Industrial and Corporate Change Advance Access published July 2, 2009

Industrial and Corporate Change, pp. 1–33
doi:10.1093/icc/dtp035

Academic collaboration and organizational innovation: the development of research capabilities in the US pharmaceutical industry, 1927–1946*

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This article investigates the historical conditions that contributed to the birth of in-house research and development (R&D) capabilities in the early US pharmaceutical industry by examining qualitative and quantitative data on university–industry interaction between the 1920s and 1940s. This evidence suggests that labor markets, collaborative research, and contract research were the principal mechanisms by which early university science contributed to the development of in-house research capabilities in the emerging US pharmaceutical industry. This article further demonstrates a pattern in which firms with lesser R&D capabilities were generally constrained to work with local partners, while firms with greater internal R&D capabilities primarily engaged local partners for smaller-scale projects requiring generalist skills and distant partners for larger-scale efforts and extraordinary projects. We conclude by examining the implications of collaboration for those firms that did engage university academic partners. Our findings suggest that pharmaceutical firms that collaborated with universities during this period achieved higher rates of patenting and laboratory growth.

1. Introduction

Although the rise of industrial research laboratories is one of the most important organizational innovations affecting technological progress in the United States in the 20th century (Mowery, 1990), the factors that contributed to this innovation and hastened the rise of private research capabilities are not fully understood. Numerous factors likely played a role in this innovation, including the increasing relevance of scientific knowledge to the problems of industry (Mowery and Rosenberg, 1998); the increasing capital (human and physical) requirements of invention

(Lamoreaux and Sokoloff, 2005); the active market for ideas (Lamoreaux and Sokoloff, 1996);[1] national institutions and policies, particularly with respect to anti-trust (Mowery, 1990); and, among other factors, even local historical dynamics (Feldman and Schreuder, 1996). We focus in this article on the importance of academic science in the emergence of industrial research capabilities, and ask about the conditions that led to these contributions, the mechanisms by which universities contributed to the development of firm-internal research efforts, and the firm-level impact of collaboration.

Economic and business historians have noted the significance of vibrant and complementary relationships between universities and industrial innovation in driving economic growth in the United States since the early 1900s (Mansfield, 1991, 1995; Rosenberg and Nelson, 1994; Mowery and Rosenberg, 1998).[2] As well, there has been a recent groundswell of interest in university–industry relationships, particularly since the passage of the Bayh-Dole Act in 1980 (e.g. Cohen *et al.*, 1998; Thursby and Thursby, 2002; Mowery *et al.*, 2003; Mowery and Sampat, 2004; Siegel *et al.*, 2007). Substantially less attention, however, has been devoted to the role of academic science in contributing to the rise of industrial research facilities and to the emergence of university–industry partnerships over time. Indeed, although their article is widely cited, Rosenberg and Nelson's 1994 lament on the lack of historical research on the emergence of university–industry partnerships remains largely unaddressed in present research.[3] Furman and MacGarvie (2007) demonstrate a statistically and economically significant relationship between the growth of university science and the rise of industrial research labs between 1927 and 1946. Their analysis suggests that the growth of academic science plays an important role in the emergence of pharmaceutical research facilities; however, this work neither clarifies the mechanisms by which academic science contributed to this phenomenon nor investigates the impact of collaboration on participant firms.

Historical research, including that of Liebenau (1984), Parascandola (1985), and Swann (1988, 1990), identifies emerging relationships between academic researchers

[1]The markets for ideas could contribute to the rise of industrial laboratories by enabling early stage inventions born elsewhere to be incorporated into and further developed as part of firms' R&D efforts; alternatively, though, the market for ideas could act as a substitute for internal R&D.

[2]See, as well, Nelson and Wright (1992), Rosenberg (2000), Siegel (2003), and Mowery *et al.* (2003). Note that there is also an interesting literature that considers the costs of increasingly tight relationships between universities and firms (Poyago-Theotoky *et al.*, 2002) and the concomitant increases in IP rights over ideas generated in universities (Heller and Eisenberg, 1998; Murray and Stern, 2006).

[3]"It is striking that the present discussion focuses so closely on the here and now (that) there is very little examination of the roles traditionally played by American universities or how these roles have evolved. . ." (1994: 324).

and private firms during this period and notes their correlation with the birth of industrial research.[4] Combining qualitative and quantitative analyses of historical data, we attempt to fill this gap in the literature. Our approach involves investigating three principal issues related to the emergence of industrial pharmaceutical research. First, through which mechanisms did US university scientists contribute to the development or R&D capabilities among biopharmaceutical firms? Second, under which circumstances did geographic proximity matter or not matter in promoting interactions between firms and universities? Third, to what extent and in which ways did these interactions affect the performance of participating pharmaceutical firms?

In order to trace the antecedents of university–industry collaborations, we briefly review the historical evolution of the US pharmaceutical industry and system of higher education toward the end of the 19th century and the first few decades of the 20th century. We then turn to the early mechanisms through which universities affected research in the pharmaceutical and chemical industries, by examining qualitative evidence on the role of labor markets and a combination of qualitative and quantitative evidence regarding the nature of collaboration and extent of contract research agreements. To investigate the role of labor markets, we examine records from the rosters of *Who's Who in Chemistry* (Haynes, 1928), finding evidence that research-oriented pharmaceutical firms hired actively from local scientific doctoral programs. Furthermore, we find that collaborative research arrangements and contract research agreements were both important precursors and useful complements to firms developing their own capabilities. We interpret these results as evidence that both direct and indirect interactions between universities and pharmaceutical firms played a significant role in fostering industrial research activities. The heterogeneity among firms with respect to the extent to which they engaged universities is also worth noting and we direct additional attention to this issue when examining the second set of issues.

Our analyses consistently point to the importance of distance. Hence, we pay particular attention to the role of location in our analysis. Informed by the qualitative evidence, we develop a number of propositions regarding the choice to collaborate across distance and investigate these in our empirical analyses. We examine the drivers of the decision to collaborate with universities and show that this decision depends both on the internal capabilities of the firm and the external opportunities

[4]It was not immediately obvious that the result of the increased value of science to firms would be the evolution of in-house firm capabilities in the United States with direct university–industry interactions and limited involvement of alternative institutions. Indeed, it is entirely possible that direct government subsidies for research or government laboratory capabilities (Jaffe and Lerner, 2001; Adams, *et al.*, 2003) rather than universities could have emerged to support the development of industrial research capabilities.

for collaboration. When examining the choice of collaborator, we find that smaller, younger firms engaged in smaller-scale projects are more likely to look to local universities as collaboration partners without particular regard to the local partner's particular strengths in research. However, we find that firms with more developed internal capabilities will engage in a geographically wide-ranging search for an academic partner with more extensive research capabilities.

In considering the impact of interacting with universities among those firms that did so, we examine data on patents, publication, and firm growth. We match patent data with data from American Chemical Society (ACS) membership rosters and find that a substantial share of pharmaceutical patents for which we can identify inventor affiliations included academic inventors. When we combine data on firm patenting and publishing with survey data from the National Research Council (NRC) and control for a number of firm and location characteristics, we find evidence of greater research output and faster growth among pharmaceutical firms that reported relationships with universities during our sample period. Prior to examining data on industry firm interactions and their consequences, we review illustrative case studies, which outline the impact of the presence and absence of local academic science on the development of two early 20th century firms, Mulford and Sterling. We are also sensitive to the fact that firms may have had a reciprocal effect on the development of academic departments during this period, so we review examples of this effect.

While our observations based on the qualitative historical evidence guide our hypotheses, we allow the data to speak for itself without imposing an explicit conceptual or theoretical structure on the analysis. We believe that this approach is most effective in elucidating the mechanisms by which universities contributed to the rise of early industrial pharmaceutical laboratories.[5] It is important to note, however, that our data are noisy and are unable to correct for potential simultaneity problems. We therefore interpret our analysis as suggestive rather than dispositive. Overall, our results suggest that the role of universities in the development of industrial research laboratories was significant and multifaceted. In addition to serving as the launching pad for the careers of individuals who found employment in private firm laboratories, US universities provided pharmaceutical firms with collaborative research and consulting. These activities appear to have played an important role in affecting the development of industrial research capabilities. Specifically, our analysis suggests a positive correlation between such collaboration and firm research output and growth.

[5]For more theoretically guided analyses of organizational innovations and their associated antecedents, see Lewin and Volberda (1999), Lewin *et al.* (1999), Murmann (2003a, b).

2. Historical context: the US pharmaceutical industry and academic science in the early 20th century

2.1 Antecedents of cooperation—developments in medical knowledge, policy, and firm capabilities

A glimpse at US pharmaceutical firms in the 1800s would have given little reason to believe that the industry would soon work closely with academic science. To begin with, the state of scientific knowledge about pharmaceutical treatments was sufficiently underdeveloped that university faculty could offer little value to private firms. US firms of the time were typically regional manufacturers, which prepared consumable chemicals based largely on centuries-old recipes or patent medicine makers, which distributed alcohol- or narcotic-based products of dubious medicinal value (Young, 1961; Liebenau, 1985).

By the end of the century, however, advances in organic chemistry, bacteriology, and instrumentation increased the usefulness of academic medical knowledge for the development of pharmaceutical preparations (Liebenau, 1990). Indeed, many leading German chemical and pharmaceutical firms, including Bayer and Hoechst, had begun to take advantage of that country's world-class universities by establishing in-house laboratories and close ties with academic researchers (Arora *et al.*, 1998; Mowery and Nelson, 1999).[6] US universities had lagged behind: the first American PhD degree was not granted until 1861 (by Yale) and the country's first research-driven university (Johns Hopkins University) was not founded until 1876. Change did take root in US universities during the final half of the 19th century, in large part due to the Morrill Acts of 1862 and 1890 and the Hatch Act of 1887.[7]

During the period between 1890 and 1940 that Goldin and Katz (1999) refer to as the "formative years" of American higher education, US universities evolved in a way that made them both attractive to and open to collaboration with medical manufacturers. Academic colleges grew in scale and scope, received substantially more funding from state and federal governments, and increasingly adopted the characteristics of research institutions (Goldin and Katz, 1999). In addition, increasing numbers of researchers and students trained at elite European (often German) institutions arrived in the United States with advanced skills in chemistry,

[6]The model of collaborative research employed by German universities appears to have given German firms an advantage in international competition. Although the initial discovery of aniline dye occurred in England, German chemical firms commercialized dye innovations more successfully, in large part because of Germany's stronger university–industry (Arora *et al.*, 1998; Murmann, 1998).

[7]For the majority of the 19th century, US universities focused on liberal arts education, conducted limited research in the natural sciences, and did not grant graduate degrees, thus lagging in research capabilities.

biology, and other natural sciences and experience in engagement with private companies (Feldman and Schreuder, 1996).

The demand for research capabilities in US pharmaceutical firms grew concurrently. One driver was the growth of urban population and density, which fostered conditions in which infectious diseases spread with increasing virulence and rapidity (Galambos, 1995). The 1905 American Medical Association (AMA) policy of critically reviewing advertising in their journals, the 1906 Food and Drug Act, and the 1938 Food, Drug, and Cosmetic Act also drove the demand for better product testing and safety.[8] The importance of university-based medical knowledge to drug makers was also accelerated by the loss of access to European medicines during World Wars I and II.

This collective set of changes had a substantial influence on the investments of US drug makers in R&D. From the early part of the century, during which R&D expenditures were minimal, Mahoney (1959: 4) reports that research expenditures increased to $15 million in 1939 and $110 million by 1956. Mahoney claims that the nature of the pharmaceutical industry changed dramatically during the 1930s and 1940s as a result of increasing average firm size and technical sophistication.

Overall, a confluence of factors—including scientific developments, changes in the structure of demand for health services and medicines, government policies and involvement in the healthcare system, the ability to imitate European medicines, and the evolution of the university system—appears to have played a role in the adoption of in-house laboratories by US pharmaceutical firms. Although numerous factors likely played a role in the emergence of in-house research capabilities, Furman and MacGarvie (2007) demonstrate a relationship between the growth in academic science and pharmaceutical research facilities. In the following sections, we investigate the specific mechanisms by which universities may have affected such investments. We begin by examining a set of illustrative case examples, which we then use to develop a framework for thinking about local and distant university–industry interaction.

2.2 Illustrative cases

In this section, we discuss the histories of a set of early pharmaceutical firms whose cases appear illustrative of the influence of local university science on firm-specific investments in innovation. We focus in particular on Mulford and Sterling.[9]

[8]See Rasmussen (2005) for an overview of the AMA's 1905 policy requiring that any pharmaceutical products advertised in their journal be approved by a council comprised of qualified chemists and other academically accredited scientists, called the Council on Pharmacy and Chemistry.

[9]Furman (2003) reviews the relationship between local resources and the strategic orientation of Mulford and Sterling.

The H.K. Mulford Company was founded in Philadelphia in 1891 when H.K. Mulford and Milton Campbell, both graduates of the Philadelphia College of Pharmacy, purchased the "Old Simes" drugstore. After initial successes in improving pill-making technologies, the founders undertook a more ambitious challenge for which they themselves were by no means sufficiently trained—the synthesis of diphtheria antitoxin. Bacteriological illness had become increasingly problematic for urban areas as a result of the increased density of city life. This problem was of particular concern to the Municipal Health Department in Philadelphia, the third largest city in the United States at the time. Philadelphia's Health Department, like that of New York, was especially active in promoting efforts to address bacteriological illnesses (Galambos, 1995).

Long known as the "Cradle of Pharmacy" (Mahoney, 1959; Feldman and Schreuder, 1996), Philadelphia was the home to some of the most advanced biomedical research institutions in North America. In addition to the Philadelphia College of Pharmacy (the oldest college of pharmacy in the country, founded in 1821), several other institutions were pursuing bacteriological research, including the University of Pennsylvania, Medico-Chirurgical College, and Pepper Clinical Laboratories of the University Hospital. Together with the Municipal Health Department, these institutions were engaged in research on diphtheria in response to "public clamor" for a diphtheria antitoxin (Galambos, 1995: 13). Galambos argues that Mulford "recognized the opportunities embodied in the 'clamor' for diphtheria antitoxin" and set out to produce a commercially viable drug (Galambos, 1995: 13). In 1894, the firm hired Dr. Joseph McFarland, who was on faculty at the University of Pennsylvania's Medical Department and the Philadelphia Polyclinic and College for Graduates in Medicine and had trained in bacteriology in Heidelberg and Vienna, and created for him a laboratory in which he could concentrate on developing diphtheria antitoxin (Galambos, 1995). In his efforts, McFarland benefited greatly from interactions with the New York City Health Department and the Laboratory for Hygiene at the University of Pennsylvania. By 1895, Mulford was able to become the first commercial provider of a diphtheria antitoxin. The firm's success with McFarland then led it to hire Professor Leonard Pearson from Penn's Veterinary School and to establish a full-fledged laboratory in 1896 in Glenolden, PA, dedicated to biological, veterinary, and vaccine research (Galambos, 1995). In the absence of these locally available academic scientific resources, it does not appear that Mulford would have engaged in the task of synthesizing a diphtheria antitoxin or, ultimately, in founding a dedicated research laboratory.

The Sterling pharmaceutical company was established under circumstances similar to those of Mulford and around the same point in time, yet it pursued a different trajectory with respect to research. Upon graduation from the Philadelphia College of Pharmacy, the same institution attended by the founders of Mulford, William E. Weiss returned to his hometown of Wheeling, West Virginia, and founded the company that became Sterling with his childhood friend,

Albert Diebold. Like Mulford, the fledgling drug maker met with considerable success. Unlike Mulford, however, the firm succeeded at marketing and distributing patent medicines. Sterling advertised widely and successfully in newspapers in rural and metropolitan areas (including Pittsburgh) and developed an active and aggressive sales force. This marketing- and distribution-driven strategy resulted in sweeping success—by 1912, Sterling was valued at $4 million (Mann and Plummer, 1991).

In the wake of World War I, Sterling acquired the assets of the Bayer Company, including all US rights to Bayer Aspirin, in the auction of seized German property rights held by the Office of the Alien Property Custodian. That Sterling was able to raise the funds required for this acquisition demonstrates the triumph of the firm's marketing and distribution resources. The firm's technical and research capabilities were substantially less well developed, however. Sterling's drug-making competence was, in fact, so limited that it was forced to solicit substantial guidance from Bayer in order to manufacture the simple products it had won at auction.

Both demand- and supply-side factors appear to have had an influence on Sterling's choice of organizing strategies. Serving the mainly rural populations of West Virginia and central and western Pennsylvania, Sterling faced relatively limited demand for medicines to fight the bacteriological illnesses for which academic science had become promising. Even if such demand had existed, Sterling did not have ready access to trained individuals who could have contributed effectively to drug-discovery research. At the very least, it seems fair to say that the comparative advantage of Sterling's West Virginia location was not based on institutions engaging in scientific research.[10]

[10]These early examples of the importance of local labor markets in diffusing biomedical research knowledge are typical of the experience of US pharmaceutical firms in the 1920s and 1930s. Firms located near universities appear to have had greater ease in recruiting scholars for their research efforts. The differences in the strength and relevance of the science bases in Philadelphia, PA, and Wheeling, WV, during the formative years of Mulford and Sterling are vast. Philadelphia was home to numerous universities with departments dedicated to biomedical sciences, including the University of Pennsylvania (which was founded in 1740 and offered its first doctorate in 1871), as well as the Philadelphia College of Pharmacy (founded 1821), the Medical College of Pennsylvania (founded 1850), Jefferson Medical College (founded 1825), Hahnemann Medical College (founded 1848), Temple University (founded 1884), and the Drexel Institute of Technology (founded 1892). The University of Pennsylvania was one of the country's leading biomedical institutions, and had granted, on its own, 919 doctorates by 1925.
By contrast, Sterling's hometown, Wheeling, WV, was 50 miles from the nearest university. The closest large universities to its home base, besides Penn State (198 miles away), were in Pittsburgh, PA, (59 miles away) and Morgantown, WV, (79 miles away). Though not immediately nearby, Pittsburgh was an emerging center of university life at the turn of the century, offering the University of Pittsburgh (which was founded in 1786 and granted its first doctorate in 1886), the Carnegie Institute of Technology (founded 1905), and Duquesne University (founded 1878). However, even if Sterling had opened facilities in Pittsburgh, these growing universities would not have been able to offer research services comparable to those of Philadelphia—by 1925, the city's largest university, the University of Pittsburgh, had only granted 86 PhDs, and Carnegie and Duquesne did not grant any PhDs until the 1920s.

While stylized, these stories seem to be illustrative rather than unique. The early history of Detroit's Parke-Davis, another one of the first chemical firms to establish science-based industrial research, resonates with that of Mulford. Similar to its Philadelphia counterpart, Parke-Davis began serious research efforts with the aim of making diphtheria antitoxin. To do so, it hired Elijah M. Houghton, a research assistant at the nearby University of Michigan, in 1895, and Charles McClintock, a research assistant in bacteriology, in 1896 (Swann, 1988). Parke-Davis established a research lab in biology and succeeded in producing diphtheria antitoxin within a few months. McClintock then turned his efforts to other biological research, which dominated the firm until the 1920s when a separate department for chemical research was established (Swann, 1988).

3. A qualitative review of the mechanisms and role of distance in early university–industry engagement

With an historical introduction and case descriptions as a background, we turn to examine qualitative evidence on the mechanisms through which universities played a role in the rise of industrial pharmaceutical research. Specifically, we examine qualitative evidence regarding the nature and extent of university–industry collaborations, consulting, and the importance of labor markets to the birth of industrial research laboratories. The evidence suggests that early pharmaceutical firms relied on a combination of mechanisms to develop in-house research expertise. Specifically, firms (i) participated in labor markets for qualified personnel, (ii) engaged in direct collaboration with academics (usually local academics), and (iii) "rented" research capabilities through agreements with nearby faculty.

Consistent with findings on the modern pharmaceutical and biotechnology firms (Jaffe *et al.*, 1993; Audretsch and Stephan, 1996; Zucker *et al.*, 1998; Feldman, 2003), geographic proximity appears to play an important role in university–industry engagement—collaboration and labor markets evidence a distinctly local character for smaller firms during the earliest part of the 20th century. The examples suggest a pattern in which firms with limited (or no) R&D capabilities are generally constrained to work with local partners while firms with greater internal R&D capabilities seek primarily local partners for smaller-scale projects and projects for which general skills are appropriate and distant partners for larger-scale projects and extraordinary projects.

While detailed firm-level R&D data are limited during this period, a few sources help shine some light on these issues. One of these sources is based on survey data gathered at semi-regular intervals by the NRC and published in the volume, *Industrial Research Laboratories of the United States*. These data enable us to observe, with some noise, those firms that report having developed industrial research laboratories. We supplement these data with information from the 1928

Chemical Who's Who in order to obtain biographical sketches of executives and researchers in the chemical (and pharmaceutical) industry.

The fact that our quantitative data are based on a survey of firms with R&D facilities in 1927, 1938, and 1946 raises questions about sample selection. Three issues are of particular note. One issue regards the extent to which these data are sufficient to reflect the phenomena we study. In this regard, the limitations of the sample are conservative in the sense that the noisiness and incompleteness of the data lower the likelihood that the results of our quantitative analysis will achieve statistically significant results. Thus, the fact that our analysis produces results of statistical and economic significance boosts our confidence in the analysis.

A second issue, whether the data are representative of pharmaceutical firms of the time, raises more complicated questions. There is, indeed, a chance that the survey reflects some response bias. This bias would, however, only affect our key results if there were a systematic difference in the propensity to collaborate with local and distant firms among firms that did and did not respond to the NRC surveys (and this difference must also vary systematically between firms with small versus larger R&D staffs). While we cannot rule out this prospect, we have no reason to believe that this type of selection problem plagues the data.

A third issue related to the NRC data sample is that we cannot conclude that those firms that did not respond to the NRC surveys did not collaborate with universities. As a result, our ability to produce counterfactuals is limited and we must be careful to frame the results of analyses using the NRC data as reflective only of those firms that self-identified as having R&D facilities. We are careful to note this in the analyses and in our discussion of the results.

3.1 Evidence on the role of labor markets

For a sample of the 30 largest labs in the NRC volume of 1927, we collected information on the educational background and location of first employment of executives listed in the *Who's Who*. Many of the executives, whether directly involved in research or not, came from scientific backgrounds, and the biographical information on the location of an individual's alma mater and postgraduate employment is instructive, indicating whether or not the individual joined the company immediately upon graduation. These data provide evidence of the way in which early R&D labor markets functioned and highlight the role of the local environment in the development of R&D capabilities.

These data indicate that the first employment after graduation from a university was often in the same city as the university and that many firms seemed to hire graduates of nearby universities. While the extent of this practice varied by firm, the firms that did hire from nearby universities ("nearby" defined loosely to include universities within 100–200 miles of the lab) tended to hire almost exclusively from those universities. For example, at Sharp and Dohme of Baltimore, Maryland, one of

the two directors of pharmaceutical research listed in the *Who's Who* in 1928 was J. C. Krantz, a former professor at the University of Maryland and a former lecturer at Johns Hopkins. The other director of pharmaceutical research graduated from the Philadelphia College of Pharmacy and had worked at Mulford and Co. in Philadelphia before becoming part of Sharp and Dohme. One laboratory superintendent (C. Neal) was a graduate of the University of Maryland department of Pharmacy, and another superintendent (E. Miller) earned a doctorate from Johns Hopkins. Of the nine employees and executives whose educational credentials are described in the *Who's Who*, six joined after studying or working at Johns Hopkins or the University of Maryland. Three were graduates of the Philadelphia College of Pharmacy (two of whom came to Sharp and Dohme after initial employment at Mulford and Co.), and one came to Sharp and Dohme after working as a professor at the University of Vermont.[11]

At Abbott Labs of Chicago, Illinois, the president, Alfred Burdick, was a former professor at the Illinois Medical College and consulting scientist Roger Adams was chair of the Department of Chemistry at the University of Illinois Urbana-Champaign. Adams' former student, Henry Volwiler, chief chemist in 1928 (later president and chairman of the board), was a graduate of the University of Illinois, as was Floyd Thayer, a former research chemist who was in 1928 manager of the chemical sales department. Of the eight people listed, six joined the firm after graduating from or working at an Illinois university. Swann notes that several of Adams' students also went on to join Abbott (1988).

Eli Lilly and Co. of Indianapolis, Indiana, provides additional examples of participation in local and national labor markets. Of the ten Lilly employees for which educational data are available, four are noted as graduates of Purdue University (62 miles away in West Lafayette), including director of research development, H.W. Rhodehamel, chief pharmacist, F.E. Bibbins, and assistant chief engineer, J.C. Siegesmund. In addition, two are alumni of other Indiana universities (DePauw and Indiana University). Of the remaining R&D staff, one joined the firm via the US Industrial Alcohol Co. in New Orleans after graduating from Louisiana State University while the others studied at Trinity College and the Philadelphia College of Pharmacy.

The list of Du Pont employees provides further examples of participation in a national labor market—it includes 55 individuals and a similar number of universities. It is clear that not every firm in the industry hired graduates of local universities, mainly because it was not always the case that local universities produced graduates with the skills required during this period.

[11]Sharpe and Dohme acquired Mulford around this time (officially, 1929; Galambos, 1995), which may explain the number of Sharpe and Dohme executives that *Who's Who* credits with Mulford experience.

Overall, the data are consistent with two conjectures: (i) that even as early as 1928 leading scientific and technical personnel at firms that developed R&D capabilities had been trained in the academic sector rather than internally and (ii) that smaller firms and firms with more nascent R&D efforts were more likely to take advantage of local labor markets while the largest firms, such as DuPont, participated to a greater extent in a nationwide labor market.

3.2 Evidence on the role of collaboration and contract research

Evidence on firm–university collaborations and contract research implicates that each of these factors was important in developing in-house R&D capabilities and casts light on the role of location in affecting partner choice. Table 1 lists the industrial labs in the NRC data that in 1938 identified the names of the universities at which they funded consultants or research fellows. In the NRC publication, this funding is described as "grants to university labs for research projects in support of program of association." Local universities, where they exist, predominate. While other more distant universities were supported by firms with larger research efforts (like Merck, with a research staff of 111), even these firms continued to be associated with nearby universities.

Alfred Newton Richards' work for Merck constitutes one example of how academics played active roles in the establishment of in-house R&D capabilities. Richards essentially acted as a head-hunter and recruiter when Merck set up its in-house facilities starting in 1930. Richards was professor of pharmacology and vice-president of medical affairs at the University of Pennsylvania. Richards acted as a liaison between Merck and the academic community, helping not only in recruiting but also in the organization of collaborative projects (Swann, 1988). Students and clinicians at Penn carried out the investigation and testing of methylcholine, a vasodilator eventually marketed by Merck as Mecholyl Chloride. Despite the fact that Vinethene, an anesthetic, was invented by scientists at the University of California Medical School, Merck engaged clinical faculty at the nearby University of Pennsylvania for investigation and testing. (Merck felt that the distance from Rahway to San Francisco was a barrier to effective collaboration.[12]) Here we see another example of a case in which a firm preferred to collaborate with local universities for more routine testing and development, whereas firms were often willing to incur the costs of long-distance collaboration when working toward drug discovery with a scientist with particular expertise. While firms with larger R&D budgets often engaged academic consultants at more distant universities who were specialists in a specific field (as we saw with Du Pont), younger and smaller firms appear to have

[12]Merck "did not feel that it would be advantageous to spend a great deal of money for the pharmacological study of vinyl ether in California. The distance was so great that a true cooperation could not be obtained." Letter from Merck scientist R.T. Major to A.N. Richards, quoted to Swann, 1988: 77.

Table 1 Pharmaceutical and chemical research labs and academic collaborators, 1938

Laboratory	Location	University
Bauer and Black	Chicago, IL	Northwestern, U Chicago, U Michigan
Breon and Company, Inc., George A	Kansas City, MO	U Nebraska, U Kansas, U Cincinnati
Bristol-Meyers Company	Hillside, NJ	Carnegie Institute Technology, Rutgers, Stanford
Carbide and Carbon Chemicals Corporation	South Charleston, WV	Mellon Institute Industrial Research
Commercial Solvents Corporation	Terre Haute, IN	Purdue University
Drackett Company	Cincinnati, OH	Ohio State University
Emerson Drug Company	Baltimore, MD	U Maryland, U Illinois, Yale
Endo Products, Inc.	New York, NY	NYU
Harshaw Chemical Company	Cleveland, OH	Western Reserve University
Hynson, Westcott, and Dunning, Inc.	Baltimore, MD	John Hopkins University, U Maryland
Jergens Company, Andrew	Cincinnati, OH	U Cincinnati
Kessler Chemical Corporation	Philadelphia, PA	Philadelphia College Pharmacy and Science
LaMotte Chemical Products Company	Baltimore, MD	Western Reserve University
Merck and Company, Inc	Rahway, NJ	U California, John Hopkins, U Pennsylvania, Princeton, NYU, Tulane, MIT, Philadelphia College Pharmacy, Cornell, Rutgers
Monsanto Chemical Corporation	St. Louis, MO; Dayton, OH	U Cincinnati, U Illinois, Michigan U, U Nevada, U Wisconsin, and Princeton
National Oil Products Company, Inc.	Harrison, NJ	Harvard Medical School, U Iowa, Lehigh, Columbia
Sharp and Dohme, Inc	Glenolden, PA and Baltimore, MD	U Pennsylvania, Bryn Mawr College, Johns Hopkins Hospital, Philadelphia College Pharmacy and Science, U California, Yale, Northwestern, Rochester
U.S. Industrial Alcohol Company	Stamford, CT and Baltimore, MD	Kalamazoo College, Stanford, Temple, U Connecticut, U Chicago, U Detroit, U Michigan, U Tennessee

Source: Industrial Research Laboratories of the United States (1938).

been more likely to collaborate with local academics. Starting in 1925, Northwestern University chemist Arthur Tatum did routine testing a few times a year for the small Chicago firm Cook Laboratories. Tatum had no unique knowledge of the drugs he tested, and Swann notes that "Cook probably engaged Tatum simply because of his proximity to the firm" (Swann, 1988: 103). Selman Waksman worked part-time at nearby Cutter Laboratories when he was a graduate student at University of California, Berkeley, and worked at New Jersey's Takamine Labs while a young assistant professor at Rutgers (Israel, 2004).

Lilly provides illustrative examples of both local collaboration and engagement with distant research partners. Lilly had four general consultants at nearby universities by 1943: an organic chemist from the University of Chicago ($2000/year), a chemical engineer from Purdue ($600/year), a biochemist from the University of Illinois ($600/year), and an organic chemist from the University of Indiana ($2400/year) (Swann, 1988: 52). As early as the 1920s, Lilly also made pioneering advances in collaboration with distant partners, including cooperation in Banting and Best's groundbreaking work synthesizing insulin at the University of Toronto. While Banting and Best had discovered insulin, the practicalities of large-scale industrial production could be developed only by a company of Lilly's size and experience in drug development. It is clear that the difficulties of long-distance collaboration (scientists traveled between Indianapolis and Toronto regularly during the development phase) (Bliss, 1984) were outweighed by the expected benefits associated with such a dramatic breakthrough in the treatment of diabetes. Lilly also worked with scientists at Harvard and the University of Rochester on the treatment of pernicious anemia in the 1920s (Swann, 1988: Chapter 5).

3.3 Propositions regarding the role of distance in early university–industry collaboration

In addition to providing evidence regarding the mechanisms through which universities aided the development of R&D capabilities in the early US pharmaceutical industry, the preceding examples highlight the role of location in partner choice. To our knowledge, only limited research has examined the role of distance in affecting firms' decisions to collaborate with specific university partners. One notable exception is Mansfield (1995), who demonstrates that firms prefer to work with local partners (those within a 100-mile radius) rather than those that are further away. Mansfield does note a key distinction between basic projects and applied projects, finding that firms are more willing to bridge distances in basic research projects if doing so enables them to work with high-quality faculty. Considering the qualitative evidence we examined above and the evidence presented by Mansfield (1995), we develop a simple, cost–benefit model of collaboration from which we can derive some propositions about the choice of local and distant partners.

The benefits associated with collaborating with university researchers appear to depend on a firm's current level of capabilities and the potential spillovers that can be appropriated from collaboration. Firms that lack R&D capabilities may achieve relatively greater benefits from early hiring, collaboration, and contract research; however, the benefits of collaboration appear to be consistent with an absorptive capacity argument in which firms benefit from engagement with universities to a greater degree when their internal capabilities are more advanced. The benefits of collaborating with specific universities also appear to vary based on the experience and specific expertise of each university. The costs of collaboration appear to depend on the "communication costs" associated with achieving access to local knowledge: the costs of collaborating with nearby universities are likely lower than the costs of collaborating with distant universities.

At the project level, the benefits and costs of collaboration across distance are likely to vary as a function of the nature of the skills needed for project completion. Those projects that are simpler are likely to require general skills, which may be found in a larger number of universities. Projects that are more complex are more likely to require specialized expertise, which is less likely to be found in any one particular university department. We also expect that projects that are larger and more complex are more likely to have higher benefits for firms that complete them successfully than those that are smaller and simpler.

This simple conceptual model yields a number of predictions. First, we expect that less experienced firms and firms will smaller R&D staffs are more likely to have simple projects and will have lower expected benefits from collaboration. As well, since the potential net benefits of their collaborative projects are likely to be low (and, thus, not overcome the costs of collaboration across larger distances), they will be more likely to collaborate locally in the event that they collaborate at all. By contrast, we expect firms with greater R&D capabilities and experience (potentially proxied by larger R&D staffs) to participate both in smaller projects, for which local collaboration may make sense, and larger projects, for which distant collaborations may have positive net benefits. Thus, we anticipate that larger firms will potentially have both local and distant projects in their portfolio of activities.

4. Collaboration and the role of distance in early university–industry engagement: larger-scale data analysis

To supplement our qualitative analyses and propositions of the previous section, we turn now to analyzing data regarding the extent, the drivers, and the consequences of pharmaceutical firms' collaborations with academic researchers during the 1930s and 1940s. Although large-scale data on these topics are limited, we are able to take advantage of survey data gathered at semi-regular intervals by the NRC and published in the volume, *Industrial Research Laboratories of the United States.*

Table 2 Descriptive statistics

	Obs.	Mean	Std. Dev.	Min	Max
Firm-level data					
Laboratory employment	346	39.36	93.11	1	931
Year firm founded (only available for 1946 data)	311	1916.31	23.18	1828	1945
Patents received	360	4.73	27.38	0	470
Cooperative agreement with university (not available for 1927 data)	360	0.37	0.48	0	1
Firm sales (Moody's) in thousands	98	114332.60	260376.80	736.37	1662339
Firm employment (Moody's)	91	9811.60	22393.83	66	137000
Data on universities in sample					
Total PhDs granted	342	16.97	29.23	0	171.55
PhDs granted in Science	342	12.58	19.92	0	105.91
PhDs granted in Chemistry	342	4.60	7.32	0	43.45

The Ph.D. counts by discipline for 1946 are obtained by taking the yearly average of the total count for 1939–1950, obtained from "American Universities and Colleges" (6th edition, 1952) published by the American Council on Education. This explains why the maximum in these fields is not an integer.

These data enable us to observe those surveyed firms that report having adopted industrial research laboratories. We report descriptive statistics for these data in Table 2. In addition to asking questions about the extent of resources devoted to R&D, the NRC surveys for 1938 and 1946 inquire about firms' collaborative efforts with universities and other organizations. Though insightful in a number of ways, these data are also subject to some limitations. Most notably, the firms that appear in the NRC data have already adopted research laboratories. As only a subset of firms with laboratories report collaborations, we can investigate the incidence of research collaboration and its covariates. Of the 145 firms identified in our 1938 sample, 32 reported research collaborations with universities, an incidence of 22%. By 1946, however, 100 of the 215 responding labs, 46.5% of all firms in the data, reported active collaborations with universities. In order to control for firm size, we obtain data on firm sales and firm employment from the volumes of Moody's Manual of Industrial Securities published in 1939 and 1947.[13]

[13]Because Moody's only includes large, publicly traded firms, we are able to identify firm size and employment data for only about 25% of the firms in our sample. For observations for which firm size and employment are missing, we include a dummy variable in the empirical analysis to indicate that this data is missing. When firms are listed as subsidiaries of the parent and report no firm-level sales or employment in Moody's, we use the sales/employment of the parent company.

We can also use these data to obtain insight into the relationship between academic science and firms' local and distant collaborative efforts. In the first step in this analysis, we model the firm-level decision to collaborate with any university as a function of the extent of research undertaken at universities in the same county as the focal firm, controlling for firm-level factors (sales, age, and R&D staff) and county-level population and economic activity. Table 3 presents the results of logit models in which the dependent variable is the firm-year choice to collaborate with a university. The results suggest that local science is associated with collaboration in 1938 though not in 1946. Specifically, firms located in counties with an academic program that graduates chemistry PhDs in 1938 are significantly more likely to engage in collaborative research efforts, as are firms located in countries with a larger fraction of chemistry PhDs. These results are not obtained for 1946, however. A number of factors may explain this difference. On the one hand, these results may arise simply because the data are relatively noisy during this period. Another possibility, however, is that proximity to universities may have been more important for collaboration when industrial research laboratories were at a relatively early stage of development.

We investigate this possibility further in Table 4, which reports the results of conditional logit regressions of the choice of academic collaborator. The data are restricted to firms that reported collaboration with an academic institution in 1938, and only those that listed the name of the collaborating institution are included (16 firms reported an association with a university but did not list the university). The unit of observation is a firm–university pair and all US universities granting PhDs in science by 1938 are included. The dependent variable is equal to 1 if firm i collaborated with university j by 1938 and 0 otherwise.

In column 1, only the distance between the firm and university in hundreds of miles and the number of Chemistry PhDs graduating from the university in 1938 are included. The coefficients are reported as odds ratios. One additional Chemistry PhD at university j increases the odds it is chosen as a partner for collaboration by approximately 6% while an additional 100 miles of distance between the firm and the university reduces the likelihood of collaboration by about 9%. Column 2 presents results obtained when the effects of distance and the scientific strength of the university are estimated separately for firms at or below the median size for labs in 1938 and firms above the median R&D laboratory size. The results show that the effect of the scientific strength of the university on its attractiveness for collaboration is slightly larger for firms above the median laboratory size. In contrast, the effects of distance are more pronounced for smaller firms, for whom an additional 100 miles between firm and university reduces the odds of collaboration by 23%. Larger-than-median firms see no statistically significant reduction in the probability of collaboration when distance increases. Similar results are found when the effects of distance and university

Table 3 Determinants of cooperative research

	1938			1946		
	(1)	(2)	(3)	(4)	(5)	(6)
Number of universities in county	1.013 (0.178)	0.705 (0.184)		0.921 (0.069)	0.919 (0.082)	
D(Chemistry PhDs in county)		5.948 (4.208)**			1.015 (0.475)	
Science PhDs in county			0.989 (0.010)			1.003 (0.005)
Share of PhDs in county in Chemistry			1.037 (0.017)**			0.988 (0.009)
Total laboratory staff[a]	1.718 (0.346)***	1.892 (0.413)***	1.863 (0.411)***	2.574 (0.421)***	2.575 (0.418)***	2.595 (0.424)***
Firm sales[a]	0.828 (0.160)	0.839 (0.173)	0.831 (0.158)	0.799 (0.154)	0.799 (0.154)	0.789 (0.152)
Firm age	1.003 (0.010)	1.001 (0.011)	1.001 (0.010)	1.001 (0.007)	1.001 (0.007)	1.001 (0.007)
Population in county[a]	1.115 (1.006)	1.171 (1.255)	1.098 (1.102)	1.770 (1.009)	1.765 (1.018)	1.773 (0.998)
Mfg establishments in county[a]	0.834 (0.658)	0.765 (0.726)	0.782 (0.663)	0.760 (0.369)	0.761 (0.371)	0.708 (0.335)
Observations	136	136	136	234	234	234

Note: Regressions based on laboratory-level data. Dummies indicating missing sales, firm R&D staff, and Firm age data are included in the regression but not reported here. Logit model of collaboration decision, by year: Dependent variable = 1 if firm *i* collaborates with a University in Year *t*; Coefficients expressed as odds ratios; Robust standard errors in parentheses, coefficients expressed as odds ratios; *significant at 10%; **significant at 5%; ***significant at 1%;

[a]In logs.

Table 4 Drivers of university–firm collaboration

	(1)	(2)	(3)
Chemistry PhDs at university	1.059 (0.015)***		
Distance between lab and university[a]	0.912 (0.034)**		
Chemistry PhDs at university X D (small)		1.052 (0.026)**	
Chemistry PhDs at university X D (large)		1.064 (0.020)***	
Distance between lab and university X D (small)[a]		0.774 (0.083)**	
Distance between lab and university X D (large)[a]		0.948 (0.036)	
Chemistry PhDs at university X D (young)			1.120 (0.087)
Chemistry PhDs at university X D (old)			1.061 (0.016)***
Distance between lab and university X D (young)[a]			0.030 (0.046)**
Distance between lab and university X D (old)[a]			0.933 (0.033)**
Observations	1215	1215	1215

Conditional logit model of collaboration partner choice: Unit of observation: firm-university pair; Dependent variable = 1 if firm *i* collaborates with university *j* in 1938; Coefficients expressed as odds ratios; Standard errors in parentheses; *significant at 10%; **significant at 5%; ***significant at 1%;

[a]All distances measured in 100's of miles.

Notes on classification: Lab considered "small" if R&D personnel in 1938 $\leq$ 19 and "large" if R&D personnel in 1938 $>$ 19. Lab considered "young" if laboratory age in 1938 $\leq$ 26 and "old" if laboratory age in 1938 $>$ 26.

strength are estimated separately for young (median age or below) and old (above median age) firms. University scientific strength does not significantly attract young firms, though it does for older firms. The effects of distance are especially pronounced for young firms (with an odds ratio of 0.03) when compared to older firms (OR 0.93).

These results are consistent with our qualitative evidence and our theory that small, young laboratories are most likely to collaborate with nearby universities while larger, more mature laboratories will seek out stronger scientific partners. For the latter firms, whose internal capabilities increase the benefit of collaboration with specialized scientists in drug development, proximity to the laboratory does not appear to be as important a determinant of collaboration as it is for smaller, younger firms.

5. Evidence regarding the impact of university engagement on collaborating firms

Building on prior research that suggests that the presence of local academic science was important in the rise of industrial research laboratories, our historical discussions and data analysis in Section 3 provides evidence that local labor markets, consulting, and local and distant collaboration were among the key mechanisms through which firms engaged university scholars. In this section, we examine whether firms that participated in such interactions were fundamentally different from those that did not and we speculate about the impact of such collaborations on firm-level outcomes. In particular, we examine the impact of collaboration and local academic science on firm-level patenting and publication behavior and on performance characteristics, such as growth and survival. Lastly, we acknowledge that the relationship between universities and local firms was reciprocal and investigate evidence regarding the impact of firms on the nature of graduate education at proximate universities.

5.1 Descriptive evidence from patent data

Some of the fruits of the early collaborations between universities and pharmaceutical firms can be found in data on firm-level patenting in the 1930s. Combining data gleaned from original patent documents[14] with the 1930 and 1935 registries of the American Chemical Society (ACS), we have identified the affiliations of many of the inventors listed on the patents granted to the firms in our sample in 1938. Among the subset of patents for which we were able to identify at least one inventor's affiliation, approximately 13% included at least one academic inventor. (We were able to identify the inventors for 184 of the 384 patents we examined.) Among prominent pharmaceutical firms Abbott, Lilly, and Parke-Davis, 50%, 56%, and 67% of patents granted, respectively, included academic inventors (when the inventor could be identified in the ACS directory). Other well-known firms with academic inventors include Merck (1 of 8 patents whose inventors could be identified had an academic inventor) and Sharp and Dohme (1 of 1). Some smaller firms, including Ostro Research Labs, Lewis Chemical Co., Sonneborn and Sons, Zonite Products Corp., and Commercial Solvents Corp. also included academic inventors on their patents, as did Monsanto (although for only 2 of 21 patents with identifiable inventors). While this sample is not sufficiently large to derive substantial statistical power, it provides suggestive evidence of considerable academic involvement in important research-oriented tasks in some pharmaceutical firms as early as 1938.

[14]Patents were downloaded from the website of the European Patent Office.

5.2 University–industry interaction and firm research output and growth

In Table 5 we present the results of negative binomial regressions predicting the number of patents firms received in 1938 and 1946 as a function of collaboration with universities, controlling for firm sales, employment, age, R&D staff, and year. We measure collaboration with a dummy variable equal to 1 for firms that indicated active cooperation with a university in their 1938 and 1946 NRC survey. Consistent with our historical, qualitative evidence, the results suggest that (conditional on firm sales, age, and R&D effort) those firms that cooperated with universities received more patents than those that did not. Specifically, the coefficients on cooperation in (1) and (2) imply that those firms that cooperated with universities received more than 60% more patents than those that did not, all else equal. The relationship appears to be stronger for those firms classified as primarily in the pharmaceutical industry (as opposed to firms identified in chemical industries, which also manufactured some medical preparations); in (3) and (4), cooperation is associated with approximately twice as many patents. Models (5) and (6) take advantage of additional features available in the data in specific years. The 1938 NRC data include information on the names of universities with which firms collaborated. Defining "local" universities as those within the same state as their firm partners, we find that those firms that work with *only* local universities produce fewer patents, while those that collaborate with partners outside of their local areas have significantly more patents. This result is consistent with an interpretation in which firms with greater R&D capabilities collaborate with firms outside of their geographic region.[15] The NRC data for 1946 do not list the names of partner universities but do provide information (admittedly incomplete) on the number of grants and fellowships. Somewhat surprisingly, there is no statistical relationship between the number of grants and fellowships and firm-level patenting. Also surprisingly, the relationship between collaboration and patenting loses its significance at the 5% level (though it continues to be significant at the 10% level). This finding may result from increasing noise in the data but is also consistent with the possibility that collaboration was especially important during the earlier phases of the development of the pharmaceutical industry's research capabilities.

The 1938 NRC survey also requested information about whether firms sponsored an internal scientific publication series, which we interpret as another indicator of a firm's commitment to scientific output.[16] In Table 6, we report the results of probit

[15]This finding turns out to be fairly robust with respect to the definition of "local universities," and also is obtained when we employ definitions based on a 50-mile radius or that includes in-state relationships and those with universities in immediate-neighbor states.

[16]For example, Loeser Laboratories reported publishing the *Journal of Intravenous Therapy* while Merck noted its publication of the *Merck Index*.

Table 5 Determinants of firm patenting

	All firms		Pharma firms only		Pharma firms in 1938	Pharma firms in 1946
	(1)	(2)	(3)	(4)	(5)	(6)
Cooperation	0.517 (0.260)**	0.514 (0.260)**	1.098 (0.306)***	1.104 (0.295)***	1.668 (0.814)**	0.790 (0.469)*
Cooperation with local universities in 1938 (dummy)					−2.889 (1.256)**	
Count of total fellowships/ grants in 1946						0.006 (0.029)
Total laboratory staff[a]	0.882 (0.149)***	0.754 (0.151)***	1.107 (0.173)***	1.087 (0.167)***	0.972 (0.227)***	1.072 (0.254)***
Years since research initiated[a]	0.173 (0.260)	0.241 (0.256)	−0.145 (0.269)	−0.169 (0.263)	0.042 (0.406)	−0.344 (0.232)
Firm sales[a]		0.301 (0.164)*	0.344 (0.177)*	0.148 (0.145)	0.177 (0.103)*	0.052 (0.185)
Firm employment[a]		0.071 (0.199)	−0.182 (0.200)			
Year = 1938	1.803 (0.197)***	1.818 (0.215)***	2.293 (0.306)***	2.242 (0.320)***		
Constant	−3.687 (0.746)***	−9.114 (2.171)***	−8.205 (3.128)***	−6.039 (2.993)**	−5.373 (2.694)**	−3.334 (3.158)
Observations	357	357	213	213	77	136

Note: Regressions based on firm-level data from 1938 to 1946. The data on the identity of collaborating universities are only available in 1938, so column 5 is restricted to that year. Similarly, column 6 incorporates data on the total number of fellowships and/or grants made to universities; these data are only available in 1946. Dummies indicating missing sales, employment, firm R&D staff, and firm age data are included in the regression but not reported here.

Negative binomial regressions: Dependent variable = Number of patents received by firm-year.

[a]In logs.

Standard errors clustered by firm in parentheses; *significant at 10%; **significant at 5%; ***significant at 1%.

Table 6 Determinants of firm publishing a scientific series

			Pharma firms only	
	(1)	(2)	(3)	(4)
Cooperation in 1938 (dummy)	0.461 (0.379)	0.618 (0.416)	0.983 (0.542)*	1.031 (0.541)*
Total laboratory employment in 1938[a]	−0.072 (0.183)	−0.025 (0.174)	−0.435 (0.315)	−0.324 (0.370)
Years since research initiated[a]	−0.159 (0.381)	−0.198 (0.408)	−0.068 (0.520)	0.064 (0.540)
Firm Employment in 1938[a]		0.526 (0.279)*		
Firm Sales in 1938[a]		–0.762 (0.354)**		
Constant	−1.095 (1.153)	6.567 (5.044)	−0.653 (1.621)	−1.240 (1.806)
Observations	134	134	71	52

Notes: Regressions based on firm-level data from 1938 to 1946. Dummies indicating missing sales, employment, firm R&D staff, and firm age data are included in the regression but not reported here. Probit regressions: Dependent variable = Dummy variable if firm reported publication in 1938; Robust standard errors in parentheses; *significant at 10%; **significant at 5%; ***significant at 1%.

[a]In logs.

estimations in which we predict whether a firm reported publishing an in-house scientific series as a function of cooperation and firm size. Columns 3 and 4 suggest a positive and statistically significant at the 10% level relationship for firms with a pharmaceutical industry designation, although this result loses its significance when we include firms with a primary chemical industry designation in the model as well (columns 1 and 2).

In addition to examining the relationship between collaboration and firm research, we investigate the relationship between collaboration and firm growth in Table 7. In this regression, we examine the correlation between the growth of firms between 1938 and 1946 and a dummy capturing whether the firm was collaborating with universities as of 1946. In all regressions in the table, we control for firm age, sales, and employment. The results of OLS regressions using the natural logarithm of firm growth as a dependent variable suggest that firms that engaged in collaborative research with universities achieved 56–73% greater growth in R&D Staff and between 82% and 99% greater growth in total staff between 1938 and 1946 than those that

Table 7 Determinants of firm growth

	DV = ln (growth in R&D personnel)			DV = ln (growth in total staff)		
	(1) All firms	(2) Pharma firms only	(3) Pharma firms only	(4) All firms	(5) Pharma firms only	(6) Pharma firms only
Cooperation by 1946	0.457 (0.197)**	0.453 (0.256)*	0.550 (0.265)**	0.617 (0.193)***	0.597 (0.262)**	0.687 (0.264)**
Total laboratory employment in 1938[a]	−0.332 (0.125)***	−0.274 (0.163)*	−0.340 (0.170)*	−0.386 (0.132)***	−0.266 (0.187)	−0.337 (0.196)*
Years since research initiated[a]	0.113 (0.149)	0.071 (0.255)	0.058 (0.251)	0.141 (0.153)	0.036 (0.254)	0.028 (0.250)
Firm employment in 1938[a]	0.657 (0.211)***	0.599 (0.211)***	0.533 (0.207)**	0.463 (0.154)***	0.378 (0.185)**	0.302 (0.182)
Firm sales in 1938[a]	−0.515 (0.172)***	−0.605 (0.208)***	−0.572 (0.203)***	−0.328 (0.142)**	−0.318 (0.180)*	−0.269 (0.179)
Firm patents in 1938			0.019 (0.007)**			0.020 (0.007)***
Constant	4.715 (2.237)**	6.285 (2.506)**	6.327 (2.447)**	2.949 (1.858)	3.259 (2.424)	3.145 (2.399)
Observations	94	49	49	102	53	53
R-squared	0.21	0.23	0.26	0.21	0.19	0.22

Notes: Firm-level regression including firms listed in both 1938 and 1946 volumes. The cooperation dummy equals 1 if the firm collaborated with a university in 1946. Columns 1–3 include firms on which data are reported separately for R&D personnel; columns 4–5 also include firms that report total laboratory employment without distinguishing between R&D and non-R&D workers. Dummies indicating missing sales, employment, firm R&D staff, and firm age data are not reported. OLS regressions: Dependent variables = ln (growth of R&D staff, 1938–1946) and ln (growth of total staff, 1938–1946); Robust standard errors in parentheses; *significant at 10%; **significant at 5%; ***significant at 1%.

[a]In logs.

did not.[17] These findings are obtained both for the overall sample as well as the sample of firms identified as principally in the pharmaceutical industry. There is also a significantly positive correlation between firm growth and the number of patents assigned to the firm in 1938.

Taken together, the analyses in Tables 5–7 provide suggestive evidence that firms that collaborated with universities in the 1930s (i) produced greater knowledge-based outputs (especially those that collaborated with distant universities) and (ii) grew more rapidly than those that did not engage in collaborations with university scientists. Since our sample is pre-screened to include firms that reported having research facilities, it is possible that our research finding on research output is somewhat conservative—i.e., that the extent of research output for firms that have research facilities and collaborated with universities is substantially greater than those that had no research facilities and did not collaborate with university researchers.

5.3 Reciprocal relationships: historical evidence of the influence of early 20th century firms on academic science

In addition to the documented episodes of academic researchers' roles in nurturing industrial pharmaceutical research outputs, the historical record suggests that a number of companies were influential in shaping the evolution of university research programs. Indeed, evidence suggests that private firms often played an important role in contributing to establishing enduring scientific programs in universities. Geiger (1986) reminds us that the role of universities as the primary institutions of research in the United States was not secure at the beginning of the 20th century:

> but if the universities were dedicated to science, broadly speaking, by the beginning of the twentieth century, it was not yet evident that science was or ought to be beholden to universities. Scientific investigation was undertaken in government bureaus and in semi-independent laboratories . . . [E]ven by 1920 the research universities could not be assured of being the primary locus of basic research.

Indeed, as universities in the latter half of the 20th century needed to address issues associated with increasingly close ties with industrial concerns (Argyres and Liebeskind, 1998; Mowery *et al.*, 2003), some universities at the end of the 19th century needed to adjust to circumstances in which private firms helped shape their academic evolution.

[17]In cases in which the NRC volume entry lists the number of scientists of different specialties (e.g. biologists, chemists, etc.) or separately reports the number of technical/scientific staff, we use this information to count the laboratory's R&D employees. The total staff count includes assistants, technicians, and other laboratory personnel. In some cases, no distinction is drawn between R&D workers and total laboratory staff, and in these cases our two variables (R&D employees and total laboratory employees) are equal.

Noble (1977) traces a number of such examples in electrical and chemical engineering. In addition, Noble highlights the importance of the Industrial Fellowship program designed by University of Kansas professor, Robert Kennedy Duncan, in increasing industry involvement with and influence upon universities. Duncan, he notes, developed an Industrial Fellowship system, "through which manufacturers were able directly to support research personnel in the university laboratories and to define their research work" (122–123). Similar to programs of the current millennium, Duncan's program was one of sponsored research and involved a Chemistry department member working on an issue as defined by the supporting firm, which committed to financing the project in exchange for the intellectual property rights associated with its discoveries.[18] Ultimately, Duncan's program was imported or imitated by other universities.

In addition to the influences of firms on the specific research agendas of individual faculty members, evidence suggests that firms occasionally shaped the entire research trajectories of nearby institutions. The relationships between Merck and Rutgers University and DuPont and the University of Delaware appear to be illustrative of the general phenomenon. Merck's choice of Rahway, NJ, as the location for the plant it built in 1899, which was influenced in part by a board member who owned land in the community (Feldman and Schreuder, 1996: 856), proved propitious for nearby Rutgers University. In the 1930s, Merck developed a relationship with microbiologist Selman Waksman of the College of Agriculture at Rutgers. Starting in 1939, Merck agreed to supply assistance for antibiotics developed by Waksman, who would assign all ensuing patents to Merck in exchange for a 2.5% royalty to be paid to Rutgers. In 1943 Waksman developed streptomycin, a new blockbuster antibiotic that was less toxic and more effective (particularly in treating tuberculosis) than existing alternatives. Motivated by fear of a public outcry over the monopolization of such an important drug, Waksman and Rutgers convinced Merck to relinquish their rights to Waksman's patents to the Rutgers Research and Endowment Fund, which licensed the patent to several competing companies. The Fund collected $12 million in royalties from Waksman's discoveries over the next 40 years. Swann quotes Waksman, whose work earned the Nobel Prize for Medicine in 1952, as suggesting that he owed more to support from Merck than to support from Rutgers for the discoveries (Swann, 1988).[19]

[18]Noble anticipated many of the current concerns about privatizing the academic commons and believed that industry involvement in supporting academics had a pernicious effect on progress. For example, he argued that industrial patenting "petrified the process of science" (110).

[19]Waksman stated that, "Without the help. . .of an industrial organization that took over a major part of the pharmacological evaluation of the antibiotic [streptomycin] and large-scale production our contribution would have never attained its goal." (Swann, 1998: 90).

The University of Delaware's relationship with Du Pont proved to be similarly beneficial to that institution. Established in 1802 on the banks of the Brandywine River, in part because the location provided easy access to waterpower and an abundant supply of willow trees (from which charcoal could be produced), Du Pont was founded long before chemical research was widespread in American universities and, consequently, without regard to the availability of local academic science. Nonetheless, Du Pont played an important role in the subsequent development of scientific research at the University of Delaware through a number of significant gifts from the Du Pont family and other individuals associated with Du Pont. In 1924, the first physics professor was brought to the University of Delaware with the help of Lammot Du Pont, who contributed $2000 for equipment and pledged an additional $600 a year for five years, half for research equipment and half to top off the new professor's salary (Munroe, 2004: Chapter 9). The university's chemical laboratory was established between 1935 and 1937 with a $300,000 gift from Fletcher Brown, a former Du Pont Vice President. Brown also made a donation to supplement the salary of Allan Colburn, a Du Pont engineer who became the first professor of Chemical Engineering at the University of Delaware in April 1938. Chemical Engineering quickly became the most active field of research at the university, with the possible exception of the agricultural experiment station (Munroe, 2004: Chapter 10).

Consistent with these examples as well as more general conjectures about the influence of firms on the development of university research environments, Furman and MacGarvie (2007) document a statistically significant relationship between the birth of new academic programs in chemical engineering and the growth of country-level industrial pharmaceutical research.

6. Discussion

The birth of industrial research laboratories and the transformation of the system of higher education were two of the most fundamental innovations affecting technological change in the United States in the 20th century. This article attempts to shed light on the mechanisms through which academic science helped contribute to the development of industrial research capabilities in the early US pharmaceutical industry. To take advantage of historical evidence, we incorporate qualitative analysis, including reviews of small-sample data and case-based evidence, along with quantitative analysis of the most comprehensive data we were able to identify for the time period. Our analysis suggests that the transformation of US leading pharmaceutical firms from primarily manufacturing apothecaries to research-intensive institutions between the 1920s and 1940s was accomplished through active engagement with universities, specifically via engagement in labor markets for university-trained scientific and technical staff and via collaboration and contract

research with university faculty. Opportunities for such engagement arose as a result of supply-side factors that increased the value of academic science to industry and the ability of universities to work with firms, as well as demand-side factors that increased the desire of pharmaceutical firms to develop products using the knowledge and technical skills resident in the academic sector. The combination of the ability to incorporate trained R&D workers into private firms and the ability to borrow and achieve instruction from leading university scientists appear to be crucial in firms' efforts to develop internal R&D capabilities and to create new institutions—private R&D laboratories—dedicated to creating medically efficacious new products. Moreover, these interactions appear to have had a positive impact on the research outputs (patents and publications) of early pharmaceutical firms and on their rate of growth.

We interpret this analysis as providing insight into the evolution of the institutions supporting industrial research in the United States. In particular, firms appear to have achieved the organizational innovation of developing industrial research facilities by "bootstrapping capabilities" from academic science—i.e., by building capabilities through the hiring of university-trained individuals and borrowing capabilities by collaborating with and contracting with researchers at nearby and distant universities. This type of engagement with universities is not a surprise in the current time period but did constitute a significant innovation in the United States in the first half of the 1900s. Moreover, it would not have been possible in the decades prior to 1900, neither for the industry nor for the academy, as neither set of institutions was prepared for such interaction. Overall, our historical and quantitative analyses provide a rich example of step-by-step institutional change (North, 1990) and help elucidate the micro-mechanisms that helped bring about what Mowery (1990) describes as one of the key organizational innovations of the 20th century.

Our analysis also sheds light on the role of distance in early collaboration. As our data are relatively noisy and do not enable us to correct for potential endogeneity, we interpret our analysis as suggestive rather than dispositive. The results are, however, consistent with a model of collaboration in which firms balance the benefits and costs of interacting with universities and in which these costs and benefits vary as a function of firm R&D capabilities, project size, and distance. Specifically, labs at early stages of development (or firms with historically limited R&D efforts) appear most likely to collaborate locally (if they collaborate at all) while firms with greater R&D capabilities and both simple and complex projects find it worthwhile to engage in both local and distant collaboration. Our observations about the role of distance in collaboration may characterize university–industry partnerships in other industries and other eras for which data may be more complete. More research into the role of distance in collaboration seems to be an opportunity for follow-up work on this subject.

Acknowledgements

The authors are grateful to Lisa Bassett, Ann-Marie Crain, Henan Cheng, Anna Harrington, and Vanessa Wong for excellent research assistance. Scott Stern provided inspiration for the project and insightful suggestions throughout; Nick Argyres, Bronwyn Hall, Zorina Khan, Petra Moser, David Mowery, Toby Stuart, and Sam Thompson contributed helpful suggestions. This work builds on research initially prepared for the NBER Conference on Academic Entrepreneurship and Innovation; the authors thank Adam Jaffe, Josh Lerner, Marie Thursby, Scott Stern for organizing that event, and to Ken Sokoloff for insightful commentary. M.M gratefully acknowledges support from the Center for Studies in Higher Education and the John M. Olin Foundation and both authors gratefully recognize support from the Boston University Junior Faculty Research Fund.

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