we found strong support for our arguments with covariates based on aggregated and undifferentiated alliance types is encouraging.

Another legitimate concern about this study is the generalizability of the paper's argument. Biotechnology is a distinctive industry, and any claim to the contrary teeters upon a shaky foundation. Indeed, Gans et al. (2002) describe conditions that are most likely to induce startups to pursue cooperative commercialization strategies with incumbents (as we have observed in this paper). These include the existence of incumbent-owned complementary assets that are expensive to replicate and the ability of startups to secure effective intellectual property protection for novel inventions. Both of these conditions are met in biotechnology, but certainly not in all technology-based sectors.

We would, however, offer two comments about the issue of the broader relevance of the paper's claims. First, because of the significant number of influential studies – particularly work on alliance activity – that are set in the industry, we believe that a slightly different perspective on the dynamics of alliance strategies in the industry is worthwhile in its own right.

Second, although biomedical research has proven to be the area of university science in which commercialization has been most vigorous, there are many other fields of active technology transfer. Moreover, some emerging science-based companies appear to bear a structural resemblance to young biotechnology firms. Consider, for instance, the company Nanosys, a 3-year-old nanotechnology firm that recently filed an IPO prospectus. Nanosys has an intellectual property portfolio of about 200 issued or pending patents, many of which were licensed from MIT, Harvard, University of California, and Columbia. The firm also has enlisted 11 prominent scientists to participate on an advisory board, including faculty from Caltech, Cornell, and University of Chicago, in addition to scientists at the four universities that formally licensed intellectual property to Nanosys. And, the company has established commercialization alliances with Dupont, Intel, and Matsushita Electric Works, among others. Thus, like biotechnology firms, emerging companies in nanotechnology are positioning themselves to broker university science to established firms. Based on this and many other examples, we expect that the core of our argument will apply in a number of settings, although we leave to subsequent work empirical assessments of generalizability.

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