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AMPHIBIOUS ENTREPRENEURS AND THE EMERGENCE OF ORGANIZATIONAL FORMS

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We study the emergence of organizational forms, focusing on two mechanisms—reconfiguration and transposition—that distinguish the founding models of the first 26 biotechnology companies, all created in the industry's first decade, from 1972 to 1981. We analyze rich archival data using hierarchical cluster analysis, revealing four organizational variants of the dedicated biotech firm (DBF). Three were products of reconfiguration, as executives from Big Pharma used past practices to incorporate new science. One DBF variant resulted from 'amphibious' scientists who imported organizing ideas from the academy into their VC-funded start-ups. We argue that such transpositions are fragile, yet charged with generative possibilities. Copyright © 2012 Strategic Management Society.

INTRODUCTION

Entrepreneurial activity is so often equated with economic growth and innovation that its role as an engine of social invention has been comparatively overlooked. We, therefore, examine how entrepreneurs cobble together different practices and templates to fashion new organizational forms and theorize why these forms vary in the degree to which they transform and reorder the social world. To do so, we utilize an original data set that affords insight into the building blocks used to assemble the first generation of biotechnology companies. Central to our inquiry is a conceptual distinction between two types of recombination: *reconfiguration,* a mechanism through which familiar attributes and elements are put together in new but recognizable ways; and *transposition*, a mechanism through which attributes and elements are introduced into foreign domains, spawning new-to-the-world forms of organizing.

Our temporal setting is the 1970s, an era rife with scientific breakthroughs in the biological sciences, but murky with respect to the commercialization of these discoveries. Initial ideas about how to convert novel science into a business were routinely wrong. The retrospective accounts of key participants stress that if they had known all the obstacles and costs, they surely would not have undertaken their efforts (Perkins, 2002; Byers, 2006). In a departure from the linear process of discovery and exploitation often described in the entrepreneurship literature, we show that chance, necessity, and naïveté—rarely mentioned in explanations of entrepreneurial outcomes—were essential in the invention of new organizational models (Boyer, 2001; Hughes, 2011: 34–44).

An apt image for this process of genesis is playing with Lego pieces: some parts fit together, some do

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not, and some are attachable but unstable. If new pieces from a different Lego set are introduced, previously unrecognizable shapes often result. In a similar manner, we contend, new organizations are created. We argue that such emergence is fundamentally relational. In building new models, individual agency takes a back seat to the social forces of juxtaposition, where at the intersection of previously separate networks, ideas and models flow and new career pathways are formed (Powell *et al*., 2005; Padgett and McLean, 2006; Vedres and Stark, 2010). From this vantage point, the earliest biotechnology companies are odd compounds of elements from the worlds of academic science, venture finance, and the established pharmaceutical industry. Guided by habit as much as foresight, biotech's founding scientists, financiers, and managers created new organizational forms that were neither entirely random nor fully predictable, in some cases reconfiguring existing practices, in others forging novel arrangements with no recognizable precedent and little chance of survival.

We emphasize that our goal is *not* to evaluate which firms proved to be commercially viable. Instead, we seek to understand *how* and *why* certain attributes combined. Our approach conceives of organizational forms as bundles of attributes and practices. In a nascent field, uncertainty and controversy surround what a firm should look like and what elements it should contain. Our aim is to explicate how familiar practices were innovatively rearranged and how foreign elements were thrust together to trigger social invention.

We create an original data set that affords insight into how the different attributes that formed the first generation of companies were assembled. Founded in the late 1970s and early 1980s, these firms were unusual for their time because they hewed neither to an industrial nor an academic model. They emerged out of the academy but utilized elements from the fields of finance and industry to produce a new type of science-based firm. To be sure, technologically sophisticated companies had long used scientific knowledge to create novel products, and university labs were not averse to industry-sponsored research projects. But the biotech model was different in three respects. First, these firms attempted to both advance science and derive economic value from such advances. Second, a considerable portion of the investment in these early firms was contingent on the quality of the science they created. Third, no university department followed the collaborative approach to science that many of these companies pursued, in which a researcher would drop what she was working on to help others advance their project.

We employ hierarchical cluster analysis (HCA) to identify two fundamentally different models among these early firms: a commercially oriented prototype and a science-oriented prototype. We find that not all possible options for organizing bioscience research were pursued during this formative era. For example, no new nonprofit research institutes were created, nor did any large corporation attempt a stand-alone corporate R&D enclave along the lines of Bell Labs. Nor did an established player build an incubator to shepherd start-ups. Our analysis of how elements were pieced together suggests that some models were not conceivable, whereas others depended upon which attributes adhered to, and followed on, one another.

The archival evidence illuminates how ideas and organizational practices crossed significant boundaries and eventually combined to produce novel forms of organization and new careers. These new spaces were created by trespassers, not by professional managers, university administrators, or government officials. We label such boundary crossers 'amphibious' entrepreneurs because they occupied positions of influence in disparate social worlds: the academy and the biotech start-up. More generally, we assert that amphibious entrepreneurs play a crucial, if unintentional, role in the emergence of new forms by carrying practices and assumptions across domains.

RECONFIGURATION VS. TRANSPOSITION: A PRAGMATIST VIEW OF ENTREPRENEURSHIP

All novelty involves some form of recombination, but we argue that it matters greatly whether the recombination incorporates familiar elements (i.e., borrowed from related or adjacent sectors or industries) or foreign components imported from distant settings. Hounshell (1984), for example, documents how Henry Ford and his advisors appropriated practices from other production industries—flour milling, food canning, breweries, and stockyards—to create the modern assembly line. More recently, the movement of digital technology from computing to photography provides another example of an innovative *reconfiguration* (Tripsas, 2009). In both cases, the imported elements were recognizable and credible. They were proximal

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combinations drawn from 'the adjacent possible' (Kauffman, 2000), a kind of shadow future that hovers on the edges of the current state of things—a map of the ways the present can reconfigure itself.

In contrast, some recombinations involve the movement of ideas and practices from a *nonadjacent* domain, across social terrains to a place where they are not initially recognized. Scholars have labeled these *transpositions.* The best seller *Moneyball* provides an example: novel management practices came to major league baseball via Wall Street analysts, whose ideas about arbitrage resulted in new statistical metrics that supplanted decades-old player evaluation practices and were labeled sacrilege by traditional talent scouts (Lewis, 2003).

Clearly, such transpositions are distinguished by the distance that the ideas and practices travel. We propose that social distance has both *cognitive* and *moral* dimensions.[1] On the cognitive side, transposed practices are not readily recognized; they seem out of context, off-key, or irrelevant; they do not fit existing category structures. On the moral side, transpositions may be attacked as inappropriate, outrageous, even profane. We find Howard Becker's (1963) work on 'moral entrepreneurship' useful in this regard. Becker characterized moral entrepreneurs as 'rule creators' who label deviance and mobilize support to proscribe it. Our view of transposition involves a different sort of moral entrepreneur—one whose insistence on doing things the 'wrong' way rewrites the rules. Such violations are much less frequent and less likely to be successful than reconfigurations, which take place on uncontested moral ground. We argue, however, that even failures of this sort generate 'fresh' action, which may be subsequently exploited by others in different domains (White, 2008: 279–283).

As further illustration of the difference between reconfiguration and transposition, we emphasize that innovation is an interstitial phenomenon (Owen-Smith and Powell, 2004). Reconfigurations occur between domains characterized by cross-traffic and ongoing conversation—that is, across existing interstices. Transpositions occur between domains where traffic is scarce and communication infrequent, thus forging new interstices. As Simon (1982) pointed out, interactions within and between subsystems are of different orders of magnitude. By extension, because they involve interactions between previously distant social systems, transpositions are both less likely to be accepted and more likely to produce radical social novelty than 'within-system' reconfigurations.

Symbolic interactionist scholars refer to transposition-like activity as traffic across social worlds (Strauss, 1978; Fujimura, 1987), wherein participants create new social spaces and synthesize existing cultural practices in unfamiliar circumstances. Although the effect can be revolutionary, the intent need not be. Padgett and McLean (2006) trace the invention of the partnership form in Renaissance Florence, with its unforeseeable spillovers in the realms of art and science, to an attempt by ruling elites to preserve the existing social order. We similarly contend that the novel organizational forms that emerge from transpositions owe more to pragmatic action than to visionary planning. Put simply, in the face of unprecedented situations, people search and experiment. Drawing on their existing knowledge and routines, they survey their social worlds for cues about appropriate action. People whose cognitive frameworks and moral assumptions bear the imprint of distant social worlds are more likely to forge new tools for coping with an unfamiliar domain because their knowledge, routines, and networks are imported—*transposed*—from another context.

As an illustration of how a pragmatist perspective shapes our view of agency, consider the first encounter in 1976 between the eventual cofounders of Genentech, biotech's earliest success story. Recently let go from his analyst job at a venture capital firm, Robert Swanson cold called UCSF associate professor Herbert Boyer. After ascertaining that Swanson was going alphabetically through a list of attendees at a recent scientific conference and that Stanford scientist and future 1980 Nobel Prize winner Paul Berg had refused a meeting, Boyer suggested an appointment at 4:45 p.m. on a Friday (Boyer, 2001; Swanson, 2001). Such a response affords many potential interpretations: 'You are unimportant and have only 15 minutes;' 'If the meeting goes well, we can get a drink;' 'I'd prefer that my colleagues not see me meeting you;' 'Traffic and parking on a Friday afternoon around UCSF are terrible, so this will test his mettle,' etc. Our point is that the circumstance was pregnant with multiple rationales and opportunities and could have as easily led nowhere as to the founding of Genentech.

The literature on organizational foundings emphasizes that entrepreneurs must work especially hard to mobilize resources to launch new organizations (Stinchcombe, 1965; Freeman, Carroll, and Hannan,

[1] We thank Joachim Lyon for helping us clarify these two dimensions.

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1983; Burton, Sorenson, and Beckman, 2002). Nascent fields are characterized by ambiguity. There is an absence of a dominant logic that guides activity and a void regarding product definitions and industry structure (Eisenhardt, 1989; Hargadon and Douglas, 2001; Santos and Eisenhardt, 2009). Clearly, the resource-building aspect of new venture formation is critical. But we also suggest that coming up with a novel template in an unfamiliar domain might be easier when the canvas has yet to be painted—an advantage enjoyed by industries whose founding companies are all *de novo* entrants (McKendrick *et al*., 2003). Newcomers to a domain are unencumbered by the baggage of established practices (Kaplan and Tripsas, 2008). Instead, their baggage comes from their domain of origin. When introduced into a foreign context, even ingrained *modi operandi* afford startling possibilities for novelty.

THE EMPIRICAL SETTING

Many analysts of the early days of biotechnology have assumed that the economic opportunities created by scientific advances in the 1970s were transparent to entrepreneurs and that these breakthroughs clearly opened up new markets for companies to exploit (Kenney, 1986a; Orsenigo, 1989; McKelvey, 1996). Seen in this Schumpeterian fashion, the subsequent organizational transformations in both the academy and industry followed directly from this technological disruption. We want to challenge the idea that technological opportunity is paramount in the emergence of organizational forms. Without question, laboratory advances had outpaced commercialization. Ron Cape (2006:16)), a cofounder of one of the first biotech companies (Cetus), captured the pent-up feeling of the times: 'It was like maybe a dam waiting to burst or an egg waiting to hatch, but the fact is, there were a lot of Nobel Prizes in molecular biology, but no practical applications.'

Yet the people who built the commercial field of biotechnology lacked a formal blueprint for constructing a new organizational form. Brook Byers, venture capitalist and founding CEO of Hybritech, San Diego's first biotech company, put it bluntly: 'We did not have the business model mapped out, or the ultimate value proposition, which are all things we do today in doing a start-up. We're much more sophisticated now. Back then, we didn't have any of that' (Byers, 2006: 21–22). Instead, these founders carried tacit blueprints from the domains they knew well. Those who were new to commercial activity brought with them governance practices from running academic labs (Zucker and Darby, 1996; Jong, 2008). Refugees from the pharmaceutical world carried a very different model of corporate R&D. These scientists, financiers, and business people all drew on their existing networks and prior skills to develop a form that operated according to quite different principles from either the traditional vertically organized corporate hierarchy or the university laboratory. A new model of a science-based company was constructed, based on fundamental scientific research, horizontal flows of information, porous organizational boundaries, a strong reliance on intellectual capital and collective know-how, and a strategy of pursuing innovation through collaborative ventures with other organizations.

Few, if any, of the participants set out to create new organizational models. Rather, the unprecedented challenges of organizing life science businesses created an era of ferment. Some founders, such as Amgen's George Rathmann and Genzyme's Henri Termeer, felt confined by existing corporate constraints and practices. Others, such as Ron Cape and Peter Farley at Cetus, sought to minimize formal organization in favor of a freewheeling, 'anything goes' environment. Genentech was a virtual entity for two years, using the UCSF laboratory of one of its cofounders as an R&D site—which prompted a nervous academic colleague to put a lock on the freezer in his lab, for fear of losing his proprietary reagents (Penhoet, 2001:96–97).[2] The venerable Salk Institute got into the fray, creating a commercial spin-off (SIBIA). Even Harvard, a bastion of academic purity, entertained a proposal to invest endowment funds in a biotech venture to be headed by Mark Ptashne, then-chair of molecular biology (Robb, 1981). When Harvard faculty protested, Ptashne secured external VC funding and launched

[2] In the first two years of its existence, 1976 to 1978, Genentech had no labs or location of its own; instead it had contractual agreements with cofounder Herbert Boyer to pursue research on insulin and human growth hormone in his lab at UCSF and with City of Hope Medical Center researchers in Los Angeles to work on synthetic DNA. Although tensions arose over Boyer's starting a firm inside the university and an investigation was conducted by the faculty senate committee on rules and jurisdiction, the university administration eventually approved the relationship by reclassifying it in more conventional terms as an R&D contract and licensing agreement (McKelvey, 1996: 99–107).

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the company anyway (Genetics Institute). Centocor began by licensing a patent for a monoclonal antibody developed by two of its founders at the Wistar Institute on the University of Pennsylvania campus; the license was later seen as a conflict of interest, and the Institute required that the two scientists relinquish their seats on Centocor's board prior to its IPO (Vaughan, 2000: 185).

These founding stories illustrate the initial absence of a dominant organizational design. Instead, a variety of novel (and in many cases, unstable) arrangements resulted from the introduction of new practices into old contexts, or the continuance of old practices in new contexts. As the constraints grew intolerable, groups of scientists, business people, and financiers established new venues to pursue genetic engineering. We turn now to a discussion of how we built a sample of these initial entities and coded their defining attributes.

DATA AND METHODS

Our sample is drawn from U.S.-based biotech companies founded from 1972 to 1981, the first decade of the nascent industry. The period begins with the founding of the first biotechnology firm (Cetus) and the presentation of the seminal Cohen and Boyer research on recombinant DNA at conferences (Cohen *et al*., 1973). We close the sampling window at the end of 1981, the year of Cetus' record-setting IPO and a year after Genentech's landmark public offering. By then, the regulatory environment had stabilized, with congressional and judicial actions that allowed venture capitalists to tap into new pools of money (a relaxed interpretation of the so-called Prudent Man Rule), encouraged universities to license scientific breakthroughs for commercialization (the Bayh-Dole Act, 1980), and permitted the patenting of man-made organisms (*Diamond v. Chakrabarty,* 1980). Our choice to focus on the industry's first 10 years is, thus, historically grounded, reflecting a founding era in which the widest variety of types of biotech ventures were formed (Kenney, 1986b; Kaplan and Murray, 2010).

Using a database collected by Powell *et al*. (2005), we identified all biotech-related firms founded from 1972 to 1981, resulting in a population of 52 potential candidates. To be included, firms needed to have pursued human health applications either from founding or within their first five years. This eliminated a number of botanical and veterinary genetics ventures, as well as companies focused on supplying the new field, yielding a final list of 26 companies dubbed dedicated biotech firms or DBFs.[3] A short lifespan was not grounds for exclusion; indeed, one of the early firms (DNAX) survived as an independent entity for less than two years before being acquired by Schering-Plough.

We gleaned information on each company from a variety of sources, including newspaper and magazine articles from the 1970s and 1980s, speeches, S-1 and 10K filings, company profiles from the *Mergent* and *Hoover's* online services, scholarly and popular books on the birth of biotechnology, and interviews with biotech pioneers. The Regional Oral History Office at UC-Berkeley's Bancroft Library was especially helpful; we combed more than 2,000 pages of interviews with scientists, entrepreneurs, venture capitalists, and early employees of the first biotech ventures. We also found relevant interview archives from the Chemical Heritage Foundation, the Smithsonian Institution, and the San Jose Tech Museum. We consulted numerous scholarly studies, including historical accounts (Kenney, 1986b; Wright, 1994; Rabinow, 1996; Hughes, 2001; Vettel, 2006), as well as doctoral dissertations and science journalism (Hall, 1987; Hybels, 1994; Teitelman, 1989; Robbins-Roth, 2000; Porter, 2004; Jones, 2005; Berman, 2007; Nelson, 2007). Where the documentary record was thin, we supplemented with semi-structured phone interviews with company founders. Each of these 10 interviews lasted from 45 minutes to two hours, generating 200 additional pages of interview data.[4]

Our analytical approach builds on comparative case methodology (Eisenhardt and Graebner, 2007), but we apply its inductive logic to a larger number of cases than is typical. We distilled the copious archival and interview data into histories of each

[3] The choice to focus only on human biotech, and not plant and veterinary science, has been made by numerous researchers (Audretsch and Stephan, 1996; Powell, Koput, and Smith-Doerr, 1996; Zucker and Darby, 1996; Oliver and Montgomery, 2000).

[4] To guard against *post hoc* impression management, we triangulated accounts from the interviews with real-time archival data, such as company press releases, IPO prospectuses, newspaper and magazine articles, and numerous books written during the mid-1980s on the burgeoning biotech industry. Here again, we sought direct statements, not retrospective reflections, from company founders. This allowed us to corroborate their recollections in recent interviews with statements recorded during the time period in question, with the aim of minimizing retrospective bias.

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firm's founding, iteratively refining a 'table shell' to ensure that we extracted the same information for all cases (Miles and Huberman, 1984). We were most interested in firm-level attributes that reflected distinct domains of both origin and function. Prior work identified three institutional sectors from which crucial elements of the biotech form were borrowed: science, finance, and commerce (Powell, 1996). Accordingly, we analyzed our cases for answers to three questions: (1) How did the firm engage with the world of science?; (2) How did it acquire funding?; and (3) How did it approach the market? For each firm, we listed the answers associated with these questions. This selective coding was a pragmatic necessity, allowing us to avoid the unrealistic task of cataloging hundreds of unique features exhibited by each of the 26 firms.

Our coding required complete agreement between the two researchers. We discussed any disputes until all differences were resolved regarding an attribute's manifestation in the company and its predominant domain of origin.[5] Once the focal attributes were selected for each case, we compiled and consolidated lists across all 26 firms, resulting in a master list of 28 notable characteristics that were central to how the first-generation biotech firms approached the scientific, financial, and commercial aspects of their enterprises.

Given our interest in how different configurations of attributes were assembled into stable groupings, we winnowed the list to eliminate those that were shared by fewer than four DBFs. Our reasoning was that unless an ingredient was salient in more than 15 percent of the cases, it could not be considered the raw stuff of assemblage. Thirteen attributes met this criterion.[6] Table 1 provides a brief description of the attributes, the domain from which they were drawn, and their frequency of occurrence. Arriving at these 13 required a set of decision rules precise enough to accommodate yes/no coding. The scheme we used could be reliably replicated by other researchers.

Table 2 shows a correlation matrix for these 13 attributes, along with the location of each company and its year of founding. Note the weak correlations between year, location, and attributes. There is no evidence of regional DBF variants (e.g., 'Bay Area' vs. 'Boston' models), as in Saxenian's (1994) work on information technology. Moreover, there is no pattern of temporal accumulation, with later firms copying the earliest ones. Nor do the attributes coalesce into a single, emergent DBF identity near the end of the 10-year observation window. Correlations between pairs of attributes are difficult to interpret given the small sample (n = 26, df = 24), although correlations greater than 0.5 (Pearson's r) are generally considered statistically significant at the $p < 0.05$ level even for samples of this size (Cohen, 1992). Using this criterion, correlations can be definitively identified between two pairs of attributes: a positive relationship ($r = 0.573$) between 'amphibious' founders and publishing and a negative relationship ($r = -0.575$) between having an academic scientist in a top management role and the hiring of a senior manager from the pharmaceutical industry. The relationships between these pairs of attributes make intuitive sense, and their fateful implications for the clustering are discussed later.

With these 13 attributes coded '1' (present) or '0' (absent) for each of the 26 firms, we generated a rectangular 'attribute-by-firm' affiliation matrix. Such matrices have long been used to determine social structure within network data (Breiger, 1974; Wellman and Berkowitz, 1988). Our objective is analogous: to determine underlying patterns of cohesion among attributes that, prior to these early biotech ventures, had not appeared together in stable configurations. The sample size prohibits approaches favored by inductive case studies, which typically rely on either manual or mental techniques. Indeed, 'tweener' sample sizes have been problematic in organizations research: too large for unaided cross-case comparison and too small for OLS-based analytics. Therefore, we employed hierarchical cluster analysis (HCA), a proven multivariate method, for our cross-case analysis (Tan, Steinbach, and Kumar, 2005). HCA is well suited to explore what we term a sociology of compounds—the ways in which diverse elements form composites. Indeed, Ruef (2000: 706) employed HCA in tracing the emergence of organizational forms in health care, arguing that 'many of the most interesting organizational forms are more properly seen as the evolutionary

[5] We soon discovered that the same attribute served different purposes for different companies. For instance, a 'just-off campus' location allowed some DBFs to continue active participation in scientific research; for others, such locations merely provided access to commercializable ideas. The different meanings attached to identical practices are discussed in the findings.

[6] To test our attribute selection process, we conducted the hierarchical clustering analysis (HCA) described later with the full set of 28 attributes, as well as with the reduced set of 13. The resulting clusters did not change. Rather, with the idiosyncratic attributes included, three of the firms simply did not attach to any cluster and remained outliers.

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Table 1. Attributes of early biotech companies

Attribute and domain of origin	Criteria for coding	No. (%) of firms for which code = 1
1. Research contracts with large corporations (finance)	Research contracts cited as a critical source of operating revenue during company's first five years	21 (81%)
2. Noted scientist(s) (science)	At least one founder listed in *American Men & Women of Science*[1]	19 (73%)
3. 'Just-off campus' location (science)	Original company address located within 10 driving miles of the research institution with which scientific founder(s) associated	18 (69%)
4. Amphibious scientist(s) (science)	At least one founder was a company officer and (1) occupied an academic position simultaneously or (2) soon returned to full-time academic research	14 (54%)
5. Nontherapeutic focus (commerce)	Company's espoused strategy centered on diagnostics, vaccines, or other nontherapeutic products	11 (42%)
6. Nontraditional initial public offering (finance)	Firm went public prior to having (1) any products in its pipeline and/or (2) any patented intellectual property	11 (42%)
7. Pharma veteran hired to run the company (commerce)	Within the first five years, company hired an experienced pharmaceutical company executive as president or CEO	10 (38%)
8. All-star scientific advisory board (science)	Firm (1) had a formal scientific advisory board (SAB) and (2) this SAB included at least one renowned scientist	9 (35%)
9. Scientist in charge (science)	Academic scientist served as president or CEO at some point during first five years of the company's existence	9 (35%)
10. Encouraged scientific publication (science)	Firm's publication record in its first five years was above the sample median on quantity and quality measures[2]	8 (31%)
11. Prior entrepreneurial experience (commerce)	At least one founder had been involved in a prior start-up	7 (27%)
12. Growth through acquisition (commerce)	Within the five years following its founding, the firm made at least one acquisition	6 (26%)
13. Venture capitalist served in operational role (finance)	Venture capitalist (1) occupied executive role or (2) actively intervened in day-to-day operations during first five years	5 (19%)

[1]*American Men and Women of Science* has been published since 1906. Nominees are selected by the editors or recommended by current listees and by leaders of academic, government, and private research programs and associations. Inclusion in the book is based primarily on 'research activity of high quality in science as evidenced by publication in reputable scientific journals' (GCL, 2012).

[2]All publications that list a company scientist as an author were totaled for the five years following the year the company was founded. *Quantity* was measured as the total number of publications (min = 0, max = 174, mean = 36.77, and median = 31). Quality was measured as the average number of non-self citations per publication (min = 7.27, max = 425.43, mean = 85.44, and median = 70.6).

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Table 2. Correlations of organizational attributes

Attributes	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Geographic location of venture	1														
2. Year founded	0.158	1													
3. Noted scientist founder(s)	–0.205	–0.042	1												
4. Amphibious scientist founder(s)	–0.158	–0.142	0.482	1											
5. All star science advisory board	–0.013	–0.144	–0.105	–0.137	1										
6. Encouraged scientific publication	–0.298	–0.120	0.480	**0.573***	–0.077	1									
7. Academic scientist in charge	0.282	0.121	0.259	0.187	–0.359	0.256	1								
8. 'Just off campus' location	–0.200	0.093	–0.029	0.051	–0.040	0.356	0.135	1							
9. Research contracts with large cos.	0.133	–0.086	0.144	0.331	0.150	0.386	0.150	–0.114	1						
10. Venture capitalist held operational role	–0.133	–0.005	–0.144	0.060	0.260	–0.185	–0.355	0.114	–0.010	1					
11. Nontraditional IPO	–0.087	0.013	–0.007	0.168	0.195	0.123	–0.132	–0.104	0.023	–0.220	1				
12. Grew by acquisition	0.069	–0.023	–0.285	–0.225	0.177	–0.058	–0.015	–0.426	0.036	–0.036	0.085	1			
13. Prior entrepreneurial experience	0.024	–0.283	–0.023	–0.308	0.470	–0.123	–0.442	–0.159	–0.144	–0.076	–0.169	0.285	1		
14. Pharma veteran hired to run the co.	–0.010	0.251	–0.411	–0.378	0.089	–0.463	**–0.575***	0.013	–0.216	0.417	–0.037	–0.058	0.233	1	
15. Nontherapeutic focus	0.196	–0.352	–0.007	0.012	–0.132	–0.197	0.195	–0.104	–0.175	–0.023	–0.103	0.085	0.007	–0.037	1

* $p < 0.05$

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product of two or more parent forms.' HCA, then, accommodates our focus on the assembly of attributes borrowed from three 'parent' forms (academic science, venture finance, and pharmaceutical commerce).

Each of the 26 companies is represented by a unique vector of dichotomously coded attributes. We computed distances between each pair of company attribute vectors using the Jaccard matching coefficient, defined as the size of the intersection divided by the size of the union of the sample sets. This coefficient is subtracted from one to yield the Jaccard distance between a pair of companies, A and B:

$$J_\delta(A, B) = 1 - J(A, B) = \frac{|A \cup B| - |A \cap B|}{|A \cup B|}.$$

The result is a symmetrical 26 × 26 matrix of numeric distances between each pair of companies. This dissimilarity matrix forms the input to the hierarchical clustering analysis, which systematically agglomerates observations, starting with those that are least dissimilar and progressing until all observations are members of a single cluster.[7] In effect, the technique searches for identical patterns of attributes, iteratively relaxing the standard of exact correspondence to produce a series of ever-larger clusters. The technique seeks to optimize within-cluster similarity and between-cluster dissimilarity simultaneously (Rawlings and Bourgeois, 2004). The result is graphically represented as a textual dendrogram, sometimes referred to as an 'icicle diagram,' presented in Figure 1. Reading from top to bottom, the diagram displays the order in which the earliest biotech firms clustered together, based on similar attribute profiles.

As with most clustering procedures, HCA does not compute an optimal number of clusters. Our decision was aided by a common measure of cluster adequacy, Krackhardt's E-I ratio (Krackhardt and Stern, 1988).[8] The ratio ranges in value from 1 to −1. An E-I ratio of 1 would indicate clusters of companies with no internally shared attributes. In our data, this limit is approached at the lowest level of agglomeration (i.e., where the most similar two companies cluster together and each of the remaining 24 companies is considered its own cluster). At the other extreme, an E-I ratio of −1 would indicate a cluster in which *all* attributes were shared (i.e., all 26 companies would have identical profiles).

We plotted the E-I ratio against the number of clusters for each level of agglomeration. The plot revealed two 'elbow' points, at four and nine clusters (see Figure 2). We analyzed the change in slope of the best fit line before and after $x = 9$ and $x = 4$, determining that the change in the E-I ratio was much more drastic below four clusters. At fewer than four, the agglomeration rapidly erases meaningful dissimilarities between groupings of firms; at greater than four, within-group similarity increases at a decreasing rate, adding scant explanatory purchase.

Based on these four clusters, we parsed the original affiliation matrix to create an aggregate attribute profile for each group of companies. Comparing these attribute profiles clarifies which elements were most consequential in determining the branching structure. Put differently, the cluster profiles reveal how new organizations in an emerging field vary in form. The final step in our analysis was to reexamine the detailed firm case histories by cluster, gleaning insights into what McKendrick *et al*. (2003: 63) have termed the 'composition rules about appropriate combinations of features' in emergent forms. We turn next to an explication of these patterns of combination.

FINDINGS

The results of our analysis are fittingly framed by a comment made by Robert Luciano, CEO of Schering-Plough at the time his pharmaceutical firm acquired DNAX, a tiny Palo Alto-based start-up, in 1982. Luciano said, 'Schering-Plough is not in business to do research. It's in research to do business' (Kornberg, 1998: 138). Not only does the phrase portray the

[7] Other analysts have used the more common Euclidean distance measure to compute dissimilarities (cf. Ruef, 2000). In a comparison of various distance measures, however, Finch (2005: 96) determined that Euclidean distance is less appropriate for dichotomous data, commenting further that 'the simplest of the four measures of distance, the Jaccard index, works as well as its more complicated competitors in terms of correctly grouping individuals based on a set of dichotomous variables.' In the spirit of choosing the simplest measure, we chose Jaccard distance as the input for our cluster analysis.

[8] Typically used in social network analysis, the E-I ratio is computed according to the following formula: (# external ties-# internal ties) / # total ties. In our data, a 'tie' represents a shared attribute among firms. Thus, the E-I ratio provided a computational basis for balancing commonality within clusters and differentiation between clusters.

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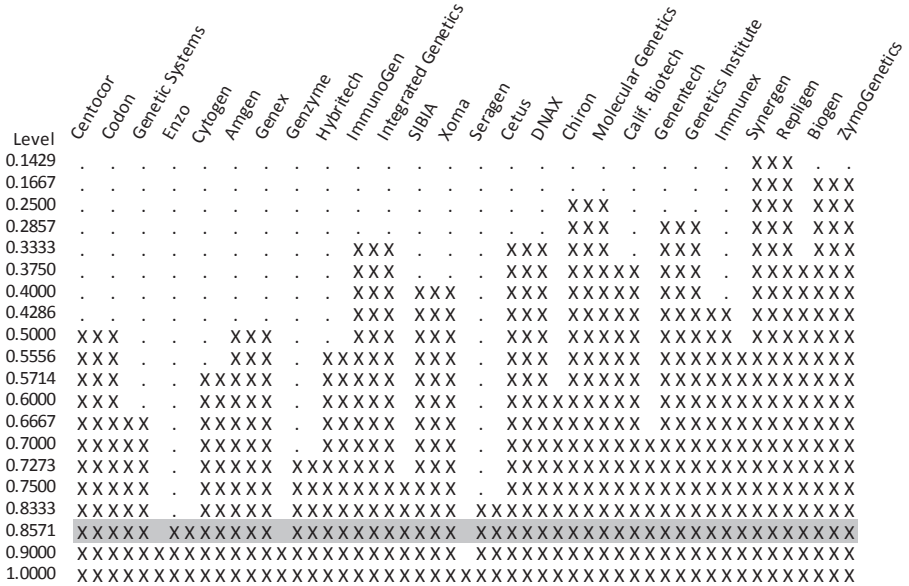

Figure 1. Results of hierarchical clustering*

*This textual dendrogram is read top to bottom, showing which companies were the first to cluster (Repligen and Synergen, based on minimal dissimilarity) and proceeding downward as the clusters tolerated greater dissimilarity. The vertical axis indicates the distance at which the clusters were agglomerated at each level. The level highlighted indicates the number of clusters—four—we deemed optimal, based on the E-I ratio (see Figure 2). Clusters were computed using the hierarchical clustering tool in UCINET 6.0. We employed the 'complete-link' method (i.e., 'farthest neighbor'), which computes similarities on the basis of the similarity of the member of the new cluster that is least similar to each other case not in the cluster.

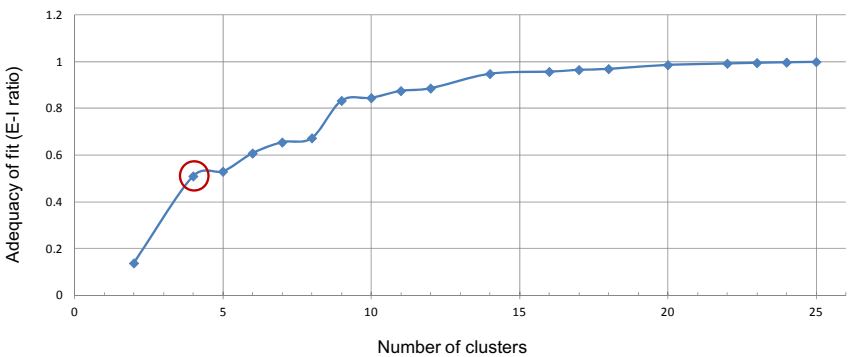

Figure 2. Determining the optimal number of clusters

Note: The elbow point circled on the above plot suggests that four clusters offer the best fit. At fewer than four clusters, the agglomeration rapidly erases meaningful dissimilarities between groups of firms; at greater than four clusters, within-group similarity increases at a decreasing rate, adding little explanatory power.

collision of values and organizing principles that propelled the earliest biotech ventures, it also evokes the two mechanisms—transposition and reconfiguration—that resulted in different degrees of organizational novelty. On the one hand, reorienting entrepreneurial activity to the purposes of basic life science research required unprecedented financial and organizational gymnastics (transposition); on the other hand, harnessing complex and costly bioscience research to the goals of business demanded innovative admixtures of existing commercial practices (reconfiguration).

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The cluster analysis reveals critical constellations of attributes that were associated with scientific vs. commercial primacy. Starting with all 26 DBFs (the 'base' of the icicle diagram in Figure 1), the sample initially divides into two large clusters of 13 firms each. The first cluster remains intact through five successive reductions in allowable dissimilarity, losing only one outlier (Seragen). This group, labeled Cluster 1, bears the strong imprint of academic science. As shown in Table 3, three attributes were disproportionately consequential in separating Cluster 1 from Cluster 2: (1) a noted scientist on the founding team; (2) an amphibious scientist/founder who alternated between academia and the start-up; and (3) absence of a senior executive from Big Pharma.[9] Of these, the presence of an amphibious founder is the most influential, accounting for 30 percent of the total distance between the initial clusters. Twelve of the 13 companies had such a founder.[10]

We first examine the attributes that characterize Cluster 1, paying attention to the social worlds they represent. Our findings illustrate how traffic across these social worlds resulted in the invention of a new organizational form that exemplified the notion of 'in business to do science.' We then apply the same analytical framework in explaining three variants of the 'in science to do business' pattern seen in Cluster 2.

Cluster 1: In business to do science

Dominant influence: academic science

Cluster 1 firms were research driven, led by amphibious scientist-founders who moved back and forth between campus and company. It may seem puzzling that Cluster 1 firms were half as likely as Cluster 2 firms to have an 'All Star' Scientific Advisory Board (SAB). Their histories make clear, however, that such boards were considered superfluous by these firms' scientist-founders. Because they remained connected to the world of academic science, these founders were not dependent on a high-powered external committee. The most extreme example is Biogen, where the founding team itself was a 'who's who' of life scientists from top universities in the U.S. and Europe. Worried about oversight from a nonscientist, Biogen's founders wrote into their articles of incorporation that the CEO would report to the scientific board, not vice versa (D'Andrade, 2001). The practice did not catch on among biotech firms and was abandoned by Biogen after seven years when the company hired Jim Vincent, an executive at Abbott Laboratories, to run the company. His description of Biogen's founding culture characterizes the operating assumptions that were constitutive of the Cluster 1 firms: 'The perception had been that everything else would take care of itself if we had good science' (Feder, 1992: 31).

'Good science' is a networked enterprise, dependent on the free flow of ideas and findings across organizational boundaries to all corners of the research community. Although active participation in this global community was unusual for a fledgling commercial entity, it was second nature for the amphibious founders of these companies. Robert Swanson (2001: 57) of Genentech characterized the scientific openness of his academic cofounder, Herbert Boyer, as follows:

> 'Boyer's philosophy…was that you gain more from interaction with your academic peers than you give up by telling the competition where you are. So with interaction you can move quicker; you gain more people willing to collaborate with you. We knew then we weren't going to have all the best ideas, and we said, where do the academic scientists go when they have an idea that they think needs to be commercialized? We want them to come to Genentech first…'

From a strategic perspective, scientific prominence helped Cluster 1 firms attract valuable external collaborators. For the younger scientists who joined these firms, however, moving from a prestigious university to an unproven start-up was a huge gamble. Staying active in the community of science mitigated some of the risk. The following comment

[9] To compute the influence of each attribute, we used the squared Euclidean distance measure, defined as the sum of the squared difference scores for each attribute. Squared Euclidean distance is especially appropriate because the data are no longer dichotomous, and it allows separate distance measures to be computed for each attribute in order to isolate those that contribute most to the overall distance between the clusters. These three attributes account for 66 percent of the overall dissimilarity between Cluster 1 and Cluster 2.

[10] The lone exception, Seattle-based Immunex, struggled over this very choice. Steven Gillis, scientific cofounder of Immunex, recalls the decision to sever ties with Fred Hutchinson Cancer Research Center in 1981: 'Most of our competitors who were involved in starting companies at the time were…staying in academia. We thought that might be a real conflict of interest. We wanted to make a clean break' (pers. comm.). More tellingly, Immunex did not hire a senior executive from the pharmaceutical industry, and its founders remained in close contact with researchers at 'the Hutch' (Wilson and Heath, 2001).

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Table 3. Differentiating characteristics of the four DBF clusters

	Cluster 1: *'In business to do science'*	**Cluster 2:** *'In science to do business'*		
		2a: Spin-off	2b: Broker	2c: Tech start-up
N	13	6	3	4
Ratio of firms with:				
Notable scientist/founder	1.00	0.33	0.67	0.50
Amphibious founder	0.92	0.33	0.00	0.00
Senior pharma exec. in charge	0.08	0.83	0.67	0.50
Serial entrepreneur among founders	0.15	0.17	0.33	0.75
Nontherapeutic focus	0.31	0.33	1.00	0.50
Publications per firm (avg.)*	584.54	185.83	148.67	266.25
Citations per publication (avg.)*	66.63	29.12	45.35	44.76
List of firms	*Biogen, California Biotech, Cetus, Chiron, DNAX, Genentech, Genetics Institute, Immunex, Molecular Genetics, Repligen, Seragen, ZymoGenetics*	*Genzyme, Hybritech, ImmunoGen, Integrated Genetics, SIBIA, Xoma*	*Centocor, Codon, Genetic Systems*	*Amgen, Cytogen,Genex, Enzo*

*Publications tracked for the first 10 years post-IPO. Citations are as of October 2010, self cites excluded. Self cites disproportionately boost Cluster 1's citation counts. Source: ISI Web of Science.

from Axel Ullrich (2006: 22), an early Genentech employee and now internationally known scientist, gives new meaning to 'publish or perish:'

> 'We were worried that if we started doing commercial research we would have problems returning to academia if things wouldn't work out. We were discriminated against at that time. We thought that if we (did) all this applied stuff, we couldn't publish. It would be terrible. We would never get a job if the company failed…we would be in the streets. So we had to publish…we had to establish a university-like atmosphere.'

Another university-like aspect of the Cluster 1 firms was the way they used corporate R&D contracts as substitutes for government grants, with renewal of the contracts contingent on the achievement of specific research objectives (Kenney, 1986b). The founding of Cetus is illustrative. Cofounder Donald Glaser (2006: 83), a Nobel laureate in physics who had moved into molecular biology, saw the venture as a way to replace the loss of a key NIH grant:

> 'The NIH funding cut had more to do with starting Cetus than it did with starting (a previous consulting firm). Cetus was in the 70s'…I wanted to continue the general idea of trying to use computer automation for important goals in biology. They (the NIH) told me that they were going to terminate my project at that time, and I was really furious because I'd put in an enormous amount of effort and it was just beginning to be really productive.'

Similarly, Genentech began its R&D efforts by funding two researchers at the City of Hope Medical Center in Southern California who had just been denied NIH funding (Kiley, 2002: 11).

Strange bedfellow: venture finance

Although corporate R&D contracts were comprehensible to Cluster 1's scientist-founders via analogy to renewable government grants, venture capital financing represented a brave new world. The influx of investment capital into the hallowed halls of academia challenged established norms. Tom Maniatis, a professor of molecular biology at Harvard and cofounder of Genetics Institute, told the *Washington Post* in 1981:

> '(It's) fascinating to see the effect on the minds of all these scientists—the worry about whether you

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> should dive into the money pile or whether the pile is dirtying everybody . . . Over the years the sense of academic purity is something which developed out of necessity . . . since there was no money a sense of saintlihood was required in the situation. Now it's not required.' (Hilts, 1981: A1)

For their part, many investors were equally ill at ease putting money into something as unpredictable as fundamental scientific inquiry. A stock analyst's criticism of Molecular Genetics could have been leveled at many of the Cluster 1 firms: 'It didn't seem the company had a clear focus . . . It seemed to me that I was funding a university' (Lerner, 1987). Such dissonance evinces the interpenetration of previously distant social worlds: venture capitalists faced unprecedented challenges in their efforts to justify investment in mini-universities; academic researchers were conflicted (and often persecuted) over involvement in science-for-profit.

Out of this turmoil emerged financial and organizational inventions—junior stock, limited research partnerships, co-location of commercial and academic researchers in a university lab—some of which were eventually ruled illegal (Perkins, 2002:10), while others resulted in lawsuits (Fox, 2000). A successful (and non-controversial) practice, however, involved the conversion of scientific output into investment dollars. Given the enormous costs and unpredictable timelines involved in discovering, developing, testing, and bringing to market genetically derived human therapeutic agents, venture capitalists needed a way to signal that the biotech start-ups were making progress worthy of additional investment. In traditional technology ventures, inventors build prototypes to make their ideas tangible. Creating a working demo of a cancer therapy, however, is a different matter. The publication of experimental results in a world-class journal served as a proxy. Using research papers to attract funding was an activity at which amphibious scientific founders excelled. Leveraging scientific reputation and output into research grants was a familiar activity for any top scientist. This practice was readily ported into the start-up setting. In a 2009 interview with us, Immunex cofounder Steve Gillis (pers. comm.) explained:

> 'It was interesting that Genentech . . . would publish in their annual report the number of times their articles were cited by other scientists. They would have a graph of how many times Genentech scientists were cited vs. other companies. And they were proud that they were always in a leadership position. But we were always either second or third. That was something that gave us pride, and, believe it or not, in the early days, Wall Street analysts looked at that, too.'

Influential by its absence: the pharmaceutical industry

As noted in Table 3, having an academic scientist in charge was inversely correlated with the presence of a senior pharmaceutical industry executive guiding the start-up. Genetics Institute was unique among the Cluster 1 firms in its combination of a seasoned academic leader (Mark Ptashne, then-head of Harvard's microbiology department) and an established pharma manager (Gabriel Schmergel, a Harvard MBA and 14-year veteran of Baxter Travenol). More commonly, a noted scientist took on the role of CEO or president (Biogen, Chiron, Molecular Genetics, Repligen) or was paired with a business manager of lesser stature (Cetus, Genentech, Immunex, Synergen, ZymoGenetics). Such asymmetries meant that Cluster 1 scientist-founders encountered minimal resistance to their ideas. An academic culture took root.

The absence of an influential executive from the pharmaceutical industry was also reflected in product development choices. Less than a third of these firms pursued diagnostic applications. Rather, their initial choices of therapeutic targets often were new-to-the-world medicines, such as interferon, with unproven applicability to the war on cancer. There were exceptions, of course, most notably Genentech's calculated cloning of human insulin. But in general, existing markets and specific target customers figured less into the decision calculus than opportunities at the cutting edge of science. DNAX, for example, produced a plethora of highly cited scientific papers, but never brought a product to market. The same was true of Cetus and Zymogenetics.

Although nearly all of these companies eventually hired a pharma veteran as top executive, the values and practices imprinted during their formative years proved durable. The 'invisible college' model, funded by corporate contracts and venture capital, fostered an impressive level of scientific output, which was then converted into financial and intellectual capital. In many technology start-ups, scientific research spawns technological applications whose development then proceeds along trajectories

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that are largely independent of university science. In contrast, biotechnology start-ups collaborate with university-based researchers, relying on input from the cutting edge of basic science (Powell *et al*., 1996; Cockburn and Stern, 2010).

Cluster 2: In science to do business

In Cluster 2 firms, academic organizing principles were superseded by commercial concerns. Only two of the 13 companies in Cluster 2 were founded by amphibious scientists. These firms did not actively publish in their formative years, and just under half could claim a notable scientist among their founders. Instead, more than two-thirds of the Cluster 2 firms recruited senior managers from Big Pharma as CEOs. Thus, where seasoned pharma executives held the maestro's baton, the ventures were less susceptible to the odd rhythms and tonalities of academic science. Instead, they remixed existing commercial elements to produce innovative variations on the start-up theme. We should note, however, that the executives who left the cozy confines of pharmaceutical executive suites for unproven start-ups were risk takers in their own right. Although they did not pursue radically inventive organizational models, they did have strong ideas about pursuing R&D in a different manner than had been done previously in corporate settings. But publishing cutting-edge science for all the world to see ran counter to their instincts.

As shown in Figure 1, the HCA results for Cluster 1 show remarkable cohesion, remaining essentially unchanged across five levels of agglomeration. In contrast, Cluster 2 splits into three subclusters at the next level of allowable dissimilarity. Each subcluster's attribute profile aligns with a distinct but preexisting approach to commercializing scientific breakthroughs (see Table 3).

Cluster 2a

These six firms resembled commercial spin-offs, except that the parent entity was a university or nonprofit research institute rather than a corporation. SIBIA (Salk Institute Biotechnology Industrial Associates, Inc.) was literally a spin-off of the storied Salk Institute, with a charter to commercialize the Institute's scientific advances (Froelich, 1984). Guided by experienced pharma executives, Cluster 2a firms were located close to their scientist-founders' academic labs, yet did not adopt a laboratory model of organizing. The unifying theme in these firms' histories is *separation of the academic from the commercial,* whereas Cluster 1 firms were characterized by the *transplant* of the academic into the commercial. The following statement by David Housman, a scientific founder of Integrated Genetics, delineates a business vs. a university laboratory: 'One reason I called this company Integrated Genetics instead of something else was because I wanted a company with the integrated functions of research, development, and sales and marketing, and not just R&D' (Curwood, 1983).

Dominant influence: the pharmaceutical industry

Cluster 2a firms featured an experienced business executive with a junior (or a minimally engaged senior) academic scientist. Hybritech recruited a mid-career pharma executive as CEO, while its founding scientist was an assistant professor. Genzyme's president and CEO boasted a decade of pharmaceutical management experience; its scientific founder was the assistant, not the lead investigator, on an NIH grant. Xoma's founder had just finished his medical residency; its first CEO was the former president of Becton Dickinson's microbiology systems division. Integrated Genetics' chief scientist-founder was a tenured professor at MIT, yet he spent less than a day a week at the company. This gave wide latitude to CEO Robert Carpenter, a West Point graduate and Harvard MBA who had been a division president at a multinational pharmaceutical company.[11] These disparities shaped the Cluster 2a firms, none of which duplicated an academic research culture. Instead, Cluster 2a firms favored quick-to-market diagnostic technologies (Hybritech, Integrated Genetics) or orphan drugs tailored to specific, small patient groups (Genzyme, ImmunoGen).

More than financiers: venture capital

Cluster 1's venture capitalists were deeply engaged in channeling money into the firms' basic research programs. In contrast, Cluster 2a's VCs engaged in management. In two companies (Hybritech and

[11] Ted Greene of Hybritech, Henri Termeer of Genzyme, and Robert Carpenter of Integrated Genetics were all recruited from the pharmaceutical corporation Baxter Travenol. Higgins (2005) has shown how Baxter and, to a lesser extent, Abbott, had outsize influence on biotech, as numerous executives with experience at managing product teams or divisions left these second-tier companies for the allure of biotech.

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ImmunoGen), the VC was the founding CEO. In two other companies (Genzyme and Integrated Genetics), VCs occupied more traditional positions on the board of directors, but exerted considerable influence on day-to-day operations. The practical orientation of the VCs complemented the pharma-bred focus on penetrating existing markets with superior, genetically engineered products, seeking a rapid return on investment. In the words of David Anderson, Integrated Genetics' hands-on venture capitalist, 'What most (biotech firms) lack is a real product focus and a real intense desire to get something out on the market. Not us' (Curwood, 1983).

Application oriented: academic science

Only two of the six companies featured notable scientists among their founders. In one of these cases, the distinguished scientist limited his involvement to serving on the Science Advisory Board.[12] Consistent with a 'spin-off' model, the science conducted in Cluster 2a companies led to marketable products, but did not generate a large volume of highly cited publications (see Table 3).

Cluster 2b

A second path to commercialization is signified by three attributes: the lack of a blue-ribbon SAB, little reliance on R&D contracts, and exclusive focus on diagnostic products. These attributes cohere around a brokerage model: rather than invest in expensive R&D, these companies partnered with academic labs, from which they licensed promising ideas and tried to bring them to market.

Harvesting science for commerce

Without an internal R&D group pursuing basic science, Cluster 2b firms had minimal need for an SAB and offered few attractions as research partners. Their strategy was succinctly stated by Hubert Schoemaker, Centocor's first CEO: 'We realized it was a lot cheaper to roam academe and pay a royalty back for what we developed than start our own research facilities' (Vaughan, 2000: 186). A more aggressive brokerage approach was practiced by Seattle-based Genetic Systems, whose founder, Robert Nowinski, negotiated exclusive rights to 37 antibodies from his former employer (the Hutchinson Center), then sublicensed them to another company for $3.7 million (Wilson and Heath, 2001). Like Cluster 1 companies, Cluster 2b firms were located close to major research centers. Unlike Cluster 1 firms, however, their locations were not motivated by proximity to labs, research seminars, or other aspects of knowledge production. Rather, Cluster 2b firms sought to maintain close relationships with suppliers of potentially commercializable ideas.

Focus on existing markets

Going after diagnostic applications was a more rapid path to profits. Genetic Systems' initial product was a chlamydia diagnostic. Codon's initial focus was on vaccines and the production of enzymes. Centocor's first product, a rabies test, was based on a monoclonal antibody licensed from the lab of one of its founders. The test was designed to run on equipment manufactured by Abbott Laboratories and Warner-Lambert. Thus, Centocor not only made minimal R&D investments, it also avoided developing its own manufacturing and sales.

Nonamphibious scientists

Noted scientists were associated with the start up of two of these three companies (Centocor and Genetic Systems), but they played very different roles. Centocor's scientist-founder retained his position as director of the Wistar Institute, a renowned research center in Philadelphia, and was forced to resign his directorship in Centocor prior to the company's IPO. In contrast, Genetic System's Nowinski was head of the virology lab at the Hutchinson Center prior to joining the start-up. When he left the laboratory to become chairman and CEO of the new venture, he brought his entire 16-person research team with him. He told *Fortune* magazine in 1987,

> 'I had been totally absorbed with research. All of a sudden I was dealing with stockbrokers, bankers, accountants, and pharmaceutical executives. It gave me a tremendous sense of being in the middle of the world. It changed my values fundamentally' (Gannes, 1987: 9).

[12] This scientist was Baruj Benacerraf, who earned the Nobel for physiology/medicine in 1980 for his pioneering work in immunology. Benacerraf was pivotal in attracting top scientists to serve on ImmunoGen's advisory board. In its first two years, ImmunoGen had no lab space of its own, instead contracting all of its research to the Dana Farber Cancer Institute, of which Benacerraf was the president and CEO. Yet in his 1998 autobiography, he never mentions his involvement with ImmunoGen (Benacerraf, 1998).

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That change—from doing science to doing deals—illustrates the stark contrast between Cluster 1 and Cluster 2b companies. With limited internal research capability but ties to academic laboratories, these companies played the role of brokers between public science and commercial health care, a classic source of recombinatorial innovation (Burt, 2009).

Cluster 2c

In contrast to Clusters 2a and 2b, the firms in Cluster 2c were located at some distance from the nearest academic lab, three times as likely to have a repeat entrepreneur among their founders, and almost seven times more likely to grow through acquisition. This attribute profile and the details of the case histories suggest a deliberate 'by the book' approach to assembling a new biotech venture. Whereas many of the other innovators were experimenting with new organizational forms (essentially making it up on the fly), the founders of Cluster 2c firms followed a conventional template for high-tech ventures, with some adjustments for the substantial investments in R&D required for biotech.

Dominant influence: venture finance

That this formula was replicable is evidenced by the presence of two companies with the same founder: Genex and Cytogen, the first and second forays into biotech by Princeton-based dealmaker Robert Johnston. In fact, when Johnston set out to assemble Genex in 1977, he sought a CEO steeped in science yet comfortable in commerce. In an unorthodox move, he placed a 'CEO wanted' ad in the journal *Science.* He selected Leslie Glick, a 37-year-old scientist with a PhD in zoology from Columbia, a postdoctorate at Princeton, and an entrepreneurial track record as founder of his own profitable tissue culture company. Johnston and Glick began researching the business opportunities opened by recombinant DNA technology, while searching for an accomplished academic researcher to join the founding team. Like Genex, Amgen was the brainchild of experienced financiers—Silicon Valley investors William Bowes and Franklin 'Pitch' Johnson. They, too, recruited a senior scientist, a scientific advisory board, and a PhD-carrying CEO.

A subordinate role for science

Bowes had been an investor in Cetus (see Cluster 1) and did not want to replicate its chaotic atmosphere of academic exploration (Duncan, 2005). His handpicked CEO—George Rathmann, an Abbott vice president with a PhD in chemistry from Princeton—insisted on having Amgen's high-powered scientific advisory board report to him, rather than vice versa (Rathmann, 2004:21). Ironically, one of Rathmann's first tasks as CEO was to fire Amgen's amphibious chief scientist, a noted UCLA biologist. At Genex, Johnston and Glick persuaded David Jackson, a tenured molecular biologist at the University of Michigan, to join the venture—in Jackson's words, 'just this incredibly countercultural thing to do at that point' (pers. comm.)—and leave behind the academic emphasis on knowledge production:

> 'It takes a lot of time to publish stuff, and (at Genex) we were always under enormous time pressure to meet various milestones. And there was a concern about disclosing stuff prematurely, before we'd really had a chance to capitalize on it' (pers. comm.).

Moreover, the dealmakers who assembled Amgen, Genex, and Cytogen chose corporate locations that were physically and symbolically removed from their academic headwaters, prioritizing instead such practicalities as the smog-free air and affordable housing of Thousand Oaks, California (Amgen), and proximity to regulatory agencies in the Washington, D.C., area (Genex).

Serial entrepreneurs

Three of the companies—Amgen, Cytogen, and Genex—are distinguished by the presence of a serial (but not amphibious) entrepreneur on the founding team. The fourth– Enzo Biochem—is an outlier, though it too exhibited the attributes of a deliberate, business-focused bioscience venture. Enzo's business initially focused on DNA probe diagnostics, which offered quicker profitability than developing new medicines. Like Amgen and Genex, Enzo also grew by acquisition, and its location—New York City—never became a hub of biotech activity (Whittington, Owen-Smith, and Powell, 2009).

Implications: do templates shape outcomes?

Our findings highlight how the attributes clustered into two camps: ventures that were 'in business to do science' vs. those that were 'in science to do business.' We found that the science-based firms formed

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a more coherent cluster, whereas the commerce-oriented firms split into three subclusters, each with a distinctive stamp. The organizations literature is replete with studies that build upon Stinchcombe's (1965) imprinting hypothesis, which emphasizes the tenacity with which circumstances at the time of an organization's founding continue to exert an influence on its evolutionary trajectory. Most studies stress how the prior experiences of founding teams shape organizational performance through the transfer of status and/or experience (Burton *et al.*, 2002; Helfat and Lieberman, 2002; Phillips, 2002; Shane and Stuart, 2002; Chatterji, 2009). Precisely how imprinting shapes work practices is seldom explored (see Johnson, 2007, for an exception). And how outcomes are experienced in new settings is mistakenly assumed to be straightforward.

Consider the ambiguity of 'performance.' In terms of time-to-IPO and time-to-acquisition, the averages for Cluster 1 and Cluster 2 are identical: five years to IPO and 20.7 years to acquisition. Our familiarity with the circumstances of each firm's survival or demise, however, makes us wary of attaching a common meaning to such metrics. Hybritech, for example, survived for eight years before being acquired by Eli Lilly at a high valuation. Standard entrepreneurial performance metrics would count this a success—a profitable liquidity event (Stuart and Sorenson, 2003). But Hybritech's founders and senior staff soon chafed under the oversight of a corporate parent and within a year, most resigned to start or join new ventures of their own (Mitton, 1990). Immunex mourned its 1991 acquisition by Amgen, seeing it as the end of its cherished 'Immunoid' culture and the beginning of life in a large corporation (Dietrich, 2003). In contrast, DNAX was acquired by Schering-Plough less than two years after its founding, yet it was allowed to continue as an autonomous research lab for another decade. Researchers there seemed to not notice the change in ownership, except that Schering-Plough required key card security be installed on DNAX's formerly open doors (Kornberg, 1998: 130). Genetics Institute staff chose a subterranean strategy of resistance after its 1996 acquisition and continued to publish and patent under the GI label, reckoning that merger activity was so widespread among Big Pharma that it would not be noticed. And Genentech launched a vociferous campaign of opposition to Roche's 2009 takeover, decrying an end to Camelot and the death of its scientific mission (Chang, 2009). Finally, a small group of companies—ImmunoGen, Repligen, and Xoma—survive as independent entities, yet have never made a profit and are derisively labeled 'biotech zombies' by some observers (Pisano, 2006).

Such contradictions point to the impossibility of judging something as subjective as success across divergent registers of worth and support a view of organizations as malleable entities, capable of being bent to a variety of purposes by founders with different goals. What was success to a commercially oriented firm was a loss of independence to a science-oriented variant. Similarly, publishing was an important metric for the Cluster 1 firms, yet much less so for those in Cluster 2. Accordingly, we searched the ISI Web of Science database for all scientific publications with at least one author who was affiliated with one of the early companies in our sample. This produced a publication count for each firm for the 10 years following its initial public offering. We use the post-IPO period, rather than founding date, because firms might have published to attract Wall Street's attention then stopped doing so after they went public.

From the publication counts, we generated a citation analysis for each firm and aggregated these by cluster (again, see Table 3). Cluster 1 firms produced, on average, 584 scientific publications during the 10 years following their IPOs—more than double the number of the next-closest cluster (Cluster 2c). In addition, the papers produced by Cluster 1 firms boasted 50 percent higher average citation counts. Clearly, the rules of the invisible college, transposed into these ventures, dictated continued engagement with the domain of open science. As active participants in the worldwide scientific community, such firms set in motion a series of changes that are still playing out in the labs of academic and commercial science. Indeed, Liu and Stuart (2011) trace the present day tendency by private firms to participate in open communities of science and technology to these early biotech boundary crossings.

CONCLUSION

We sought to answer the questions of where new organizational forms come from and how bundles of practices are combined in science and technology-based ventures. We added to this central concern an accompanying question about different types of entrepreneurs and their role in the emergence of

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novel organizational forms. Rather than emphasize the discovery of opportunities or broader population-level patterns, our contribution is a relational approach that focuses on two mechanisms of assembly and highlights how 'amphibious' entrepreneurs are able to bring organizing assumptions from one social domain into another. Previous studies of organizational genealogy have emphasized both an entrepreneur's prominence as a signal of the quality of a new venture and the transfer of experience from previous employers. The former highlights the inheritance of legitimacy, whereas the latter stresses the transfer of technical knowledge and capabilities. Our analysis underscores both factors: social capital, in the form of distinguished scientists and proven pharmaceutical executives; and routines, expressed through scientific, corporate, and venture finance knowledge. But we point out that how routines are transferred and legitimacy conferred are contingent on both context and social distance. When resources and status are moved to a proximate domain, reconfigurations occur; but when they travel to unfamiliar settings, novel conceptualizations of what a firm should look like are rendered possible.

In the short run, the impact of the skilled individuals involved in assembling these earliest biotech firms loomed large, yet the pivotal skill set in generating a novel organizational form was not the individual creativity of the improviser (Miner, Bassoff, and Moorman, 2001) nor the resourcefulness of the bricoleur (Baker and Nelson, 2005). Rather, our emphasis on how attributes fit together is a story of pragmatic search, where the tools of everyday practice were used in new and unfamiliar settings, at a time when there was a greenfield. This leads us to stress that relationships constituted both founders and their companies. In those settings where the organizing principles of an academic life science lab were installed *in toto* with financing from the capital markets in lieu of government grants, the ensuing interactions formed novel entities with effects that extended far beyond their creators' initial intentions. For example, publishing in top-tier scientific journals was unusual for start-up companies; but project-based work in which scientists dropped their current research to assist others on whatever leads proved hottest was equally uncommon in the academy. The companies published *and* patented, even as they collaborated with ostensible competitors. Venture financing was necessary, but of a magnitude and duration not encountered in prior information technology start-ups, so new ways of repurposing scholarly outputs as prototypes had to be fashioned. In contrast, when science took a back seat to commercial goals, innovative steps were climbed to bring new biotechnology products to market, albeit in companies that looked more comparable to other high-tech ventures.

Thus, our fundamental finding is that when entrepreneurs launch new businesses in adjacent fields with which they are familiar, the organizing process is marked by *reconfiguration*, the reassembly of borrowed elements from known sources. Such bricolage generates innovations, and often produces new organizations, but does not result in novel *forms*. In contrast, when entrepreneurs enter a distant domain, they are incapable of drawing on that domain's established templates and tools of organizing. Instead, they rely on the frameworks from the former domain with which they are familiar and, in the process, generate dramatically novel models. We argue that this mechanism of *transposition* may result more from naïveté than prescience and is more pragmatic than calculative.

Periodically, scholars call for new theories to make sense of contemporary organizations (Daft and Lewin, 1990; Greenwood and Miller, 2010). We counter that understanding novel forms of organizing does not require 'new' theories. Instead, we have followed more classic ideas from the Carnegie School (March and Simon, 1958; Simon, 1982) and symbolic interactionism (Mead, 1934; Blumer, 1969; Becker, 1986) and paired them with fresh insights from the networks (White, 2008) and evolvability (Kauffman, 2000) literatures. All forms of organization face the challenge of coordinating work and mobilizing resources. The manner in which a division of labor is fashioned and resources accessed determines whether an organizational form is novel or not. Some organizations tackle these challenges by assembling recognizable routines in creative ways; others bring unfamiliar routines together to produce something that stands apart from previous practice. We have offered both an analytical and methodological lens on this question of design—a focus on how distant and proximate attributes are combined. Our sociology of compounds can be readily applied to the study other domains—the open source world of Linux and Wikipedia, political reforms that mix state funding with private provision, or newer modes of contracting. The key is to isolate the elements that are used to 'solve' protean organizational problems. Our use of HCA represents a fruitful methodological approach.

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Nelson and Winter (1982: 130) define innovation as 'a recombination of conceptual and physical materials that were previously in existence.' We take a further step in removing the prefix from 'recombination' and articulating a mechanism by which previously unfamiliar elements are combined for the first time. Consider, as but one example, how inserting scholarly practices into a new firm transforms the nature of science. Nobel laureate and DNAX founder Arthur Kornberg (1998: 139) commented that:

> 'In a conventional academic department, there are a dozen professors and each one is an entity unto himself; a duchy I would call it. Professors are self-sustaining . . . one can be successful and surrounded by failures; it is possible. DNAX is not organized that way . . . when a discovery is made at DNAX, everyone has access to it and can build on it, advance it. That doesn't occur in any academic organization . . . or in pharmaceutical companies where there are layers of authority and bureaucracy.'

We maintain that the role of naïveté has been underestimated, if not completely overlooked. In the case of biotechnology, the cadre of scientist-entrepreneurs that founded the first-generation companies may not have known 'how to run a business,' but they most assuredly knew how to run a top-flight research laboratory. As this type of organizing knowledge was transposed into a new setting, radical social novelty was unleashed, eventually reverberating back into the domains from which it was transported. What began as an odd experimental approach to mounting a new venture is described today as the 'life sciences innovation system' that 'replaced the traditional divide between university science and pharmaceutical innovation' (Cockburn and Stern, 2010: 26). This disruptive organizational model not only led to a distinctive DBF form, it fed back into the conservative halls of the academy and the large pharmaceutical laboratories and led to the remaking of the boundaries between public and private science. Today, both domains are fundamentally transformed—interdisciplinary, project based, entrepreneurial, and intensively networked.

More broadly, we suggest that disruptive organizational models that transgress social and economic boundaries are consequential because they alter the very texture of the social worlds in which we live. Whether in the form of an evangelical church that teaches finance, a software company that purports to be the world's library by use of a search algorithm that was the product of basic science research, or nonprofit ventures that aim to assist poor women in becoming economically self-supporting, such cross-realm confluences are fertile sources of social and economic change.

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