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# Dissecting diffusion: Tracing the plurality of factors that shape knowledge diffusion

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ABSTRACT

Knowledge diffusion drives both technical progress and economic growth. In this study, we present a unique comparative case study that examines the diffusion of two comparable, foundational biotechnology inventions – recombinant DNA (rDNA) and polymerase chain reaction (PCR). Using a variety of metrics to trace knowledge diffusion, we find robust evidence that the diffusion of PCR significantly outperforms rDNA. Examining the historical record, we then consider how organizational origin, licensing strategy, complementary assets, industry stage, and early social networks play a role in shaping these processes. Ultimately, we show that reliance on a single diffusion metric or factor is insufficient in explaining knowledge diffusion. We argue for the exploration of multiple underlying factors in diffusion studies, and we highlight the utility of employing multiple complementary measures in diffusion research.

## 1. Introduction

The diffusion of scientific knowledge lies at the heart of both technical progress and economic growth. Knowledge diffusion, defined as "the process in which an innovation is communicated through certain channels over time among the members of a social system" (Rogers 2003, p. 5), has therefore attracted considerable scholarly attention (e.g., Audretsch and Feldman, 1996; Bloom et al., 2013; Romer, 1994; Jones, 2005; Jaffe et al., 1993).

Fundamentally, diffusion of anything requires people or organizations to have access to (or to be exposed to) the thing that is diffusing. In turn, several different factors may affect access to scientific knowledge. For example, a number of studies posit that the organizational origin of new knowledge matters; university research may be easier to access and may thus spread more broadly and quickly than research stemming from commercial firms (e.g., Agarwal and Ohyama, 2013; Trajtenberg et al., 1997). Other studies point to the role of intellectual property rights (Williams, 2013) or licensing terms (Fosfuri, 2006), observing that more lenient approaches may facilitate easier access. Still others highlight the importance of institutions like biological resource centers (e.g., Furman and Stern, 2011) or the availability of complementary assets such as tools that automate research processes (e.g., Furman and Teodoridis, 2020). From yet another angle, industry stage can play a role since a quickly growing industry, by definition, has more individuals and organizations able to serve as adopters and thus as subsequent diffusers (e.g., Methé, 1992; Menanteau and Lefebvre, 2000). Finally, others focus on social networks and/or geographic proximity (e.g., Audretsch and Feldman, 2004; Feldman et al., 2015; Jaffe et al., 1993; Owen-Smith and Powell, 2004), noting that these connections often enable access to new knowledge.

Much of this work strives to isolate the effect of a particular factor on knowledge diffusion, typically by examining a large dataset. But in practice, these factors do not work in isolation but rather act in consort. In this study, therefore, we present a comparative case study of the diffusion of two key technologies, highlighting the simultaneous and complementary roles of organizational origin, intellectual property approaches, complementary assets, industry stage, and early social networks.

Specifically, we examine the diffusion of two foundational biotechnology inventions. The invention of recombinant DNA (rDNA) at Stanford University and the University of California at San Francisco and of polymerase chain reaction (PCR) at Cetus Corporation marked the beginning of the biotechnology industry. These two breakthroughs share a number of common features that make them well suited for a comparative case study. Both technologies are scientific techniques that were invented in the San Francisco Bay Area. Both technologies were

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published and then patented and followed similar licensing approaches. In addition, both technologies were associated with Nobel Prizes that were granted within ten years of the initial invention. However, the technologies also differ in key ways: rDNA was invented in a university setting, whereas PCR was invented by a commercial firm. PCR benefitted from a concerted effort on the part of the inventing organization to develop complementary assets; rDNA did not. rDNA emerged in 1973 at the inception of the industry and prior to major shifts in university licensing, including the Bayh-Dole Act; PCR emerged 12 years later. And the first major conference focused on PCR attracted more than twice as many participants as the first conference on rDNA.

Using a wide variety of comprehensive metrics to trace knowledge diffusion, we compare and contrast rDNA and PCR along several different dimensions with the goal of understanding both the commonalities among and differences between their diffusion patterns and processes. Specifically, we find that PCR outperforms rDNA in terms of patent and publication output, in terms of the number of scientists and types of organizations involved in follow-on activity, and in terms of the geographic spread of knowledge. Furthermore, the follow-on publication activity that builds on PCR encompasses a broader knowledge space than that of rDNA, suggesting wider application. We next explore evidence on a plurality of diffusion factors including organizational origin, the technologies' licensing strategies and complementary assets, the stage of the industry, and social networks around the original inventors. We find that the confluence of these factors usefully explains the diverging diffusion patterns we observe.

Our results provide broader implications for diffusion studies. In documenting and examining diffusion patterns, we argue that it is critical to account for the multiple factors that influence access to the original technologies. Narrow assessments of individual factors may be insufficient – and, potentially, misleading – towards understanding and explaining knowledge diffusion. For example, had we only examined the role of organizational origin, we would have drawn insufficient (and perhaps misleading) conclusions. In addition, we document how a firm invention can diffuse *to* universities, thus reversing the oft-studied process by which university inventions diffuse to firms. Finally, our work highlights the value of employing multiple diffusion measures, thus moving beyond patent citations alone to consider complementary lenses on diffusion processes. Collectively, these contributions offer important insights for policymakers and managers alike as they work to identify how strategic choices may inhibit or enhance diffusion.

## 2. Literature review

Scholars and policymakers have directed considerable attention to the diffusion of scientific knowledge. From a policy perspective, diffusion is important because it underlies both innovation and economic growth. For example, the US government has spent around two percent of GDP annually on research and development (R&D) since Vannevar Bush's report, "Science, the Endless Frontier" (Bush, 1945), posited that public investments in science diffuse to firms and, ultimately, generate economic impact.Elsewhere, the EU's Europe 2020 Strategy called for three percent of GDP to be invested in R&D, with one percent coming from public funds. Although scholars have since refined Bush's linear model by showing how public investments, private investments, and economic impact are shaped by a variety of influences, the fundamental insight that knowledge diffusion is key to innovation has remained a pillar of both economic policy and associated academic research (Feldman & Kelley, 2006; Stephan, 2012; Mazzucato, 2011).

Prior work has investigated a wide array of factors that influence knowledge diffusion, ranging from narrow features tied to the inventing organization to broader characteristics that define the larger environmental landscape. These factors include organizational origin, licensing strategy, complementary assets, industry stage, and early social networks. Although prior scholarship tends to focus on these factors in isolation, we argue that diffusion is best explained by considering them in tandem. Here, we review each factor in turn to provide a conceptual baseline and comprehensive framework.

First, a great deal of work has focused on whether the knowledge at risk of diffusion stems from a university or a firm (e.g., Breznitz and Feldman, 2012; Fini et al., 2011; Goldfarb and Henrekson, 2003; Siegel et al., 2003; Wright et al., 2006). The special attention offered to universities is based on the observation that universities and firms differ in fundamental ways. Specifically, many scholars claim that universities and firms subscribe to different "institutional logics" or underlying principles, incentives, norms, and goals (Thornton et al., 2015). Thus, university-based researchers may be motivated primarily by a desire for community recognition and prestige. This desire can lead them to openly share research with the scientific community, since that is how their peers come to learn of their work and contributions. By contrast, firm-based researchers may be motivated by the (potential) commercial fruits of their research. To protect these fruits, they may keep research results from the broad community, since sharing could enable others to copy or otherwise build on the research (Dasgupta and David, 1987, 1994; Fini and Lacetera, 2010; Nelson, 2016a; Sauermann and Stephan, 2013). These observations, in turn, may underpin an expectation that university-generated knowledge might diffuse more quickly, across a wider geography, to more organizations and, therefore, to a wider range of applications. In contrast, firm-generated knowledge might diffuse less quickly, within a more constrained geography, to fewer organizations and, therefore, to a narrower range of applications.

Other work on diffusion and access to scientific knowledge focuses on organizational policies, such as intellectual property rights and related licensing approaches (e.g., Fore et al., 2006; Goldfarb and Henrekson, 2003; Kenney and Patton, 2009; Siegel et al., 2003). For example, Williams (2013) documents how Celera's intellectual property tied to the human genome has shaped subsequent innovation in the space. She finds that IP depressed subsequent scientific research and product development by 20 to 30 percent. Examining the case of universities, specifically, Kenney and Patton (2009) argue that university-owned IP can have similar effects, while also pointing to the importance of the specific licensing terms that a university offers to potential users (see also Arora et al., 2004; Fosfuri, 2006).

Another stream of work focuses on institutions and tools that may directly enable or ease access to scientific knowledge. For example, Furman and Stern (2011) explore how biological resource centers, which serve as depositories for scientific models, organisms, and data, facilitate access and thus diffusion (see also Stern, 2004). Furman and Teodoridis (2020) show how the availability of tools that automate research processes enables broader knowledge access and use. This work thus builds on Teece's (1986) seminal insight that the successful diffusion and adoption of a technology depends not only on the focal technology but also on the existence of complementary assets that enable the further development and distribution of a technology.

From yet another angle, many scholars acknowledge, implicitly or explicitly, that both industry stage and market size shape both access and diffusion. Specifically, when an industry is growing quickly, it has more individuals and organizations able to serve as adopters and thus as subsequent diffusers. By contrast, the earliest and later stages of an industry may see less diffusion due to a limited number of diffusers in the early case and due to market saturation in the later case. Methé (1992), for example, documents this pattern in a study of DRAM market over a 16-year period. Complementing this work, Menanteau and Lefebvre (2000) note that very early-stage industries often have numerous adoption barriers, whereas these barriers are reduced in more mature industries. Similar insights underlie more general discussions of industry stage and technology development, such as those described by Abernathy and Utterback (1978), Abernathy and Clark (1985), and Geroski (2000). At the same time, market size also can shape diffusion. Put simply, larger markets can provide more opportunities for diffusion to occur.

Finally, other work explores network connections and geography.

Scholars have long recognized that social networks play an important role in diffusion. For example, in the 1950s, Coleman et al. (1957) demonstrated that a physician's willingness to prescribe a new drug depended largely on whether that physician's network ties had prescribed the drug. More recently, scholars have examined how social networks serve not only to influence adoption decisions but also to spread knowledge that may not be readily available to those outside of a network. Specifically, if one is closely connected to a knowledgeable source, then one is more likely to access knowledge (e.g., Abrahamson and Rosenkopf, 1997; Ceci and Iubatti, 2012; Whittington et al., 2009). For example, Saxenian (1996) observes how engineers at competing Silicon Valley firms often shared proprietary knowledge with one another. Owen-Smith and Powell (2004) show how Boston universities and biotechnology firms collaborated around knowledge sharing, highlighting how network connections can undergird a localized system of scientific knowledge sharing. Indeed, several studies find that knowledge diffuses more readily to organizations that are geographically proximate (e.g., Audretsch and Feldman, 2004; Belenzon and Schankerman 2013; Jaffe et al., 1993). These geographic effects can be particularly strong for scientific knowledge that informs subsequent innovations. For example, Gittelman (2007) finds that research collaborations among geographically-clustered firms are more likely to result in papers that are later cited in these firms' patents (see also Audretsch and Feldman, 1996; Feldman and Desrochers, 2003).

Collectively, these and other studies provide convincing evidence of the myriad factors that shape access to new knowledge and subsequent diffusion. Many of the studies cited above strive to isolate the effect of a particular factor on knowledge access and diffusion. Yet in practice, diffusion is shaped by several factors simultaneously; moreover, the factors cited above may, in fact, work in consort. Thus, whether and how a researcher accesses particular scientific knowledge is likely to depend on the organizational origin of that knowledge, the associated IP approaches, the availability of complementary assets, the stage of industry development, *and* the researcher's position in a network – simultaneously. In turn, understanding how these factors work together requires detailed case-based analyses that can trace diffusion over time. This stands in contrast to the prior scholarship that typically uses large datasets. In this paper, we present just such an analysis with the aim of understanding how two seemingly comparable technologies may nonetheless exhibit rather different diffusion patterns.

## 3. Research design

Fundamentally, we aim to examine a series of factors that affect the rate of knowledge diffusion. As previously reviewed, this includes the role of the organizational origin, licensing strategies, complementary assets, industry stage, and early-stage professional networks. For the research design, we set up a comparative case study that relies on two technologies that are similar on key dimensions but also, importantly, differ in systematic ways. Thus, our empirical approach deviates from prior work that often employs a *ceteris paribus* framework by examining one key explanatory factor while holding everything else constant. Here, we aim to examine a multitude of factors that we posit affect the scale and scope of diffusion. The technologies' common features allow for comparability, while critical assessment of their differences helps explain any observed divergences in the diffusion trends between the two cases. We carefully track both to inform our conclusions.

In this section of the research design, we provide background on each case and illustrate their features. Next, we document the sample, data construction, and variables for the empirical analysis tracking diffusion trends. In the results section, we present two parts. First, as a baseline, we document the scale and scope of diffusion for both technologies drawing upon a range of metrics. Second, we examine the systematic differences between these two cases with a mixed-methods approach. Taken together, these analyses are more inductive by first documenting the trends of diffusion followed by a critical assessment to identify the range of factors that account for observed divergences. This unique approach provides a more comprehensive analysis of the confluence of factors that drive knowledge diffusion.

### 3.1. Two cases

We focus on two key techniques in biotechnology: recombinant DNA (rDNA) and polymerase chain reaction (PCR). Recombinant DNA enables the transfer of fragments of foreign DNA into other organisms. Essentially, it is a process for combining genetic material from different sources. The technique involves cutting a loop of bacterial DNA, called a plasmid, and then attaching another plasmid with a complementary attachment but different DNA. Then, an enzyme called a DNA ligase is used to firmly paste the two plasmids together. Finally, the recombinant DNA is transferred into a bacterial cell, which quickly replicates and thus manufactures copies of the inserted gene. Stanley Cohen and Herb Boyer, professors at Stanford University and the University of California San Francisco (UCSF) respectively, co-developed this technique in 1973. Today, rDNA-based products are widespread in medicine, agriculture, and bioengineering and include synthetic insulin, human growth hormone, and insect- and herbicide-resistant crops (Betlach, 2002; Hughes, 2001).

Kary Mullis developed the polymerase chain reaction technique in 1985 while working at Cetus Corporation, an early biotechnology company in Emeryville, California (about 10 miles from San Francisco). PCR enables the rapid reproduction of precise segments of DNA at an exponential magnitude. It is based on the fact that a DNA molecule consists of four bases – adenine (A), cytosine (C), guanine (G), and thymine (T). These bases always match to the same partner in a double-helix structure, such that A and T always pair and C and G always pair. The PCR technique involves heating a sample, thus causing the double-stranded DNA to separate into single strands. When the sample is cooled, short DNA sequences bind to complementary matches on each single strand, and, raising the temperature slightly, an enzyme synthesizes new DNA strands – with a T to match each A, a G to match each C, and so on. Then, the process starts over again. Each cycle doubles the amount of target DNA, such that repeated cycles of heating and cooling yield an exponential increase in genetic material. The PCR technique is widely used in medical, forensic, and applied sciences, with applications ranging from gene cloning to diagnostic tests (including those for Covid-19) (Rabinow, 1997).

rDNA and PCR are alike in many respects. Both were developed in the San Francisco Bay Area. They are both techniques, rather than products per se. Moreover, these two techniques are the bedrock techniques of the entire biotechnology field. Accordingly, they both emerged in the earliest years of this industry; most observers characterize the 1980s as the "birth" of the industry, with rapid growth in the 1990s and maturity in the 2000s (Evens and Kaitin, 2015). However, rDNA preceded PCR by 12 years. Underscoring their importance, each technique led to a Nobel Prize less than ten years after the initial invention – in 1980 for rDNA and in 1993 for PCR. Each technique also was both published and patented. Finally, in both cases, the inventing organizations issued non-exclusive licenses to any organization that wished to use the technology. In the case of rDNA, Stanford (which managed the license on behalf of itself and UCSF) offered different licensing agreements to different organization types. For-profit licensees paid a small up-front fee and a graduated royalty schedule; nonprofit licensees paid no royalties (Feldman et al., 2007; Hughes, 2001). In the case of PCR, Cetus initially required licensing agreements with an up-front payment as well as royalties from both private and public or nonprofit organizations (Feeney et al., 2018). However, in December 1991 Roche acquired ownership of the PCR intellectual property and established a new licensing system that more closely matched the Stanford approach. Thus, they eliminated up-front fees for academics and nonprofits, and reduced the royalty rate to encourage greater use of the technology (Fore et al., 2006; Cook-Deegan and Heaney, 2010).

While no two technologies are a perfect match on every dimension, rDNA and PCR are closely matched technologies along key dimensions – and, in fact, prior qualitative work has matched these same two technologies (Nelson, 2016a). However, rDNA and PCR also have important differences. As mentioned previously, rDNA was invented in a university setting, whereas PCR was invented in a private startup firm. And while a cursory glance at the 12-year difference in timing in inventions may appear inconsequential, a more nuanced view is that the industry may be at different stages, with more organizations for PCR to diffuse to more quickly in the 1980s. Finally, PCR has proven over time to have more technological applications than rDNA. These differences have implications for diffusion that will be explored in the analysis. Table 1 provides an overview of the features for these two cases.

## 4. Sample

### 4.1. Data construction

We trace the diffusion of rDNA and PCR through publication citations and patent citations. Regarding the former, the inventing scientists published papers that described rDNA and PCR immediately after invention. Thus, Cohen and Boyer first disclosed rDNA in 1973 in an article in the *Proceedings of the National Academy of Science,* and Mullis first disclosed PCR in 1985 in an article in *Science.* To gather publication citations, we turn to the SciSearch database, which contains all records published in the Science Citation Index and additional records from about 1000 other journals. This source covers approximately 8600 leading journals in science and medicine. SciSearch has broader interdisciplinary coverage and more records than PubMed and Scopus for the years where our study focuses.[1] We download complete information for every publication that referenced one of the original publications.

Turning to patents, acting on behalf of itself and UCSF, Stanford University applied for three patents on rDNA. One patent (US Patent 4,237,224) covered the technique itself, while two additional patents (4,468,464 and 4,740,470) covered products tied to eukaryotic and prokaryotic cells. Similarly, Cetus applied for three patents tied to PCR (4,683,195; 4,683,202; and 4,965,188). We employ a custom data-scraper to download from the US Patent and Trademark Office website the complete information for every patent that referenced one of these original patents. We limit our time series to 15 years after the date of the initial invention, thus matching the most liberal window in similar studies; both Jaffe et al. (1993) and Trajtenberg et al. (1997) employ a 14-year citation window. For rDNA, the 15-year panel spans 1973 to 1987; and for PCR, the 15-year panel spans 1985 to 1999. Appendix Table A1 shows the breakdown of the original publications and patents for each technology.

**Table 1**
Features of the two cases.

| | rDNA | PCR |
|---|---|---|
| Year of invention | 1973 | 1985 |
| Location of invention | San Francisco Bay Area | San Francisco Bay Area |
| Nobel Prize | 1980 | 1993 |
| Invention disclosure | Publish first, then patent | Publish first, then patent |
| Role in biotechnology industry | Foundational technology for entire industry | Foundational technology for entire industry |
| Inventing organization(s) | Universities (Stanford and UCSF) | Firm (Cetus) |
| Licensing strategy | Non-exclusive – low upfront fee and percentage of revenues for related products | Non-exclusive – shift from emphasis on upfront fee to selling complementary assets |
| Complementary assets | Initially limited | Early development and emphasis |
| Industry stage | Emergence phase – invention marks the start of the industry | Emergence phase – invention precedes industry shift to rapid growth |
| Early professional networks | Limited | More expansive |

One concern with the use of citations to track diffusion is that, over time, people may no longer cite foundational work because they assume that everyone knows it (c.f., Lederberg, 1977; Nelson et al., 2014). Merton (1979) describes this tendency as "obliteration by incorporation." The specific concern is that obliteration by incorporation may not show the full extent of diffusion as time passes and knowledge is "incorporated." Moreover, recent work by Myers and Lanahan (2021) reports that citation paper trails may account for only about half of knowledge spillovers.

To address these concerns of undercounting, we assemble a second patent database using patent filings from PatentsView (Bloom et al., 2013). Given their significant novelty, both PCR and rDNA defined new *US mainline sub-classes*. This dataset consists of all patents that reference either of these two specific sub-classes. We report the results with this separate sample as an empirical extension.

Next, we turn to coding both the publications and patents. We begin by coding each organization with a unique identifier. Often, a single organization would appear in multiple different formats even within a database. For example, Stanford University might be listed as "Stanford," "Stanford University," "The Leland Stanford Junior University," "The Board of Trustees of Stanford University," or any number of other permutations. Thus, we use repeated sorting, text string searches, and extensive manual reviews to parse organizations and assign a unique identifier. We also code each organization by type – university, firm, or other – and geocode its location as measured in longitude and latitude. We repeat the process of creating unique identifiers for the individuals in our dataset. This process is more challenging than in the case of organizations because publications often list only first initials with a last name. Our challenge is disambiguating different individuals that share the same initials and last name. In the case of overlapping names, we examine organizational affiliations in that same year. If two matching names shared the organization in a given year, then we code them as the same person.

### 4.2. Variables

Using the aforementioned dataset of publication and patent citations, we examine knowledge diffusion from multiple angles to assess the scale and scope of diffusion and the nature of research production. Tracing diffusion from multiple angles allows a more comprehensive understanding of diffusion patterns than looking at just one measure, such as forward citation counts, alone. Table 2 reports the list of metrics, their functional form, and primary form of analysis. For all metrics, we estimate activity for both publication and patent application[2] activity, respectively.

To assess the scale of activity, first we compute the annual count of output. For publications, this includes predominantly peer-reviewed journal publications in addition to books, chapters, and conference proceedings; for patents, this includes patent application filings. Second, we report the annual count of unique organizations engaged in these two separate research areas. For patent activity, we draw upon the assignee for this organizational measure. Third, with detail on the organizational

[1] Since our interest lies in comparing two technologies, and since these technologies are in the same field, we expect alternative databases would yield similar results since any database omissions would apply similarly to both technologies.

[2] Results are robust to patent grant records.

**Table 2**
Metrics of diffusion.

| Variables | Functional Form | Primary Form of Analysis |
|---|---|---|
| *Scale of Activity* | | |
| Output | $\sum Output_{it}$ | Annual trend lines |
| Organization | $\sum Organization_{imt}$ | Annual trends lines |
| University only<br>Firm only<br>Multiple types | $\frac{\sum Output_{ilt}}{\sum Output_{it}}$ | Comparison of means |
| Geographic Distance | $\overline{km\ from\ Origin_{it}}$ | Fitted trend lines with confidence intervals |
| *Scope of Knowledge Diffusion* | | |
| Unique Domains | $\sum Domain_{ikt}$ | Annual trends lines |
| Breadth of Study | $\overline{\sum Domain_{it}}$ | Fitted trend lines with confidence intervals |
| *Nature of Research Production* | | |
| Collaboration | $\overline{\sum Scientists_{it}}$ | Fitted trend lines with confidence intervals |
| New Entrant | $\sum New\ Entrant_{it}$ | Annual trends lines |
| Joint Scientist | $Joint_{jt}$ | Comparison of means |

Notes: $i$ denotes form of research production – publication or patent application, respectively; $t$ denotes panel following initial invention ($1 \leq t \leq 15$); $j$ denotes individual conducting research – author or inventor; $k$ denotes the distinct concepts (publications) or US Classes (patents); $l$ denotes organizational type – university, firm, and multiple, respectively; and $m$ denotes the distinct organization.

type — university, firms, and other — we compute the ratio of output produced only within universities, only within firms, and by multiple organizational types, respectively. Fourth, to examine the geographic reach of diffusion, we compute the distance in kilometers between the follow-on research project and original invention. For publications or patent records with multiple organizations, we compute the average distance per output.

To assess the scope of knowledge diffusion, we rely on prominent classification schemes that identify the set of knowledge domains where each research project contributes. For publications, database indexers assign specific *concepts* to each paper, which reflect particular topics within wider subject areas. For example, concepts in our publication database include "Agronomy," "Blood and Lymphatics," and "Enzymology." For patents, USPTO officers assign the range of *US Classes*. We use these discretized knowledge domains first to estimate the count of unique domains among the corpus of follow-on research. This provides a metric to assess the reach of influence of the initial invention across knowledge space. Second, we compute the annual average count of domains per output to assess the breadth (or focus) of the follow-on study.

Lastly, to assess the nature of research production, we rely on detail of the scientists. For publications, we assess authors; for patents, we assess inventors. First, we estimate the average size of the collaborative team for each output. Second, we identify output where the set of scientists are new entrants to the research network. This builds upon an extensive literature that disambiguates the nature of connections in professional networks (e.g., Ahuja, 2000; Rosenkopf and Padula, 2008). Specifically, these scientists do not have prior collaborative ties with other scientists who previously published or patented in the respective technology field. We define this variable as *New Entrants*. Third, while we predominantly assess publication and patent activity separately, we identify the set of scientists that produce both publications and patents within each technology. In contrast to the other metrics that report at the output level (publications or patents), this variable reports at the individual level. We define these scientists as *Joint Scientists*.

## 5. Results

We present the results in two parts. In Part 1, we document the scale and scope of diffusion for both technologies, drawing upon the range of metrics outlined in Table 2. Importantly, this offers a baseline for understanding how the diffusion trends compare and contrast across the two cases. In Part 2, we examine systematic differences in these two cases that may account for the diverging trends of diffusion observed in Part 1. In doing so, we integrate a mixed-methods approach to inform our assessment and conclusions.

### 5.1. Results Part 1: Diffusion Trends

As a baseline, Fig. 1 reports trend lines of the total unique organizations across both publication and patent activity by technology (rDNA and PCR). A distinct pattern emerges – the trend line for rDNA (thinner red) is relatively flat across the 15-year panel, while the trend line for PCR (thicker blue) illustrates a precipitous increase over the first five years of the panel. Moreover, the number of unique organizations engaged in the knowledge diffusion of PCR exceeds rDNA by a substantial amount over the duration of the extended panel.

To unpack this finding further, we report a range of statistics to compare the diffusion of rDNA and PCR. Moreover, we split the sample and report diffusion trends based on publication and patent activity, respectively. For reference, Table 2 reports the primary form of analysis for each metric to assess the differential trends across the two technologies; this includes a combination of descriptive statistics, comparison of means, and trend lines. In line with Table 2, we assess diffusion along three prominent angles: (i) *Scale of Activity*; (ii) *Scope of Knowledge Diffusion*; and (iii) *Nature of Research Production*. We report each in turn.

#### 5.1.1. Scale of Activity

Table 3 provides baseline descriptive statistics in Panel A. The first follow-on publication for rDNA and PCR occurred the same year as the initial invention (1973 and 1985, respectively).[3] However, the first follow-on patent application filing lagged five years for rDNA and two years for PCR.[4]

Panels B and C provide additional statistics and the comparison of means for metrics of scale based on activity up to 10 years following the initial invention. Panel B reports for publication activity; Panel C reports for patent application activity. In terms of output, PCR reports substantially higher levels of activity in terms of output, scientists, and organizations, exceeding the level of diffusion for rDNA by over ten times along most metrics. In terms of organizational type, we find evidence that rDNA-based collaborations producing follow-on publication output are most likely only from universities (65 percent), which aligns with the original source of invention. This ratio exceeds the comparable metric for PCR- based collaborations (41 percent); this difference is statistically significant. As an aside, however, it is worth noting that the PCR statistic also reveals a prominent trend of diffusing to university settings (even though it is a firm invention). This stands in contrast to prior expectations that knowledge generally flows from university to firm settings (Lööf and Brostrom, 2008; Szücs, 2018). Moving on, the ratio of PCR- based collaborations comprised of co-authoring teams from multiple types of organizations (34 percent) exceeds the comparable

[3] We acknowledge a discrepancy in the data between Table 3 and Fig. 1. Notably, the trend line for PCR does not capture the first follow-on publication in 1973. This coincidentally is due to incomplete data for this record. This first follow-on publication was a *News Item* in Science. As an extension, we examine the completeness of the bibliometric records for the full sample. We report the results in Appendix Table A2. With the exception of Publication Concepts, the level of missingness is minimal and thus ignorable (missing records account for less than 0.01 percent of sample). For Publication Concepts, we report a higher level of missingness; however, the proportion of missingness does not appear to differ systematically across the rDNA or PCR samples. We conclude the records are missing at random.

[4] For all trend lines, we trace activity over the first 15 years following the initial discovery. Given the lag for patent application activity for PCR and rDNA, the trend lines begin at panel five for rDNA and panel two for PCR.

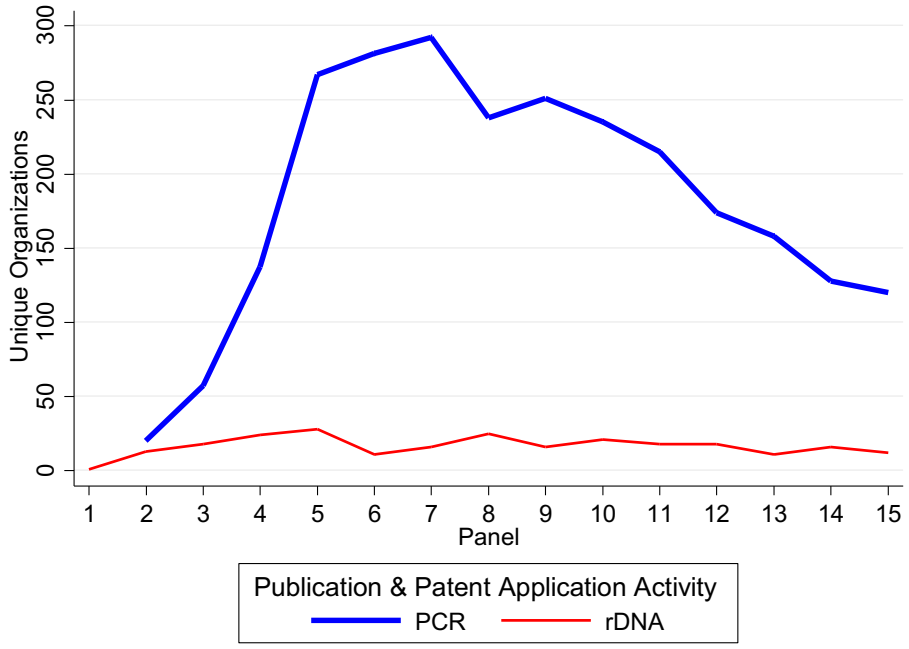


**Fig. 1.** Total Unique Organizations Notes: In contrast to Table 1, total unique organizations is based on publication *and* patent activity $\sum Organization_{mt}$, where $m$ denotes the distinct organization across entire sample and $t$ denotes panel following initial invention ($1 \leq t \leq 15$).

**Table 3**
Descriptive statistics.

| Variables | rDNA | PCR | t-stat | |
|---|---|---|---|---|
| *Panel A: Baseline Descriptive Statistics* | | | | |
| Year of initial invention | 1973 | 1985 | – | – |
| First follow-on publication | 1973 | 1985 | – | – |
| | [1] | [1] | | |
| First follow-on patent application | 1977 | 1986 | – | – |
| | [5] | [2] | | |
| Total Unique Organizations [by $t = 10$] | 173 | 1778 | – | – |
| *Panel B: Publications [by t=10]* | | | | |
| Output | 384 | 3889 | – | – |
| Scientists (Authors) | 732 | 12,012 | – | – |
| Organizations | 148 | 1672 | – | – |
| University only | 0.65 | 0.41 | 8.73 | *** |
| Firm only | 0.07 | 0.05 | 1.03 | n.s. |
| Multiple types | 0.10 | 0.34 | −13.55 | *** |
| High Quality Publication | 0.13 | 0.02 | 5.90 | *** |
| *Panel C: Patents [by t = 10]* | | | | |
| Output Count | 67 | 778 | – | – |
| Scientists (Inventors) | 114 | 922 | – | – |
| Organizations (Assignees) | 32 | 198 | – | – |
| University only | 0.19 | 0.18 | 0.30 | n.s. |
| Firm only | 0.70 | 0.62 | 1.39 | n.s. |
| Multiple types | 0.06 | 0.08 | −0.73 | n.s. |

*Notes*: Panel denoted in brackets. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$. Not statistically significant (n.s.).

rDNA-based metric (10 percent); this difference is statistically significant. Interestingly, we do not report statistically significant differences in means along these measures for the patenting sample. Lastly, for publication activity, we find that rDNA-based authors are more likely to publish in high-ranked scholarly journals (13 percent) compared to PCR-based authors (two percent). This initial set of results suggests that PCR diffused at a greater pace than rDNA.

Fig. 2 reports an additional set of trend lines to illustrate differences in the scale of diffusion between the two technologies. For all primary figures, the 15-year trend lines for rDNA (PCR) diffusion are reported by the thinner red (thicker blue) lines; moreover, the left column reports publication-based activity, while the right column reports patent application-based activity. Panels A and B in Fig. 2 report the trend lines of annual activity as measured by total output and unique organizations.[5] In alignment with Fig. 1, these trends illustrate that the scale of PCR follow-on activity exceeds rDNA follow-on activity for both modes of production (publications and patents). The initial output trends reported in Panel A appear to be comparable; however, PCR follow-on activity demonstrates a precipitous increase between five and ten years following the initial invention. We do not find a similar increase for rDNA. The rDNA trend line is relatively flat across panels.

Panel C in Fig. 2 provides an alternative metric of scale based on the geographic spread of research activity. Given that we construct the mean distance per output, we report the fitted trend lines with confidence intervals to account for the annual distribution of the metric. The results for publication activity for both rDNA and PCR report positive slopes – the distances of diffusion increase over time. However, PCR follow-on activity takes place at greater distances from the original invention compared to rDNA follow-on activity. In terms of actual distance, PCR reports a greater international impact than rDNA, with an average distance in the latter half of the panel exceeding 6500 km.

As for patenting activity, we report a contrasting trend to the publication trends. First, the trend lines are downward, suggesting that the distance among follow-on activity decreases over the panel. Second, the average distance is closer to the origin than the publication results (and appears to reflect domestic rather than international impact).[6] Third, the differences between the two inventions are negligible. We explore these results further by stratifying the sample by organization type – only firms, only universities, and multiple types. A clear trend emerges: output produced only by firms drives the downward slope for the rDNA

[5] Refer to Appendix Figure A1 Panel A for cumulative (rather than annual) trend lines.

[6] We assume that R&D occurs at the assignee's location and thus document distance based on the assignee's location. However, it is feasible that some organizations are building on their technology in different locales (or even countries) but only patenting in certain jurisdictions. This is a limitation of the data.

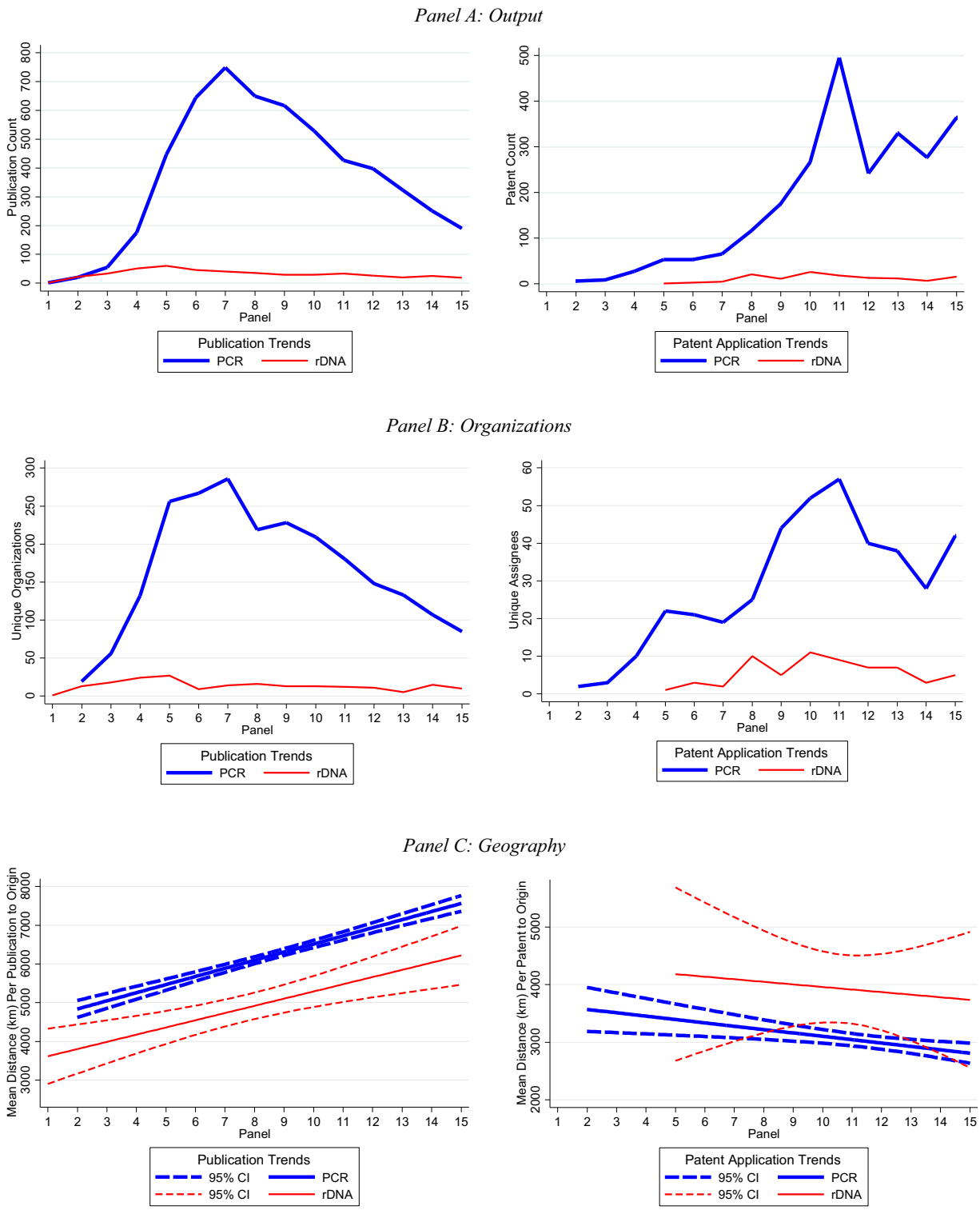


**Fig. 2.** Scale of Activity

*Notes*: Trend lines based on annual activity. Publication trends presented in left column; patent application trends presented in right column. Panel A reports count of publications and patent applications; Panel B reports count of unique organizations; and Panel C reports trend line with confidence intervals of mean distance (km) to origin of initial invention.

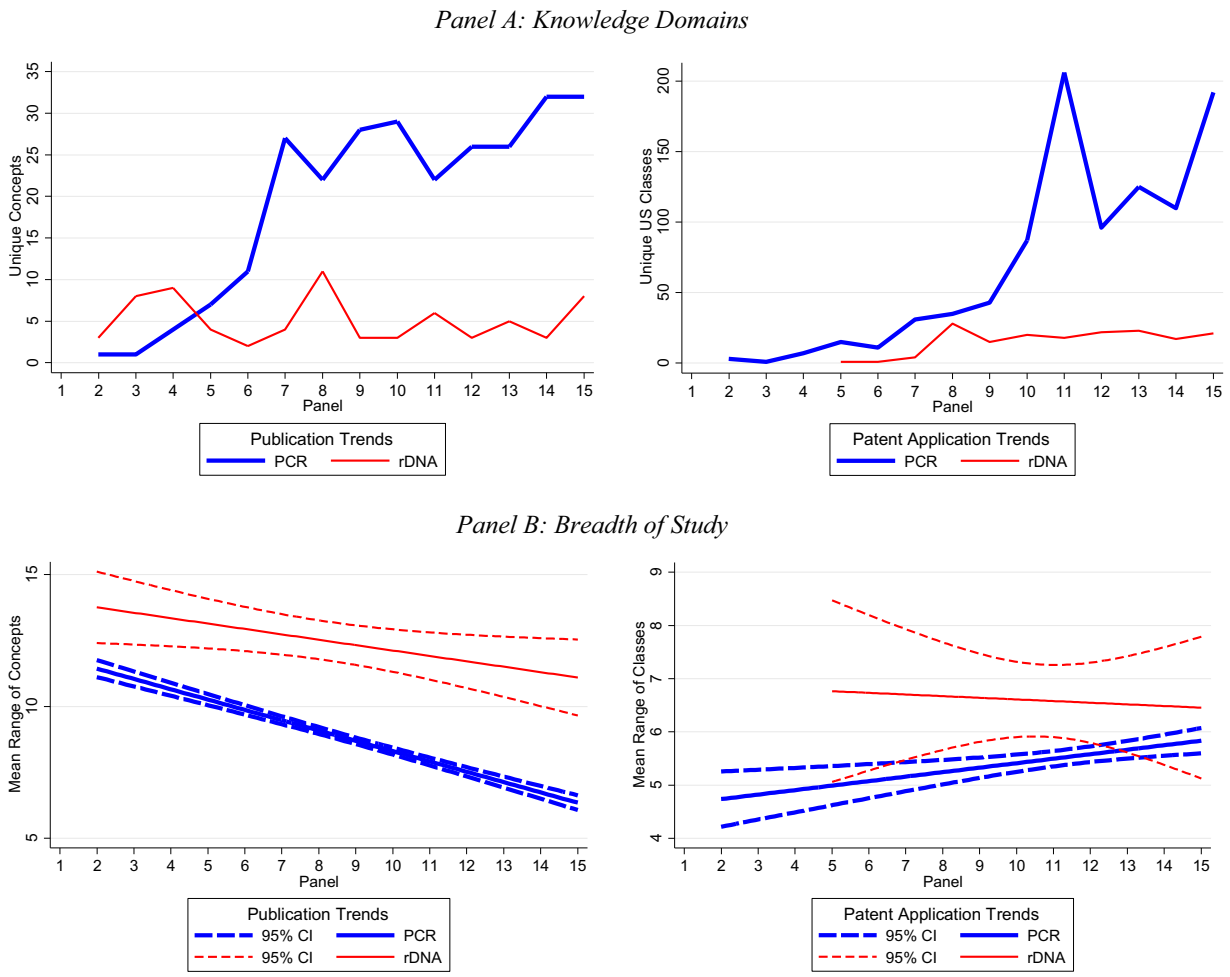


**Fig. 3.** Scope of Knowledge Diffusion

*Notes*: Trend lines based on annual activity. Publication trends in left column; patent application trends in right column. Panel A reports count of unique concepts or US classes; Panel B reports trends with confidence intervals of mean range of concepts per publications or US classes per patent.

sample for *both* patents and publications.[7] In other words, follow-on activity from firms building upon the rDNA invention decreases in geographic spread over time. This may reflect the earlier stage of the biotech industry when rDNA was discovered or the potentially smaller market size for rDNA versus PCR. We explore this result further in Part 2. Interestingly, the downward slope is robust for PCR patent output regardless of organization type.

The variability of these findings demonstrates the importance of considering multiple diffusion factors and measures. For example, tracing patents alone would not have indicated any difference in geographic scale of diffusion across the two technologies (Fig. 2 Panel C); moreover, the share of assignee organizations are generally comparable (Table 3 Panel C). Multiple measures of diffusion produce a more complete assessment of the trends.

### 5.1.2. Scope of Knowledge Diffusion

Fig. 3 illustrates differences in the scope of knowledge diffusion. Panel A reports the unique count of knowledge domains among the set of follow-on publications and patent applications, respectively.[8] For both, the corpus of activity that builds upon PCR encompasses a larger knowledge space. While rDNA demonstrates broader reach for publication activity over the initial four years of the panel, the differences flip and are pronounced in the extended panel.

Panel B reports the fitted trend lines with confidence intervals for the breadth of study. Effectively, this variable reports how broad or narrow the follow-on studies are. For publication activity, both technologies report negative slopes, indicating that the studies become more focused over time. This trend likely reflects greater application and commercialization of the technology. However, the slopes are statistically different over the entire panel. The rDNA trend reports greater breadth over the entire panel; in contrast, PCR studies are more focused, with approximately four fewer domains per study. For patenting activity, the differences are not as pronounced. PCR-based follow-on patents are slightly more focused eight to eleven years after the initial invention. Collectively, this set of results suggests contrasting differences between these two technologies. Overall, PCR diffuses to a broader knowledge space. However, the follow-on output is generally more focused, which likely reflects more directed application and subsequent commercial impact (Sørenson & Stuart, 2000; Sorenson et al., 2006).

### 5.1.3. Nature of Research Activity

We now turn to the nature of research production across the two diffusion trajectories by examining the scientists. Panel A in Fig. 4 reports the average number of co-authors or co-inventors per output. We report divergent trends across both modes of production. Not only are co-authoring teams larger for PCR follow-on studies compared to rDNA follow-on studies, but also the size of the team increases over the panel.

[7] Results available upon request.

[8] Refer to Appendix Figure A1 Panel B for cumulative (rather than annual) trend lines.

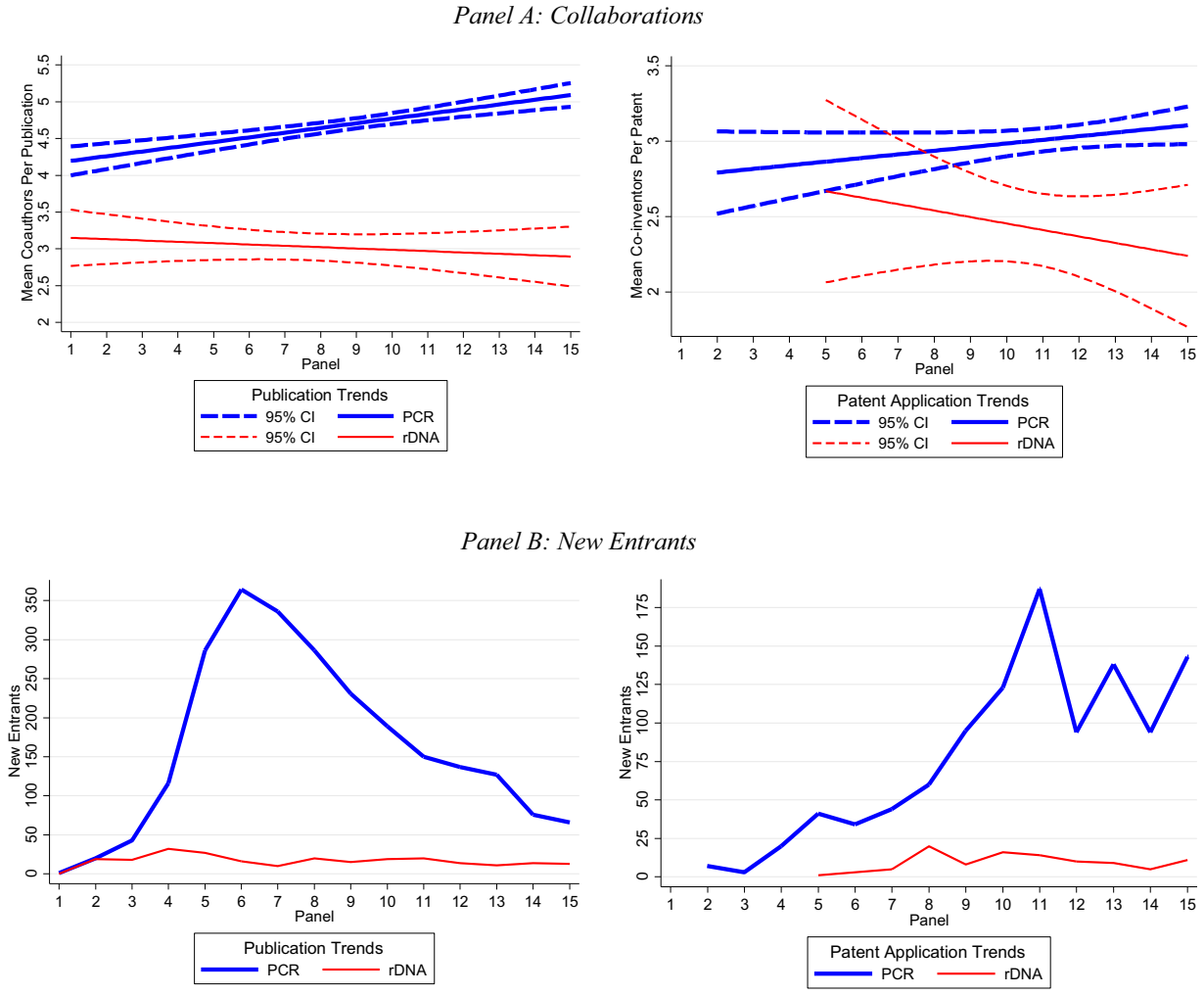


**Fig. 4.** Nature of Research Activity
*Notes*: Trend lines based on annual activity. Publication trends presented in left column; patent application trends presented in right column. Panel A reports trend line with confidence intervals of mean coauthors per publications or co-inventors per patent; Panel B reports count of new entrants.

For publication activity, the PCR-based team increases from 4.5 co-authors to five; for patenting activity, the PCR-based team increases from 2.8 to 3.2 inventors. However, for rDNA follow-on studies, the collaboration size *decreases* over the panel. The difference is significantly different across the entire panel for publication activity and statistically different for the latter part of the panel for patent activity. Not only does Table 2 report that the entire network of scientists is larger for PCR (12,012 unique authors and 922 unique inventors by 10 years post-initial-invention) compared to rDNA (732 unique authors and 114 unique inventors), but also production takes place with larger teams. In turn, this finding suggests that if larger teams are involved in follow-on activity, these larger teams are embedded in larger individual networks of scientists, which would further enhance diffusion.

To examine this last claim more critically, we assess the scientific network. Specifically, we examine the extent to which the network is based on scientists with prior collaborative ties to those producing research in the respective field or rather among new entrants who have no prior collaborative ties to scientists in the network. The trend lines in Panel B of Fig. 4 illustrate similar trends to the scale metrics. The number of new entrants for the PCR sample substantially exceeds the number for the rDNA. This holds across both publication and patenting activity. This suggests that PCR attracted greater numbers of scientists without prior ties to build upon the initial invention, whereas the diffusion of rDNA was more reliant on activity led by scientists with prior collaborative ties.

**Table 4**
Comparison of means – joint scientists.

| | Other | Joint | t-stat | |
|---|---|---|---|---|
| rDNA | | | | |
| Publication Count | 1.36 | 3.81 | −1.55 | n.s. |
| Publication Panel | 7.74 | 6.56 | 1.45 | n.s. |
| *Observations* | *986* | *27* | | |
| Patent Count | 1.34 | 1.56 | −1.26 | n.s. |
| Patent Panel | 10.81 | 9.22 | 2.47 | ** |
| *Observations* | *209* | *27* | | |
| PCR | | | | |
| Publication Count | 1.49 | 3.30 | −6.05 | *** |
| Publication Panel | 8.84 | 6.61 | 14.71 | *** |
| *Observations* | *16,489* | *370* | | |
| Patent Count | 3.23 | 4.46 | −3.59 | *** |
| Patent Panel | 11.28 | 8.72 | 15.09 | *** |
| *Observations* | *1814* | *370* | | |

*Notes*: Data based on 15-year panel following initial invention. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$. Not statistically significant (n.s.).

As a final assessment, we also identify the subset of scientists that both publish and patent within each technology (Joint Scientists). Twenty-seven scientists (2.7 percent) meet this specification in the rDNA sample, while 370 (2.1 percent) meet this specification in the PCR

**Table 5**
Summary of results.

| Metric | rDNA | PCR |
|---|---|---|
| *Scale of Activity* | | |
| Organizations | | X |
| Output | | X |
| Scientists | | X |
| Quality of Journals (pubs only) | X | |
| Geographic Distance (pubs only) | | X |
| *Scope of Knowledge Diffusion* | | |
| Knowledge Domains | | X |
| Breadth of Study | X* | |
| *Nature of Research Activity* | | |
| Collaborations | | X |
| New Entrants | | X |
| Joint Scientists | | X |

Notes: "X" indicates which invention – rDNA or PCR – leads in diffusion rate for each metric as reported in the primary results. Unless otherwise stated, results hold for both publication and patent application trends. Scale of Activity draws upon results from Table. 3, Fig. 1 and Fig. 2. Scope of Knowledge Diffusion draws upon results from Fig. 3. *For the breadth of study metric, rDNA leads over the entire panel for publication activity and only for a portion of the panel for patent application activity. Nature of Research Activity draws upon results from Fig. 4 and Table. 4.

sample. Table 4 reports a series of comparison of means to assess their activity compared to the set of only authors or only inventors. For rDNA, we report one difference: Joint Scientists are more likely to produce patents approximately 1.6 years earlier than those that only patent. We find evidence of greater differences for PCR. In this set, Joint Scientists are not only more likely to produce work at an earlier stage after the initial invention, but they are also more likely to produce more in terms of publications and patents.

A summary of our results appears in Table 5. As the table shows, by most every metric – including those tracing the *Scale of Diffusion*, the *Scope of Diffusion*, and the *Nature of Research Activity* – the diffusion of PCR exceeds that of rDNA.

#### 5.1.4. Robustness cCheck

For the primary analysis, we track knowledge diffusion by analyzing the corpus of publications and patents that reference the original invention (refer to Appendix Table A1). While tracing citations is a prominent method to examine diffusion (e.g., Jaffe et al., 1993), we also examine diffusion through tracing references to specific patent classes. As a function of the research design, each invention was so groundbreaking and foundational that it was assigned its own patent sub-class. For rDNA, the Cohen- Boyer patent (patent # 4,237,224) was granted the United States Patent Classification (USPC) sub-class '435/69.1′ (Feldman and Yoon, 2012; Feldman et al., 2015). For PCR, the main patent (patent #4,683,202) led to the establishment of the USPC class '435/91.2' (Clayton, 2020). For this extension, we rely on the patent class to identify the corpus of patents within each sub-class. Of note, we are unable to assess this robustness measure for publication activity given the structure of the schematic for knowledge domains.

We relied on patent filings from PatentsView to construct this additional dataset. This robustness check uses the sample of all granted patents with application dates through the 15-year panel with the USPC mainline sub-classes '435/69.1' for rDNA (338 patents) and '435/91.2' for PCR (2203 patents). This extension shows comparable trends to the main results for both rDNA and PCR, demonstrating the robustness of using patent classes as a diffusion measure (Appendix Figure A2).

### 5.2. Results Part 2: Factors of Diffusion

The results from Part 1 illustrate that the diffusion of PCR spreads wider, faster, and farther than rDNA by most every metric. As mentioned previously, these two cases share common features that allow for comparability. However, they also differ in important manners. Here, we explore these differences to help understand their divergences in diffusion. In this section, we explore five possible diffusion factors: (i) *Organizational Origin*; (ii) *Licensing Strategy*; (iii) *Complementary Assets*; (iv) *Industry Stage;* and, (v) *Social Networks.*

#### 5.2.1. Organizational Origin

Despite the fact that both inventions were discovered about 10 miles apart, in the same industry, and accruing notable notoriety, they have different organizational origins. rDNA was discovered within a university setting, whereas PCR was discovered at a firm. Given the association of universities with public science and of firms with private science as described in Section 2, we have strong theoretical grounds on which to expect that diffusion patterns from universities and firms will look different. Because universities subscribe to public science and because public science facilitates diffusion, university-generated knowledge might be expected to diffuse more quickly, across a wider geography, to more organizations and, therefore, to a wider range of applications. In contrast, because firms subscribe to private science and because private science inhibits diffusion, firm-generated knowledge might be expected to diffuse less quickly, within a more constrained geography, to fewer organizations, and, therefore, to a narrower range of applications.

Yet, we find evidence to the contrary. The baseline result of the firm-based invention (PCR) diffusing at a significantly greater degree than the university-based invention (rDNA) stands in contrast to these expectations. The finding that rDNA-based authors are more likely to publish in high-ranked scholarly journals than PCR-based authors is in alignment with our initial expectations around university publishing and prestige. However, when considering the broader set of results, the a priori expectation that firm competitive dynamics will reduce diffusion as compared to university diffusion does not appear to hold. The comparisons and statistics indicate different factors are involved in rDNA and PCR diffusion that do not correspond to a simplistic dichotomy of public versus private settings, or open versus closed science. Instead, we must explore additional explanations.

#### 5.2.2. Licensing Strategy

Another explanation for the diffusion differences ties to the early licensing strategy for PCR. As noted in Section 3, Cetus initially had a more restrictive strategy; however, six years after the invention, Cetus sold the rights for PCR to Hoffman-La Roche (Roche), which adopted a liberal strategy that was comparable to Stanford's approach to rDNA (Fore et al., 2006). Specifically, Roche pursued a revenue model that was not dependent on licensing the PCR method per se but rather on selling the reagents and thermocyclers required to carry out the method (Cook-Deegan and Heaney, 2010). In other words, their licensing strategy explicitly relied on their development of complementary assets, and the change in licensing strategies may explain why the PCR slope increases in the panel when it does.

Interestingly, this early discrepancy in licensing approaches highlights the comparability and subsequent validity of the research design. If PCR's licensing was overly restrictive, then rDNA should outperform PCR during PCR's early and more restrictive years; yet, it does not. As our analysis demonstrates, even in the face of a more restrictive initial licensing policy for PCR, PCR still outpaces the diffusion of rDNA along multiple diffusion metrics. In this way, our use of PCR as a comparator also reflects a conservative test since, if anything, rDNA should have had an advantage. As with the organizational origin, this factor does not provide a complete understanding of the divergence in diffusion. So again, we explore additional factors.

#### 5.2.3. Complementary Assets

Another potential explanation for PCR's greater diffusion concerns the development of complementary assets around each technology. Both rDNA and PCR depended on complementary assets. Specifically, to perform rDNA, one needs an appropriate "plasmid" matched to the

desired experimental outcome. Mary Betlach, a technician in Boyer's lab, was one of the people who created and distributed plasmids that enabled others to perform rDNA. She also worked with Boyer to distribute a two-page handwritten guide on plasmid purification, which proved critical towards teaching others how to perform the technique (Betlach, 2002).

In the case of PCR, Mullis's original demonstration of the technique was incredibly time- consuming and laborious, requiring the repeated manual heating and cooling of a sample for several hours. Moreover, the "polymerase" that Mullis used was not thermostable and was thus inactivated during each heating cycle. Cetus thus invested in the development of a new thermostable polymerase, isolated a year later, and they contracted with equipment manufacturer Perkin-Elmer to make a "thermocycler" – a machine that would automatically heat and cool a sample and thus automate the procedure. At the same time, Perkin-Elmer started an informal newsletter that shared "tips and tricks" on how to perform PCR (Rabinow, 1997). Such developments were essential towards simplifying PCR and thus enabling its broad diffusion (and are a likely explanation for why the diffusion of PCR accelerates a couple years after invention).

The key question, in turn, is whether certain organizations are more likely to possess or develop complementary assets that may aid diffusion. Here, the qualitative evidence suggests that firms may be more likely to develop such assets. For instance, Betlach, Boyer's lab technician, reported that Boyer's university lab "freely gave out all sorts of materials" to perform rDNA. But she also recalled her hesitation to continue revising the method:

> My feeling was once I got any given method to the point where I could get what I wanted out of it at a reasonable pace, I didn't want to spend any more time working on the methods. I wanted to move on and actually do the work (Betlach, 2002).

In other words, Betlach was primarily focused on doing her own research (and that of Boyer's lab) and not on facilitating the work of others. Similarly, referring to the time shortly after invention, Boyer's post- doc Herb Heyneker recalled, "In those days [shortly after the rDNA invention], you could not buy your enzymes; you had to make them yourself" (Heyneker, 2004).

Conversely, when an interviewer asked Henry Erlich and Norm Arnheim, who played key roles in the development of PCR at Cetus, how an academic institution might have approached PCR, they emphasized Cetus's ability and interest in further developing complementary assets:

> Erlich: I think it [PCR] certainly could have been conceived by an academic scientist in an academic lab, but I think that it certainly wouldn't have been developed and applied in the same way … one of the real virtues of CETUS was the ability to work as part of a complex team and draw resources from many different disciplines, so that, as we were talking earlier, the initial group that worked on PCR had chemists in it and biochemists and geneticists—you know, a small group of people with somewhat diverse backgrounds. But clearly its ultimate development required access to enzymology, a biochemistry lab like David Gelfand's, it required access to an engineering group, which most academic settings wouldn't have had. In a distinction that we were talking about quite a bit earlier where academic labs try to do everything from within, I think the kind of resources that were required to really develop PCR into a procedure that could be used broadly in molecular biology research as well as in diagnostics could really only have come in a corporate setting...
>
> Interviewer: Do you agree with a lot of this, Norm?
>
> Arnheim: Yes, I think just from a historical perspective, I think most academic scientists, or virtually any academic scientist who might have thought the technique up and actually have demonstrated it for the first time, would have applied it to his specific problem, published a paper, maybe thought it was important, but then go on and stick to the fundamental problems that scientist was interested in. So I think it would have taken a very unusual academic scientist to make the commitment, "This has potential for all sorts of things and I'm going to try and develop a machine that will automate it, and I'm going to try and develop an enzyme that can be utilized in the machine." I think all of these things were foreign to the desires of most academic scientists (Smithsonian, 1993).

Erlich and Arnheim thus contend that a firm's ability to collaborate across a wide range of expertise combined with a commitment to develop complementary assets can propel diffusion. In other words, sharing in and of itself may be insufficient to spur diffusion; it is also important to develop and share complementary assets. In turn, because universities are not in the business of manufacturing and selling complementary assets, their direct commercialization efforts may reach only so far. Of course, in some cases, firms will step into this void by developing complementary assets for and improving upon technologies originating from universities.

#### 5.2.4. *Industry Timing and Market Size*

One potential concern with our research design is that the 12-year gap between the invention of rDNA and PCR means that they occurred at different points in the biotechnology industry's life cycle. Although both inventions occur during the emergence period for the industry (Evens and Kaitin, 2015), this difference in timing may have implications for the plausible set of inventors and organizations able to build on each technology. Specifically, if there were fewer organizations active in biotechnology in the 1970s and 1980s, then rDNA may show less diffusion simply as a function of this smaller risk set. At the same time, the introduction of the Bayh-Dole Act in 1980, which streamlined the process of university patenting, may have enabled greater PCR diffusion as measured by downstream patents since rDNA initially diffused in the pre-Bayh-Dole era whereas PCR diffused entirely in the post-Bayh-Dole era. Finally, rDNA and PCR have different applications and thus they may address markets of different sizes. Again, these size differences could shape diffusion patterns.

We examine these issues in four ways. First, we provide an assessment of broader market trends for an empirical baseline understanding of the industry stage over the study period. Second, we offer two empirical extensions to the primary analysis. We re-analyze the diffusion trends with proportional distributions and then, separately, examine the diffusion trends among universities only. Third, to tackle the potential complication of the Bayh-Dole Act, we eliminate universities from our sample and examine only firm patenting. Last, we consider the potential applications for each product. We discuss each approach in turn.

In Appendix Figure A3, we examine trend lines on US higher education R&D expenditures in the life sciences (Panel A), US doctorates granted in the life sciences (Panel B), biotechnology startups (Panel C), and biotechnology patent applications (Panel D). Two vertical lines indicate the rDNA and PCR invention years (1973 and 1985, respectively). While the four graphs indicate the most expansive period of growth in the biotechnology industry occurred in the 1990s, it is clear that there are also distinct differences in the industry from when rDNA was invented to when PCR was invented. There is a positive slope in all four figures indicating a greater amount of R&D expenditures in the life sciences, a greater number of life sciences doctoral recipients, a greater number of biotechnology startups founded annually, and a greater number of biotechnology patent applications. This means that PCR invention had a larger market into which it could diffuse and makes market size itself a diffusion factor.

Given the differences in the early-market stage, we re-analyze our primary results. Specifically, we adjust the functional form of the metrics for output, organizations, and knowledge domains to proportional distributions. These adjusted measures provide a relative comparison that controls the total diffusion of each technology and thus highlights

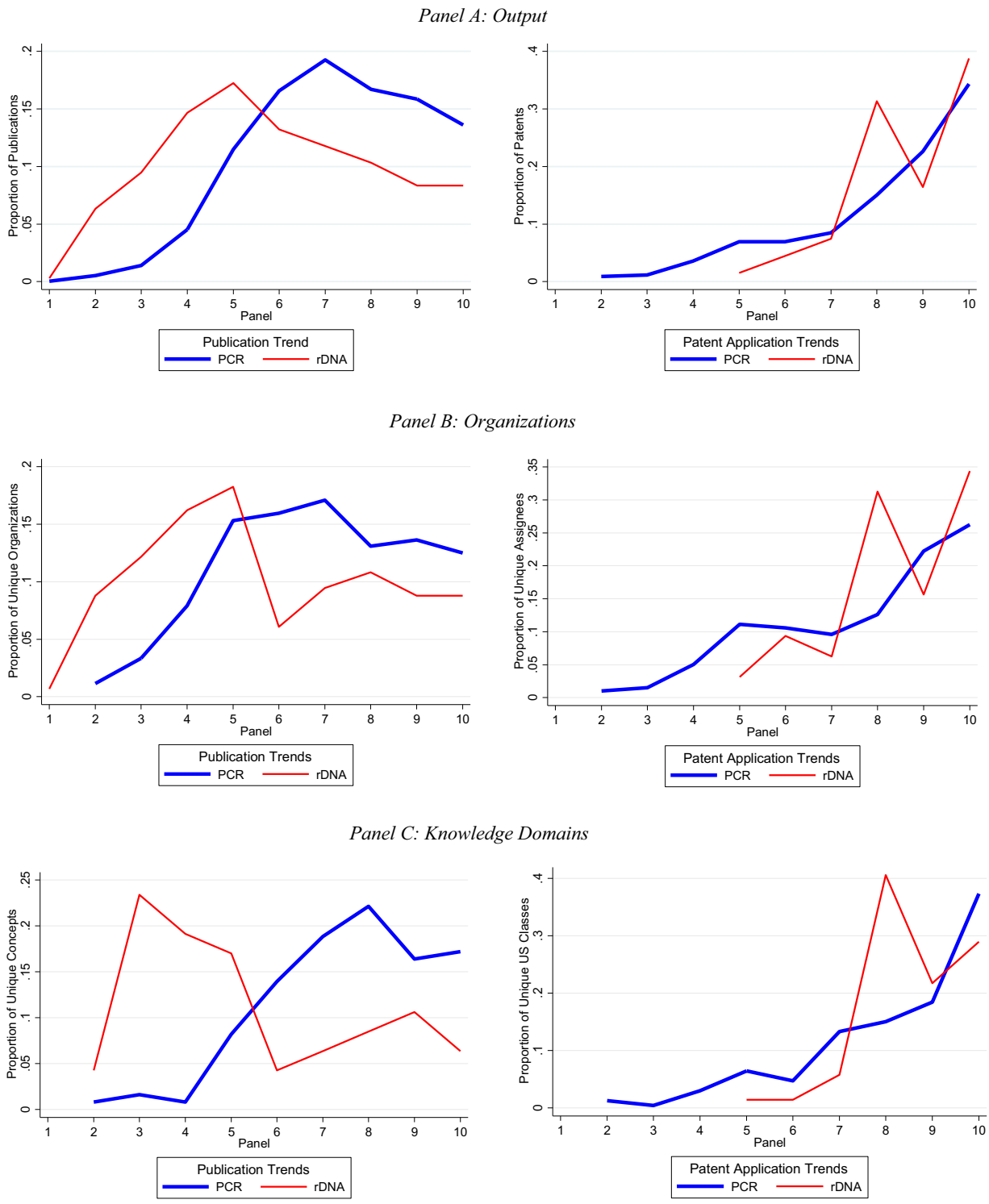


**Fig. 5.** Proportion of Total (10-year Panel) Activity
*Notes*: Proportion of total (10-year) publication activity in a given year in left column; proportion of total (10-year) patent application activity in a given year in right column. Panel A reports output; Panel B reports unique organizations; and Panel C reports unique knowledge domains.

*when* the diffusion of each technology was most prominent. This functional adjustment allows for greater comparability, given the differences in timing. Fig. 5 presents the results of trend lines for the proportional distributions over the first 10 years of the panel. Across all three panels, we identify a common feature – the diffusion of rDNA peaks *earlier* than the diffusion of PCR by approximately two to three years. While the diffusion of rDNA was more pronounced (proportionally) immediately after the initial invention, the diffusion of PCR took longer to gain traction yet sustained more demonstrably. We confirm this assessment with an additional analysis where we report the parametric plot with confidence intervals to compare cumulative publication and patent activity between the two technologies (Appendix Figure A4). For both modes of production, we find evidence that the diffusion of rDNA accelerated faster than PCR over the first seven years of the panel. This qualifies our conclusions to the results reported in Part 1; yet, the main finding holds that PCR outpaced rDNA.

Separately, we restrict the sample of follow-on activity to publications and patents produced *only by universities*. Universities, in contrast to firms, reflect a consistent set of organizations over the timeframe since almost no universities in our sample cease to exist or come into existence in the 1970s and 1980s; thus, by restricting the sample to universities, we hold the risk set of adopting organizations constant between the two technologies. We report the trend lines to illustrate differences in scale across output and organizations in Appendix Figure A5. The overall trends are consistent to the primary results as presented in Fig. 2 (Panels A and B) and provide greater assurance that the divergence in diffusion is not solely a function of the industry life cycle and timing of the initial invention.

To address the possibility that the pre-Bayh-Dole timing of rDNA limited its diffusion as reflected in patent citations, we construct a sample that eliminates universities. (Bayh-Dole primarily affected university patenting, not firm activity and not university publishing.) Appendix Figure A6 displays the resultant trend lines. As the figure illustrates, patenting differences between the technologies remain even when universities are eliminated from the sample. Moreover, as is evident from Panel A and Panel B in Fig. 2 (which includes universities), rDNA patenting actually dips somewhat in 1981 (panel year 9), the year after the Bayh-Dole Act passed. Thus, Bayh-Dole does not appear to be exerting a major influence on overall patenting patterns.

Lastly, related is the question of whether PCR or rDNA inherently possesses greater potential applications in the market. If this is the case, we would expect greater diffusion of the technology with broader applications and a larger market. Considering the history of PCR and rDNA, it does appear that PCR has more applications in a broader array of fields.[9] PCR is used in medical forensics, molecular biology, pharmaceuticals, and diagnostics (Cook-Deegan and Heaney, 2010). On the other hand, rDNA mainly has applications in genomics and pharmaceuticals. In turn, these differences may partly explain why the scope of PCR diffusion outpaces that of rDNA. However, equating greater market size or market application with greater diffusion would be a simplification of how diffusion occurs, as the previous analysis indicates.

#### 5.2.5. Social Networks

Intrinsically related to the industry stage is the state of the early social networks around the inventors. Later-stage industries will have larger networks of scientists. Qualitative histories of both rDNA and PCR indicate that, despite initial publications, full and detailed information on how to perform each technique was not widely available, especially in the period shortly after invention. Thus, social networks may have been important towards facilitating diffusion (Abrahamson and Rosenkopf, 1997; Nelson, 2016b). Our results are consistent with a scenario in which the networks around PCR were more conducive to diffusion than those networks around rDNA, and in which networks are critical to diffusion.

Of course, networks are difficult to track. Indeed, two of the most common approaches are to examine co-authorship and co-patenting ties, as we did (e.g., Ahuja, 2000; Phelps et al., 2012; Singh, 2005). Our findings indicate larger teams are involved in PCR follow-on activity. It follows that these larger teams would be part of larger individual networks of scientists, which would further enhance diffusion.[10] But these measures may not fully capture social networks. For instance, in the case of rDNA, shortly after Herb Boyer co-invented the technique, he taught it to Herb Heyneker, who was a post-doc in Boyer's lab. Heyneker then traveled to the Netherlands and to Switzerland, where he taught others how to perform the technique. As Heyneker recalled the interactions:

> Pieter Pouwels…wanted to learn the new technology, and made sure that he came to my lab in Leiden on a day-to-day basis for up to a month to really understand the ins and outs of the technology. Then he took it back to [his home institution]. … [Later,] I received an invitation from Charles Weissmann to visit his lab in Zurich with the goal to help to teach them some of the recombinant DNA technologies (Heyneker, 2004).

Thus, Heyneker describes the importance of direct personal contacts in facilitating the diffusion of knowledge about how to perform rDNA – and thus facilitating the diffusion of the rDNA technique itself. Yet the publication records for Heyneker, Pouwels, and Weissmann only partially capture these relationships: Heyneker and Pouwels have co-authored publications on rDNA, but Heyneker and Weissmann have not – even though Weissmann does have numerous publications with other co-authors on rDNA and even though he learned the technique from Heyneker. Such anecdotes provide evidence that co-publishing (and, almost certainly, co-patenting) networks – as we used in our study – are insufficient towards understanding the diffusion of knowledge through networks.

Another possible approach towards unpacking the role of social networks is by examining the events that facilitate and reflect such networks, such as symposia, guest lectures, and conferences. Of course, complete data are difficult to obtain. But as a rough assessment, we examine attendee lists for the first conferences on rDNA and on PCR. The 1973 Gordon Conference on Nucleic Acids was the first professional venue at which Cohen and Boyer presented their primary findings related to rDNA; the 1986 Cold Spring Harbor Symposium on Quantitative Biology was the first professional venue at which Mullis presented his findings related to PCR.

We draw upon archival records reporting the list of conference attendees to assess attendance overlap with the primary sample of scientists. This enables us to examine the extent to which the conference attendees at these pivotal meetings may have facilitated diffusion via subsequent publications and patenting. We report the results in Appendix Table A3 and Appendix Table A4. One-hundred and forty individuals attended the 1973 Gordon Conference (rDNA), whereas more than twice as many people (315) attended the Cold Spring Harbor Symposium (PCR). Moreover, the Cold Spring Harbor attendees were more likely than the Gordon Conference attendees to subsequently build on this work. Approximately 25 percent of Gordon attendees (33 scientists) later published or patented research that built upon the initial rDNA invention, whereas approximately 37 percent of Cold Spring Harbor attendees (117 scientists) later published or patented research that built upon the initial PCR invention.

Appendix Table A4 reports the results from a series of comparison of means between the conference attendees and the remaining larger sample of scientists that either published or patented within 15 years of the initial invention. Again, we report a stronger effect of diffusion from the Cold Spring Harbor Symposium (PCR) than the Gordon Conference (rDNA). Conference attendees of the Cold Spring Harbor Symposium produced more output (both publications and patents) at earlier panels. We also find that Gordon Conference attendees produced output at earlier panels; yet, their level of output did not differ from scientists that did not attend the conference. We recognize the very limited sample size for this latter set of statistics. However, taken together these results indicate that attendees of the Cold Spring Harbor Symposium facilitated greater levels of early-stage diffusion for PCR. They also provide evidence on the importance of events like conferences towards facilitating diffusion.

#### 5.2.6. Synthesis of Factors

As the foregoing analysis highlights, no factor on its own is sufficient to explain why PCR diffused more broadly than rDNA. Rather, a

[9] We document this empirically in Fig. 3 Panel B for publications when we examine the breadth of study. The results are not conclusive for patents.

[10] As an additional empirical extension for Fig. 4 Panel A, research teams with prior connections increase the size of their co-authoring network over time more than new entrants. This trend holds for publication output. Results are available upon request.

confluence of factors – including organizational origin, licensing strategies, complementary assets, industry stage, and social networks – shaped the diffusion of each technology. In turn, we illustrate how a complete understanding of the breadth and timing of diffusion must account for this plurality.

## 6. Discussion and Conclusion

Scholars have devoted considerable attention to understanding the diffusion of scientific knowledge and have documented a wide array of factors that shape both access and diffusion. Our study marks an attempt to understand how these factors work in consort to explain how two comparable – and enormously important – biotechnology inventions nonetheless exhibit rather different diffusion patterns. Specifically, our study makes three key contributions. First, we underscore the importance of examining multiple factors in order to understand diffusion processes. Second, we address the literature on university-firm distinctions, particularly by demonstrating how such organizational distinctions alone may be insufficient and even misleading. Finally, we make a case for empirical plurality, encouraging the use of multiple measures and approaches in innovation studies. We elaborate on each of these contributions.

### 6.1. Multiple Factors Underlying Diffusion

Prior scholarship has identified numerous factors that shape the diffusion of knowledge, including organizational origin, licensing terms, complementary assets, industry stage, and social networks (e.g., Feldman and Kelley, 2006; Fosfuri, 2006; Perkmann et al., 2013; Siegel et al., 2003). Although this work implicitly recognizes that these factors may operate in tandem, our work explicitly demonstrates the importance of considering multiple factors simultaneously. Indeed, had we focused on a single factor, we might well have reached the wrong conclusion – or, at least, an incomplete one – about diffusion trends. For example, had we followed a long line of literature in presuming that the university- versus firm-origin of rDNA and PCR might forecast their diffusion, we would have been wrong (e.g., Henderson et al., 1998; Jaffe, 1989).

Of course, a key suggestion to emerge from our analysis is that factors not only act simultaneously, but also *interact* with one another. For example, our qualitative evidence suggests that university-based researchers are not incentivized to develop complementary assets, such that organizational origin and the development of such assets are intertwined, not independent, factors. Indeed, by highlighting this interaction, our work adds a new consideration to studies that question whether university-based researchers truly are committed to open sharing. Specifically, some work establishes that commercial interests may lead to decreased sharing (e.g., Blumenthal et al., 1996), while other work highlights how academic interests, too, may be associated with secrecy rather than sharing (e.g., Murray, 2010; Nelson, 2016a). Our work builds on these insights by suggesting that even if university-based researchers openly share findings, as they did with rDNA, the lack of incentives to develop complementary assets may nonetheless limit diffusion. In other words, diffusion may depend on the *interaction* between organizational norms and complementary assets.

Other factors that we explore, too, are almost certainly interrelated. For example, licensing strategy can shape the generation of complementary assets, as the experience with PCR highlights. As another example, the size of social networks is inherently related to the stage of an industry. Rapidly growing industries tend to have more players and, therefore, larger – but potentially more disperse – social networks. In other words, our study encourages future scholarship to explore both the multitude of factors that shape diffusion and the interactions between them. In this way, our work encourages researchers to move beyond the investigation of diffusion *patterns* to also explore diffusion *processes*.

### 6.2. Contextualizing University-Firm Distinctions

Our study holds special relevance for the literature on university technology transfer and university-firm distinctions. This literature has focused on a wide array of topics, including research spinouts (e.g., Fini et al., 2011; O'Shea et al., 2005; Wright et al., 2006), technology transfer offices and policies (e.g., Breznitz and Feldman, 2012; Goldfarb and Henrekson, 2003; Kenney and Patton, 2009; Siegel et al., 2003), and regional ecosystems (e.g., Clarysse et al., 2014; Kenney, 2000). One undercurrent of some of this work is the presumed openness of universities as opposed to commercial firms, which could lead to increased diffusion from universities; if universities are more open than firms, then knowledge generated in universities might spread faster and wider. Our study lacks the counterfactual to test this assertion directly; we cannot say how PCR might have diffused had it been invented in a university or how rDNA might have diffused had it been invented in a firm. Yet, the fact that we demonstrate how a firm-invented technology, PCR, spreads more widely than a comparable university-invented technology is instructive. First, it challenges the idea the firms are "closed." Indeed, prior work by Hicks (1995), Nelson (2016a), Owen-Smith and Powell (2004), and others demonstrates that firms can, in fact, be quite open with their work. Even in their foundational work on public versus private science, Dasgupta and David (1994) distinguish between the logics that guide an individual researcher and the organizations, like universities and firms, that have been the focus of much prior scholarship. They write, "the same individual, we suppose, can be either [publicly- or privately-oriented], or both, within the course of a day" (Dasgupta and David, 1994, p. 395). In other words, the proclivities of individuals in particular moments may be just as influential as the kind of organizations for which they work (see also Fini and Lacetera, 2010).

Second, and building on the point above regarding plurality, diffusion appears to be dependent on a wide array of factors, and the type of inventing organization may not be the most important among them. In fact, as our discussion of complementary assets highlights, firms may be advantaged in some ways (and, of course, disadvantaged in others). Collectively, these insights do not aim to minimize or even challenge the important work on university-firm distinctions; obviously, universities and firms vary along a number of dimensions. But they do suggest that simple university-firm dichotomies are likely to be inadequate for understanding knowledge diffusion processes.

### 6.3. Measurement Plurality

Finally, our work holds important methodological implications. In the interest of completeness, we trace diffusion through publication citations, patent citations, and the growth of patent classes. Our work thus enables us to compare across these measures and to demonstrate the importance of using multiple measures to paint a complete picture of diffusion. For instance, had we only traced publication citations and not patent citations, we would have concluded that diffusion trailed off for PCR as compared to rDNA around panel year seven (refer to Figs. 2 and 4). In contrast, patent citations indicate continued increases in magnitude through year 11 for PCR. Even more notably, had we traced only patent citations, we would have underestimated the divergent trends in diffusion. Moreover, we would have concluded that the geography of diffusion contracts over time, when the publication data clearly show increased geographic spread.

Patent and publication citations also depict different diffusion patterns in terms of the types of organizations involved, breadth of study, and composition of inventors. For example, patent application trends indicate the breadth of study of follow-on PCR patents *increases* over the panel, while publications indicate that the breadth of study *decreases*. And while the composition of new rDNA entrants is again relatively flat over time, publication trends would lead us to believe that PCR's new entrant composition declined over time, while the patent application trends show an increased new entrant pool. Taken together, the different

measures reveal that we would have dramatically understated and mischaracterized the differences in diffusion trends had we relied on a more limited set of metrics, as other studies have done. By illustrating how different measures can amplify or obscure different organizations and trends, our work thus adds to a growing chorus of work that encourages multiple measures of innovation and comparison across these measures (Feldman and Lowe, 2015; Fini et al., 2018; Nelson, 2009).

In addition, our work highlights the potential gains from employing a mixed-methods approach to the study of scientific practices (Bansal and Corley, 2011; Koppman and Leahey, 2019). Indeed, such an approach may be the only way to fully uncover and examine the multitude of factors that shape diffusion in particular cases. At the same time, even our use of this approach is limited. For example, it is difficult for us to disentangle which of the factors that we identify are more or less influential – and when – in shaping diffusion patterns. Such observations underscore that even as our work serves as a call for plurality – of measures, approaches, and factors – it also unearths related challenges.

### 6.4. Limitations

Our work faces a number of limitations, which suggest possibilities for future research. First, and most obviously, we consider only two technologies. Future work might expand this by utilizing twin or simultaneous discoveries to track larger trends. Though scaling the number of technologies would likely yield a tradeoff in the granularity of tracing diffusion, a set of recent studies has started to employ this methodological approach (Bikard, 2020; Hill and Stein, 2019). Second, we focus only on biotechnology and, within biotechnology, only on techniques (as opposed to products). Biotechnology is enormously consequential, both economically and socially, and prior work indicates that it is a focal area for university knowledge transfer. Nonetheless, it is possible that processes look different for products and/or in different fields. Future research, therefore, might fruitfully compare and contrast across fields. Third, the techniques that we investigated are now decades old. This selection enabled us to trace diffusion over many years and to control for more recent changes in university technology-transfer arrangements and policies. Yet, the point remains that the biotechnology industry, university commercialization, and university-firm collaboration patterns have changed substantially (Bercovitz and Feldman, 2008; Perkmann et al., 2013). Finally, beyond the five factors that we consider, there may be other factors that influence diffusion – particularly if an analysis is focused on other industries, time periods, and/or geographies. Thus, future work may well move beyond our analysis to uncover and examine an even wider range of factors and relationships between them.

Ultimately, our work suggests that despite much insight into knowledge diffusion, there remains much to discover. Given the scale and scope of challenges facing the world, better understanding the dynamics of diffusion remains an important task.

## Declaration of Competing Interest

None.

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### Data Access

Data and code for the primary analysis can be found at https://doi.org/10.7910/DVN/1BZASG.

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## Supplementary materials

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