LEVERAGING EXISTING TECHNOLOGY: THE ROLE OF ALLIANCES IN CROSS-APPLICATION

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Abstract

In contrast with conventional views of R&D alliances as cooperation in upstream value chain activities critical to innovation and marketing alliances as cooperation in downstream activities critical for the stimulation of demand, this paper proposes that it is marketing alliances, rather than R&D alliances, that play a key role in helping entrepreneurial firms overcome certain constraints in innovation. Using data from Securities Data Company (SDC) venture capital and alliances databases and the United States Patent and Trademark Office (USPTO) patents database, from 1976 to 2004 (N=107 firms, n= 2305 observations), I find support that marketing alliances are a primary enabler of recombinant innovation in entrepreneurial firms as found in the cross-application of technology

INTRODUCTION

R&D alliances, partnerships involved in cooperation in upstream value chain activities, have been firmly positioned as involving the sharing and expansion of technological knowledge (Hagedoorn, 1993; Mowery, Oxley and Silverman; 1996; Dutta and Weiss, 1997; Das, Sen, Sengupta, 1998; Katila and Mang, 2003; Sampson, 2004). Meanwhile, marketing alliances, partnerships involved in cooperation in downstream value chain activities, have traditionally been considered beneficial only for the stimulation of demand (Hagedoorn, 1993; Das, Sen, Sengupta, 1998). Marketing alliances are thus seen as a signal of product maturity (Das, Sen, Sengupta, 1998), not as an opportunity for knowledge creation—the historic "exclusive" domain of R&D alliances.

However, understanding the true relationship between marketing alliances and innovation has important implications for entrepreneurial firms. Instead of using developed innovations to set marketing alliance strategy; firms could actually be using marketing alliances to develop commercially-driven innovation strategy. These trends are visible in medium- to large-size pharmaceutical companies, such as Pfizer, Merck, and Novartis, where commercially driven product development groups are being built within the larger R&D organization.

This paper investigates the entrepreneurial effort of recombinant innovation asking: how do entrepreneurial firms continue innovating beyond their initial innovation? I look to the alliance literature to identify how alliances help firms overcome constraints in innovation. In this paper, I focus on the implications of marketing alliances on innovation. I argue that marketing alliances play an essential role in exploring new application domains and leveraging technologies across those domain spaces. In doing so, marketing alliances allow entrepreneurial firms to overcome technological myopia and technological dependence; the former comes from entrepreneurial founders' inclination to focus on the narrow functionality of existing technology (Doherty, 1990) while the latter occurs because entrepreneurial firms are resource constrained (Aldrich, 1999).

This paper is organized as follows. First, I develop the concept of cross-application and explore its connection to technology trajectories and application trajectories. Next, I relate cross-application to other innovation, using a model of recombinant search across application domain and technological knowledge space. This elucidates the concept of cross-application in action, while also highlighting the constraints to cross-application. I then review the literature on strategic alliances to clearly delineate the conventional realms of R&D alliances versus marketing alliances with respect to innovation. Finally, I lay out my theoretical contribution on the role of marketing alliances in innovation through hypothesis-building and an analysis of data on 107 entrepreneurial biotechnology firms.

CROSS-APPLICATION AND TRAJECTORIES

This paper introduces the concepts of cross-application and the application trajectory to build its story. Cross-application needs to be defined as a separate choice for entrepreneurial firms and also, in the next section, related to choices regarding other types of innovation. Different paths of innovation require different skills, routines and knowledge (Nelson and Winter, 1980).

As seen in Figure 1, for any given technology-based firm, there exists at least one technological trajectory (Dosi, 1982; Nelson & Winter, 1982) and any number of sub-market customer preference trajectories (Christensen, 1997; Adner & Levinthal, 2001; Adner, 2002; Tripsas, forthcoming) that could be met. For ease of exposition, I shall consider a context where there exists one technological trajectory whose available attributes are consistently changing as the technology matures toward its natural limit (Sahal 1985; Foster 1986; Fleming 2001) and as exogenous developments in science unfold (Nelson and Winter, 1982; Dosi 1982; Fleming and Sorenson, 2000). When the firm takes a technology at a specific point in the technological trajectory with fixed attributes, the seed of an *application trajectory* is planted. The firm then may match these fixed attributes to specific customer preferences in the sub-markets by placing different weights on the attributes of the technology. C*ross-application*[1] is thus defined as the entrepreneurial effort of taking existing firm technological knowledge into new application domains. A clear *application trajectory* becomes visible as the firm creates a series of cross- applications for its technology. It is important to note that an application domain is not *how* the technology is employed (i.e. product), but *where* a technology is employed (i.e. forensics).

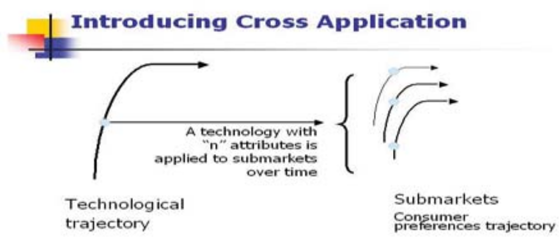

Figure 1: Introduction of the Application Trajectory

Cross-application is highly relevant in the biotechnology industry, and is illustrated at an entrepreneurial biotechnology company, MassSpec[2]. From the technology trajectory of mass spectrometry (light to gas to liquid), this particular biotechnology firm has leveraged their mass spectrometry technological knowledge (fixed in attributes) over time and extended it across three sub-markets, each with different preference trajectories, to develop an application trajectory (Figure 2). Focusing on the fixed attributes of the technology, this particular mass spectrometry technology identifies the chemicals that were highly evident in large amounts, or peaks, in certain samples. Initially, the company utilized their mass spectrometry technology in drug development applications. Products that later resulted were utilized by big pharmaceutical companies (e.g., Pfizer, Merck, GlaxoSmithKline) in testing the breakdown of drugs in the body. In this case, the attribute emphasis rests on the *timing* between the appearances of peaks. In the last five years, the firm has applied their mass spectrometry technology to forensic applications. Products that resulted from cross-application were utilized by crime laboratories (e.g., Los Angeles Police Department and New York Police Department) to detect chemicals or toxins posthumously. In this case, the attribute emphasis rests on the *height* of the peaks. In the last year, following FDA approval for the use of mass

1 The name "cross-application" is taken from the software industry, where the concept references programming code that is utilized across an entire system.
2 Under Non-disclosure agreement (NDA), the actual firm name cannot be disclosed.

spectrometry technology in newborns, the firm has applied mass spectrometry technology to clinical applications. In this final case, future products that result from cross-application will be used by hospitals in neonatal care, and the attribute emphasis rests on the *number* of peaks that appear.

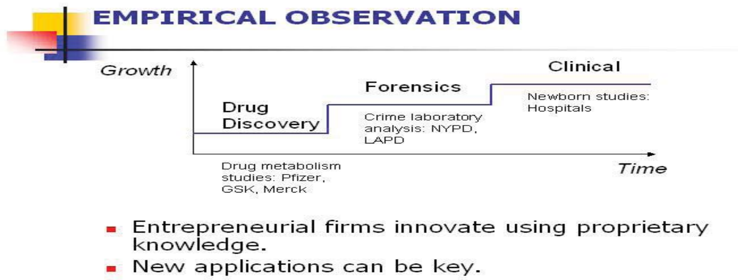

Figure 2: Example of Cross-application at MassSpec

TYPOLOGY OF RECOMBINANT INNOVATION

Cross-application is a choice among other types of innovation. The effort of leveraging existing technology to address the discovery of a new bundle of attributes from a pre-existing set of attributes valued in alternate application domains is Schumpeterian entrepreneurialism at its core. "Everyone is an entrepreneur when he actually carries out new combinations, and loses that character as soon as he has built up his business, when he settles down to running it as other people run their businesses (Schumpeter, 1934)." Innovation is thus defined as a recombination of conceptual and physical materials that were previously in existence (Schumpeter, 1934; Nelson and Winter, 1982).

To continue innovation, a firm would need to continue conducting new combinations (Schumpeter, 1934). However, in recombinant innovation, uncertainties of two main kinds combine to make technology development decisions difficult: supply uncertainty and demand uncertainty (Garud and Nayyar, 1994). The type of recombinant innovation focused on in this paper involves the knowledge surrounding these two types of uncertainties. Thus, technology is identified as the supply factors to which demand responds, and technological knowledge the "useful knowledge rooted in engineering and scientific disciplines, but also drawing from practical experience from production" (Arora, Fosfuri, & Gambardella, 2001). Likewise, application domain is identified as the demand factors to which the organization's technology supply factors can respond (Levinthal, 1998), and application domain knowledge the knowledge surrounding the particular demand factors of the domain. Note, however, that application domain demands differ significantly from market demands. Using the example of MassSpec, the technology is that of mass spectrometry, the application is that of posthumous chemical detection, and the market consists of the customer, i.e crime laboratories. The difference in application domain demands and market demands reflects the difference between knowledge creation and product creation (commercialization).

Technological knowledge and application domain knowledge are conceptualized as possibility spaces or problem spaces (Perkins, 1995; Boden 1991; Ernst and Newell, 1969; Newell and Simon 1972) and the elements being recombined (Table 1). The search for a solution is viewed as a process of search through a space of possibilities (Figure 3). The innovative search, as seen in Figure 3, models the typology of recombinant innovation in Table 1. The whole space of possibilities is divided into four subspaces. Thus four types of innovation arise as the result of recombinant innovation search where 1) firms' search actually varies across two distinct dimensions (application domain knowledge and technological knowledge) rather than one (just technological knowledge) and 2) firms can vary in their degree of usage and re-usage of existing knowledge as they can vary in their exploration of new knowledge (Katila and Ahuja, 2002).

Table 1: Categorization of Potential Movements in Possibility space

	Reuse Application Domain Knowledge	New Application Domain Knowledge
Reuse Technological Knowledge	A movement in composition knowledge results in process changes	A movement in application domain knowledge results in **CROSS-APPLICATION**
New Technological Knowledge	A movement in technological knowledge results in product changes	A movement in both technological knowledge and application knowledge results in truly novel innovation

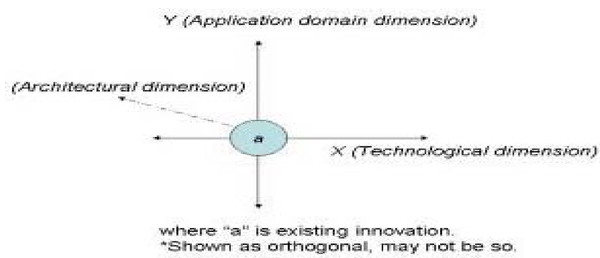

Figure 3: Potential movements in Possibility space

Namely, leveraging both technological knowledge and application domain knowledge would result in process changes, akin to architectural innovations (Henderson and Clark, 1990). Leveraging application domain knowledge and exploring technological knowledge would result in product changes, akin to component innovations (Henderson and Clark, 1990). Exploring new application and technological knowledge would result in radical innovation to the firm (Tushman and Anderson, 1986). The innovation type of interest is that of leveraging technological knowledge and exploring application domain knowledge, introduced above as cross-application.

Cross application is of special interest in recombinant innovation because of the firms' leveraging of existing technological knowledge. Successful innovation is contingent on the development of the underlying technology and introduces uncertainty, requires risk capital, and makes venture creation qualitatively more hazardous (Bhave, 1994). Development of a knowledge base is difficult, time-consuming and expensive (Ahuja, 2000). Expensive equipment, skilled personnel and large investments imply innovation is often a high-cost, and uncertain-benefit, exercise. Yet, the firm has alternatives in the magnitudes of cost and uncertainty it is willing to undertake, and prior literature expounds on the benefits of leveraging existing technological knowledge in innovation. This paper focuses on four of those benefits.

One primary benefit of leveraging existing technological resources is the need for significantly less resources. Searching recently created knowledge, for example, conserves cognitive capabilities (Cyert & March, 1963) and reduces search costs (Katila, 2002). Leveraging existing technological knowledge is "genetically conservative" (Adner and Levinthal, 2000). For example, Adner and Levinthal (2000) describe how Internet technology entailed substantial initial development effort and government sponsorship; however, leaping from government application to commercial use required less development necessary and occurred with faster speed to market. .

Additionally, searching recently created knowledge is more likely to lead to successful rewards (Cyert & March, 1963). This illustrates a second benefit to leveraging existing technology: lower risk. The quality of existing knowledge is said to be more reliable (March, Sproull & Tamuz, 1991). Organizational memory of firms is embodied in the routines of the firm, and these routines represent the capability of the firm (Nelson and Winter, 1982). These routines help firms maintain continuity and build competence (March, 1991). By leveraging existing technological knowledge, firms use embedded routines that decrease the chance of errors and increase the chance of successful recombination and successful innovation (Katila, 2002). For example, firms that build on recent knowledge are frequently better able to predict the nature of technological advances and, by investing in an area early, the firm avoids foreclosure to future developments in that area (Cohen and Levinthal, 1989; McGrath, 1999).

Third, leveraging existing technology increases potential for competitive advantage (Katila, 2002). Unlike external technology that is accessible to all firms (Mansfield, 1988), internal technologies are proprietary and not widely accessible. Existing technological knowledge thereby forms the basis for sustainable competitive advantage. In other words, leveraging existing technological knowledge uses innovative resources that are scarce, hard to imitate (Barney, 1986) and unable to be simply purchased in strategic factor markets (Diericks and Cool, 1989).

Lastly, leveraging existing knowledge has many of the characteristics of local search, but can also involve exploration. As Kogut and Zander (1992) suggest, the knowledge of a firm can be considered as owning a portfolio of options, or platforms, on future developments. Like local search, in searching for innovative opportunities, a firm's R&D activity is closely related to its previous R&D activity (March and Simon, 1958; Nelson and Winter, 1982; Helfat, 1994; Rosenkopf and Nerkar, 2001). Also like local search, the firm searches for solutions in the neighborhood of its current expertise of knowledge (Stuart and Podolny, 1996). However, leveraging existing knowledge can avoid many of the disadvantages of local search such as competency traps (Levitt and March, 1988) and core rigidities (Leonard-Barton, 1992) by incorporating feedback from the environment (Katila, 2004). While results of past innovative searches become natural starting points for new innovative searches, firms do not have to rely solely on their own established knowledge to determine what is important and useful. By involving exploration of application domain opportunities in leveraging existing technology, the firm can integrate developments both inside and outside of the firm.

Until now, only the benefits of the strategy of cross-application have been discussed. However, there are also costs. As Levinthal (1998) suggests, technological change associated with the shift in application domain is typically quite minor; indeed, in some instances there is no change in technology. Instead, the innovative development occurs in meeting the new basis of competition – the critical attributes of functionality – and meeting the resource restraints of the new application domain – that is the availability of resources.

STRATEGIC ALLIANCES AND INNOVATION

Research and industry practice agree on several characteristics that differentiate strategic alliances from acquisitions and other inter-organizational arrangements. Primarily, strategic alliances are cooperative relationships between two or more independent organizations, designed to achieve mutually beneficial longer-term business goals to the extent that the alliance is economically viable (Das, Sen, and Sengupta; 1998). Alliances provide the companies involved the opportunity to develop capabilities and learn from each other (Hagedoorn, 1993). Prior literature has established that R&D alliances are positively related to technological exploration (Mowery, Oxley and Silverman, 1996; Dutta and Weiss, 1997; Das, Sen, Sengupta, 1998; Hagedoorn, Link and Vonortas, 2000;

Hagedoorn, 2002; Hagedoorn, 1995; Katila and Mang, 2003; Sampson, 2004). Moreover, previous literature on innovation looks to R&D alliances as the essential source of new technologies. Hagedoorn (1995) additionally posits that R&D sophistication is positively correlated with technology partnering intensity, and that inter-firm technology partnering is also related to the emergence of new technologies. Finally, whether to develop internal capabilities (Kogut, 1988) or to gain access to other firms' capabilities (Grant and Baden-Fuller, 1995; Nakamura, Shaver and Yeung, 1996), R&D alliances increase new technological knowledge for all firms in the partnership (Hagedoorn, Link and Vonortas, 2000; Sampson, 2004).

Thus, R&D alliances are positioned as being beneficial to knowledge creation as opposed to marketing alliances, positioned as being beneficial to only stimulation of demand. This positioning could be due to the dichotomization of exploration versus exploitation (March, 1991). R&D alliances have traditionally been linked to exploration, or the search for new innovation opportunities. On the other hand, marketing alliances have been linked to exploitation or the refinement, implementation, efficiency of production and selection of innovation (Rothaermel and Deeds, 2004).

However, in terms of leveraging existing knowledge in innovation, marketing alliances can be critical to successful innovation. This paper posits that while R&D alliances are positively related to exploring new technological knowledge, they are not fundamental to cross-application. Marketing alliances are critical to cross-application or re-using technological knowledge to explore new application domain knowledge. This is addressed in the next section.

RESEARCH AND DEVELOPMENT (R&D) ALLIANCES AND CROSS-APPLICATION

Although R&D alliances might give a firm the ability to explore new technological knowledge, R&D alliances may not give a firm the ability to leverage existing technological knowledge particularly in new application domains. One reason why R&D alliances might not help leverage existing technological knowledge is that R&D alliances tend to focus on *creating* rather than refining technology. Firms look to other firms that have made similar commitments to build technological knowledge and seek to learn from the accumulated competence (Mitchell and Singh, 1992). Mowery, Oxley, and Silverman (1998) find that while alliance partners have significantly greater technological overlap than non-allied company pairs; partners in technology-related joint ventures do not display higher levels of technological overlap than partners in market-access joint ventures. Therefore, R&D alliances may not overcome technological myopia not because of lack of overlap but due to motivation of what to do with that overlap. Most high-tech firms have a tendency to use R&D alliances for technological knowledge development and learning, not necessarily application domain knowledge development and learning.

A second reason that R&D alliances may not enable a firm to leverage existing technological knowledge in exploring new application knowledge is that R&D alliances do not necessarily provide access to application domain insights. For example, Carmichael Roberts, the CEO of Surface Logix, expresses concern about entering new application domains with his patented technology:

> "The academic lab was not focused on customizing a technology for a specific application. For instance, in the lab we never thought about which companies were doing work in related areas, what the most important disease categories were, which micro assay formats were most widely used or how to target the technology for business development (Lassiter and Roberts, 2001)."

Therefore, R&D alliances may not get past technological dependence as they are focused on the technology and exploring new technological knowledge. In order for cross-application to occur, alliances should facilitate leveraging of technological knowledge and exploration of application domain knowledge.

Hypothesis 1a: R&D alliances decrease the likelihood of cross-application in that they decrease the likelihood that that a firm will leverage internal technological knowledge.

Hypothesis 1b: R&D alliances decrease the likelihood of cross-application in that they decrease the likelihood that a firm will explore application domain knowledge.

MARKETING ALLIANCES AND CROSS-APPLICATION

Unlike R&D alliances, marketing alliances help identify new application domains while leveraging existing technology. Namely, firms can develop new functionality by discovering the bundle of attributes valued by a new application domain that are not necessarily the same as the bundle of attributes valued by the previous application domain. As expressed by Dr. Soumya Roy, Vice President of Lieberman Research Worldwide:

> "The 'gap' in the experience is what marketing can reveal and ultimately address. The gap can be as simple as a better manual, packaging, product bundling, new form of distribution (e.g. internet-based) and not necessarily anything related to product engineering and/or product development in the classic sense (Roy, 2004)."

Definition of innovative opportunities and selection depends on the customer scheme[3] of the firm, which will give a different perspective on the application domain (Doherty, 1990). Therefore, marketing alliance might help overcome technological myopia. Marketing alliances can also provide information to familiarize the firm with the selection environment and help change understanding of the application domain. As Adner and Levinthal (2000) express:

> "In order to apply existing technological knowledge…the firm needs to focus on selecting market contexts for a product rather than selecting products for a fixed market context. There may be a variety of technologies that are sitting in the laboratory that would begin to emerge if transplanted into the right market."

Marketing alliances can help firms understand preference trajectories (Tripsas, forthcoming), or cycles of incremental and discontinuous changes in preferences, which are analogous to technological trajectories. Preference discontinuities, in the form of consumer demand for totally new functionality or features, i.e. new attributes included in the consumer's utility function or step function changes in preferences for existing attributes, can be catalysts for technological transitions. By understanding changes in preference trajectories, firms can leverage existing technological knowledge into new application domains.

Marketing alliances between firms thus allow for a more comprehensive understanding of the application domain, as application domain knowledge is tacit (Kogut and Zander, 1992; Katila, 2004) and even when it is codified, it is not asset specific (Williamson, 1981). Especially for entrepreneurial firms, marketing alliances create pressure to innovate into new application domains, e.g., to identify and satisfy unmet needs among existing and potential customers (Adner and Levinthal, 2001; Clark, 1985; Christensen, 1997) and understand government regulations, competitive landscape, and availability of complementary assets to identify and satisfy resource restrictions (Levinthal, 1998; Adner and Levinthal, 2000). Thus, marketing alliances might help

3 Dunn and Ginsberg (1986) review such orientations also labeled cognitive maps, knowledge structures, scripts, theories of action. Also see Lawrence and Lorsh (1967) for discussion of departmental cognitive orientations and Van Maanen and Barley (1984) for discussion of occupational communities.

overcome technological dependence.

Hypothesis 2a: Marketing alliances increase the likelihood of cross-application in that they increase the likelihood that a firm will leverage technological knowledge.

Hypothesis 2b: Marketing alliances increase the likelihood of cross-application in that they increase the likelihood that a firm will explore application domain knowledge.

METHODOLOGY

SAMPLE SELECTION

The concept of cross-application is studied in the context of the biotechnology industry. Biotechnology firms apply the principles of engineering and technology to life sciences. Biotechnology firms collectively and individually exhibit the highest alliance activity among all high-technology industries (Hagedoorn, 1993); and these firms are clearly engaged in the process of entrepreneurship – the creation of new wealth through opportunity discovery, evaluation and exploitation (Shane and Venkataraman, 2000). Biotechnology is a relatively new industry as the first player, Genentech, was founded less than 30 years ago. The core technologies used in biotechnology are approximately 20-25 years old. These technologies are numerous and diverse, including applications for basic drug development, agrobiology, nanotechnology, even industrial applications. As Powell, Koput, and Smith-Doerr (1996) write: "in many respects, biotechnology is not an industry per se but a set of technologies with the potential to transform various fields – pharmaceuticals, chemicals, agriculture, veterinary science, medicine, even waste disposal." This paper treats the wide array of biotechnology companies as comparable, as do many previous papers on the field (e.g. Barley and Freeman, 1992; Amburgey, Shan and Singh, 1994).

Given the importance of knowledge creation in biotechnology innovation – specifically, the need to develop and extend intellectual property – patent data can serve as a powerful metric to measure and understand the underlying knowledge base of firms. Indeed, the biotechnology industry is optimal as a population for testing the developed hypotheses as, in this industry, patent filing and citations are a core strategy for intellectual property protection (Arora, Fosfuri, and Gambardella, 2001) and least prone to problems in self-citations (Alcacer and Gittleman, 2004).

The level of analysis is at the innovation level. To identify different types of recombinant innovation (those described in Table 1), entrepreneurial firms are selected and then analyzed for their innovations, where each patent is an innovation. There are two stages in product development: science to proven technology versus proven technology to product (Grupp, 2000). This paper focuses on the first. The Securities Data Company (SDC) Venture Expert database is used to identify the population of Venture Capital (VC) backed entrepreneurial firms in the biotechnology industry. VC-backing is used to investigate firms that are early stage but that have somewhat of a viable underlying technological knowledge. Of the total 4,072 VC-backed biotechnology firms, a simple random sample (Levy and Lemeshow, 1991) of 25% or 1018 firms was used to find firms with at least two patents.[4] Patent data from the United States Patent and Trademark Office (USPTO) patent database identified 106 firms with at least 2 patents. At least two patents must exist for there to be any evidence of leveraging existing knowledge. Each patent, after the first, is then categorized. Of the 106 firms, 48 have alliances: 148 marketing alliances and 216 R&D alliances. Due to missing data for controls, the final sample consists of 2305 patents.

PATENT AND CITATION DATA

Cross-application and the three other types of recombinant innovation are measured by using patent and

4 The entire sample was not investigated due to lack of resources and time and as a simple random sample achieves a conservative estimate compared to that obtained from the entire sample.

citation data (Figure 4). Although it may have some limitations, patent and citation data have been utilized extensively in economics to understand the process of invention and innovation (Schmookler, 1996; Griliches, 1984 and 1990; Jaffe 1998). In particular, the references or backward citations that appear in a patent identify earlier inventions whose claims are sufficiently close to the claims of the citing patent (Jaffe, Trajtenberg, and Fogarty, 2000). Backward citations serve the legal function of delimiting the scope of patent protection, by identifying technological predecessors of the patented invention. The applicant has a legal duty to disclose any knowledge of prior art, but the decision as to which patents to cite ultimate rest with the patent examiner, who is supposed to be an expert in the area and hence able to identify relevant prior art that the applicant has missed or concealed. Patent citations are an accepted measure to study how older innovations are combined to produce new innovations (Griliches, 1979, 1992; Jaffe, 1986; Jaffe, Trajtenberg, and Henderson, 1993). Although, it has been shown that citations are many times added exclusively by examiners, biotechnology is an industry where such a problem might not be pertinent and references are accepted to be a satisfactory indication of prior art (Alcacer and Gittleman, 2004). Patents and patent citations in the biotechnology industry, therefore, have less potential problems making it more ideal for analysis.

DEPENDENT VARIABLES

Following the discussion above on typology of recombinant innovation, the four types of innovations are measured as follows:

TYPE 1: Leverage of technological knowledge and application domain knowledge is identified when the firm references only previously filed firm patents (self-citations) in the same technology domain (measured by 3-digit U.S. Patent Class code).

TYPE 2: Also called cross-application, leverage of technological knowledge and new application domain knowledge is identified when a patent self-cites at least one previously filed firm patent in a different technology domain.

TYPE 3: New technological knowledge and leverage of application domain knowledge is identified when the firm has only previously filed patents in the same technology domain but does not self-cite (self-citing would indicate leveraging existing technological knowledge).

TYPE 4: New technological knowledge and new application domain knowledge is identified by no self-citations and a new technology domain (different than all past patented technology domains).

Using the patent class as an indication of the application domain or the emphasis on attributes for use is supported in previous literature. Griliches (1990) pointed out that classes are based primarily on technological and functional principles. Also classes have been used to measure how a patent will be "used" (Schmookler, 1966; Scherer, 1982). The classes used in this sample (Figure 5) can be found in Table 2 and the outcomes of the categorization can be found in Table 3.

United States Patent	6,949,356
Busby , et al.	September 27, 2005

Methods for improving secondary metabolite production in fungi

Abstract

The invention relates to the production of secondary metabolites by fungi. More particularly, the invention relates to improvement of production of commercially important secondary metabolites by fungi. The invention provides methods for improving secondary metabolite production in a fungus, comprising modulating the expression of a gene involved in regulation of secondary metabolite production.

Inventors:	**Busby; Robert** (Weymouth, MA); **Cali; Brian** (Arlington, MA); **Hecht; Peter** (Newton, MA); **Holtzman; Doug** (Jamaica Plan, MA); **Madden; Kevin** (Charlestown, MA); **Maxon; Mary** (Somerville, MA); **Milne; Todd** (Brookline, MA); **Norman; Thea** (Belmont, MA); **Royer; John** (Lexington, MA); **Salama; Sofie** (Boston, MA); **Sherman; Amir** (Boston, MA); **Silva; Jeff** (Beverly, MA); **Summers; Eric** (Brookline, MA)
Assignee:	**Microbia, Inc.** (Cambridge, MA)
Appl. No.:	**487558**
Filed:	**January 19, 2000**

Current U.S. Class:	**435/41**; 435/43; 435/254.11; 435/471
Intern'l Class:	C12P 001/00; C12P 001/02
Field of Search:	435/25411,41,43,471

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Figure 4. Example of a Patent

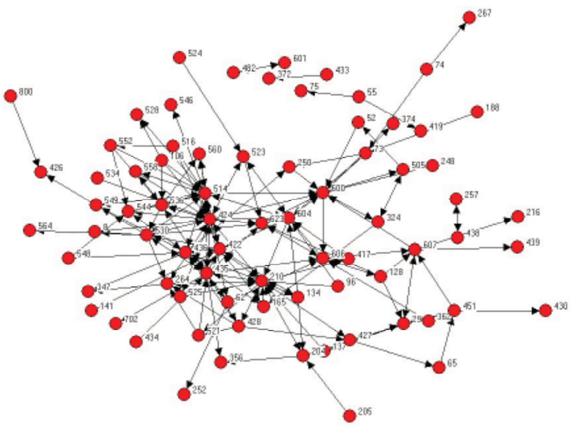

Figure 5. Sample of Cross-Application

Table 2. List of Classes in Cross-Application Sample

8	Bleaching and dyeing; fluid treatment and chemical modification of textiles and fivers
29	Metal Working
52	Static structures (e.g. buildings)
55	Gas separation
62	Refrigeration
65	Glass manufacturing
73	Measuring and Testing
75	Specialized metallurgical processes, compositions for use therein, consolidated metal powder compositions, and loose metal particulate mixtures
96	Gas separation: Apparatus
106	Compositions: Coating or Plastic
128	Surgery
134	Cleaning and Liquid Contact with Solids
137	Fluid handling
141	Fluent Material Handling, With Receiver or Receiver Coating Means
165	Heat Exchange
204	Chemistry: electrical and wave energy
205	Ectrolysis: Processes, Compositions
210	Liquid Purification or Sepration
216	Etching a substrate: processes
250	Radiant energy
257	Active solid-state devices (e.g. transistors, solid-state diodes)
264	Plastic and nonmetallic article shaping or treating: processes
324	Electricity: Measuring and Testing
347	Incremental printing of symbolic information
362	Illumination
372	Coherent light generators
374	Thermal measuring and testing
417	Pumps
419	Powder metallurgy processes
422	Chemical apparatus and process disinfecting, deodorizing, preserving, or sterilizing
424	Drug, bio-affecting and body treating compostitions
426	Food or edible material: processes, compositions, and products
428	Stock material or miscellaneous articles
430	Radiation imagery chemistry: process, composition, or product thereof
433	Dentistry
434	Education and demonstration
435	Chemistry: molecular biology and microbiology
436	Chemistry: Analytical and Immunological Testing
438	Semiconductor device and manufacturing: process
439	Electrical connectors
451	Abrading
505	Superconductor Technology: Apparatus, Material, Process
514	Drug, bio-affecting and body treating compositions
516	Colloid systems and wetting agents; subcombinations thereof; processes of

521	Ion-exchange polymers, cellular products, waste polymer recovery
523	Synthetic Resin Compositions and Nonreactant Material
524	NRM to a preformed solid polymer or preformed specified intermediate condensation product
525	Chemically Treated Synthetic Resins, Compositions of Plural Synthetic Resins
528	Synthetic Resins from Plant Material of Unknown Constitution or Specified Reactant
530	Natural Resins, Peptides, Proteins, Lignins
534	Radioactive or Rare Earth Metal Compounds, Azo and Diazo Compounds
536	Carbohydrates
544	Six-Membered Nitrogen Hetero Rings with Two or More Hetero Atoms
546	Six-Membered Hetero Rings with One Ring Nitrogen
548	Five- Four- or Three Membered Nitrogen Hetero Rings
549	Oxygen or Sulfur Hetero Rings
552	Azides, Tripheylmethanes, Quinones, Hydroquinones, Steroids
558	Esters
560	Carboxylic Esters
564	Amino Nitrogen Compounds
600	Surgery: radioactive substances
604	Medicators and Receptors
606	Surgery: devices or appliance for use in operative surgery
607	Prosthesis (i.e. artificial body members), parts thereof, or aids and accessories therefore
623	Surgery: light, thermal, and electrical application
702	Data processing: measuring, calibrating, or testing
800	Multicellular living organisms and unmodified part thereof and related processes

Table 3. Dependent Variable Categories and Distribution

	Reuse Application Domain Knowledge	New Application Domain Knowledge
Reuse Technological Knowledge	TYPE 1 354 of 2305 (15%)	TYPE 2 389 of 2305 (17%)
New Technological Knowledge	TYPE 3 447 of 2305 (19%);	TYPE 4 1115 out of 2305 (49%)

INDEPENDENT VARIABLES

The independent variables are the previous year counts of marketing alliances (*Marketing*) and R&D alliances (*R&D*). Counting numbers of alliances is an accepted method of measuring colloboration experience (Katila and Mang, 2003; Das, Sen, Sengupta, 1998; Dutta and Weiss, 1997). For example, Katila and Mang (2003) measure the cumulative number of firm R&D collaborations to measure R&D collaboration experience. Results hold for cumulative counts and different lags, however, previous year counts are used to distinguish the impact of recent knowledge gained by alliances.

CONTROLS

Patents: A firm might find it easier to leverage technical knowledge if a firm has more patents. This variable indicates the stock of technological knowledge of the firm and is measured by the count of previous patents the firm has to patent-of-interest's application date.

State: Prior literature has found that there is a significant effect of knowledge spillover in certain geographic clusters, as such a firm might get new knowledge from spillover effects (Griliches, 1995; Jaffe, 1998; Jaffe, Trajtenberg, Henderson, 1993). This variable is measured as a dichotomous variable coded one if the firm is located in California or Massachusetts where most biotechnology firms are located (2033 of 2305 observations).

Age: As a firm matures, it is more likely to exploit rather than explore (Sorenson, 2004). This variable is measured from the firm founding date to the patent-of-interest's application date and is left censored at zero (since some firms had patents before founding).

Size: Firms with more resources are more likely to utilize those resources to explore new knowledge (Cyert and March, 1963). As data could not be gathered for each firm year, the average size of the firm is used to create a categorical variable coded one if the firm employs on average less than 100 employees (410 out of 2305 observations), two if the firm employees on average less than 500 employees (522 of 2305 observations), and three if the firm employees on average 500 or more employees (1233 of 2305 observations). This categorization method is used by the U.S. Small Business Administration (SBA) to describe entrepreneurial firm size. This is also a rough way of capturing R&D and marketing budgets of the firm.

Other alliances: For some of the robustness checks, I also included counts of *licensing* and *manufacturing* alliances. These are also previous year counts of alliances like the independent variables.

ANALYSIS AND RESULTS

Analysis is performed at the innovation, or patent, level to test if indeed alliances affect cross-application (positively or negatively).[5] Multinomial logistic regression is a widely accepted method used in analyzing a categorical dependent variable that has more than two categories (Allison, 1999).[6] In this case, the categories have no ordering and the logistic regressions are run in comparison to a reference group. Descriptive statistics of the independent variables, including a correlation matrix, are presented in Table 4. Multicollinearity tests, including tolerance and variance-inflation factor (VIF), indicate pair-wise correlations are not problems in this analysis.[7]

Multinomial logistic regression compares multiple groups through a combination of binary logistic regressions. In this case, the differences in R&D alliances and marketing alliances in promoting TYPE 1, TYPE 2, TYPE 3, and TYPE 4 innovations can be explored. TYPE 2 innovations, or cross-applications, are the type of innovation of interest, as such TYPE 2 is used as the reference group to obtain the coefficients that test the hypotheses. Using multinomial logistic regression as the primary method, the analysis compares TYPE 1 to TYPE 2 innovations and TYPE 4 to TYPE 2 innovations. Multinomial logistic regression provides a set of coefficients for each of the comparisons. The group comparisons are equivalent to the comparisons for a dummy-coded dependent variable. Thus, the coefficients for the reference group are all zeros, similar to the coefficients for the reference group for a dummy-coded variable. Simple discriminant analysis provides preliminary confirmation that marketing alliances and R&D alliances are significant in discriminating between the 4 types of innovation at

5 Initial exploratory work analyzed the firm longitudinally, across years, to find that there is a significantly positive relationship between marketing alliances and cross-application. Results can be found in the Appendix.

6 This analysis examines a firm profile across time to investigate how different firm profiles trigger a set of outcomes. There is a mix of outcomes as patenting is not mutually exclusive. This objective of this analysis does not lend itself to discrete analysis, e.g. like personality tests at different times that lead to different behaviors.

7 Multicollinearity is the intercorrelation of independent variables. Inspection of the correlation matrix reveals only bivariate multicollinearity for bivariate correlations > 0.90. While simple correlations tell something about multicollinearity, the preferred method of assessing multicollinearity is to regress each independent on all the other independent variables in the equation to obtain R2 (R2=0.4597). R2's near 1 violate the assumption of no perfect collinearity. Tolerance is 1 - R2 and as a rule of thumb, if tolerance is less than .20, a problem with multicollinearity is indicated. VIF is simply the reciprocal of tolerance. VIF >= 4 is an arbitrary but common cut-off criterion for deciding when a given independent variable displays "too much" multicollinearity: values above 4 suggest a multicollinearity problem.

the p <0.001 level.

Table 4. Descriptive Statistics and Correlation Matrix of Independent Variables

Variable	Mean	Std. Dev.	Min	Max	(1)	(2)	(3)	(4)	(5)	(6)	(7)
(1)Marketing	0.1822	0.6426	0	8	1.0000						
(2)R&D	0.8265	1.4861	0	9	0.5889*	1.0000					
(3)Licensing	0.2090	0.7028	0	6	0.7508*	0.5214*	1.0000				
(4)Manuf.	.0728745	0.4013	0	6	0.7286*	0.5310*	0.6365*	1.0000			
(5)Patents	28.7692	67.7341	2	598	0.2005*	0.2768*	0.1782*	0.2890*	1.0000		
(6)State	0.8057	0.3961	0	1	0.0677	0.0534	0.0638	0.0876	0.0850	1.0000	
(7)Age	12.1936	9.0835	0	50	0.0860	0.0455	0.0661	0.0399	0.5123*	-0.0480	1.0000
(8)Size	1.7857	0.7673	1	3	0.2524*	0.2683*	0.2345*	0.2883*	0.4464*	0.1571*	0.4358*

*p<0.01

There is an overall relation between the independent variables and the dependent variable. Two tests are relevant: the likelihood ratio test and the Wald test. The likelihood ratio test evaluates the overall relationship between an independent variable and the dependent variable. The Wald test evaluates whether or not at least one of the independent variable is statistically significant in differentiating between the groups in each of the embedded binary logistic comparisons. Both are significant at p<0.0001 level. This indicates that there is an almost certain relationship between the dependent variable, type of innovation, and at least one of the independent variables.

Table 5: Results of Clustered Multinomial Regression[8]

Category (TYPE 2 is the reference group)	**TYPE 4 New Tech**	**TYPE 1 Leverage AD**
Intercept	0.6914* (0.2178)	-0.8276* (0.3280)
Marketing	-0.2399* (0.1084)	-0.2738* (0.1600)
R&D	0.1644 (0.1152)	0.1596 (0.0971)
Patents	-0.0008 (0.0007)	0.0005 (0.0006)
State	0.0517 (0.3419)	0.6340* (0.2690)
Age	-0.0213 (0.0145)	-0.0111 (0.0074)
Size	0.3258* (0.1661)	0.1184 (0.1796)

*p<0.05

8 Type 2 and Type 4 are compared to make the direct comparison of leveraging technological knowledge as that is the difference between the two. In the same logic, comparing Type 2 and Type 1 would give you the impact of exploring application domain knowledge. Type 2 and Type 3 gives you the impact of doing opposite types of recombination.

In finding support for Hypothesis 1a and Hypothesis 2a, the coefficients of Column 2 in Table 5 are interpreted as magnitude and direction in the coefficient's ability to distinguish between types of innovation.[9] Hypothesis 1a states that R&D alliances decrease the likelihood that a firm will leverage technological knowledge. Hypothesis 1a does not find full support in the coefficient for *R*&D in the regression comparing TYPE 4 (explore technological knowledge/explore application domain knowledge) with TYPE 2 (leverage technological knowledge/explore application domain knowledge). The coefficient is positive but not significant. However, multinomial logistic regression can only control for observations that are independent across groups (clusters) but not necessarily within groups.

In finding support for Hypothesis 1b and Hypothesis 2b, the coefficients of Column 3 in Table 5 are interpreted as magnitude and direction in the coefficient's ability to distinguish between types of innovation. Hypothesis 1b states that R&D alliances decrease the likelihood that a firm will explore application domain knowledge. Hypothesis 1b is fully supported by the coefficient for *R&D* when comparing TYPE 1 (leverage technological knowledge/leverage application domain knowledge) with TYPE 2 (leverage technological knowledge/explore application domain knowledge). The coefficient is positive and significant. This means that R&D alliances positively affect leverage of application domain knowledge compared to exploring new application domain knowledge. It is 17 percent more likely that firms leverage application domain knowledge than explore new application domain knowledge with R&D alliances.

Hypothesis 2b states that marketing alliances increase the likelihood that a firm will explore application domain knowledge. Hypothesis 2b is fully supported by the coefficient for *Marketing* when comparing TYPE 1 (leverage technological knowledge/leverage application domain knowledge) with TYPE 2 (leverage technological knowledge/explore application domain knowledge). The coefficient is negative and significant. This means that marketing alliances negatively affect leverage of application domain knowledge compared to exploring new application domain knowledge. It is 24 percent less likely that a firm will leverage application domain knowledge than explore new application domain knowledge with marketing alliances.

To control for heteroskedasticity in testing Hypothesis 1b and Hypothesis 2b, a fixed effects logitistic regression model is used (Table 6). The dependent variable is a dichotomous variable where zero indicates leveraging of application domain knowledge and one indicates exploration. There is a positive and significant effect of marketing alliances on exploring application domain knowledge, while there is a negative effect of R&D alliances on exploring application domain knowledge.

Table 6. Logit with Firm Effects

Category (TYPE 2 is the reference group)	**TYPE 4 New Tech**
Marketing	0.2949* (0.1461)
R&D	-0.1764 (0.0964)
Patents	-0.0033* (0.0012)
Age	0.1346* (0.0355)

*p<0.05

9 An exponentiated value reveals the percentage change in the expected odds of the dependent variable for a one-unit change in the independent variable. The generic transformation formula is: (exp(B) - 1)(100%)

Other robustness checks were performed. To test if primary results hold true for more distant application domain knowledge, lagged counts of alliances were used. This test shows robustness for the effect of marketing alliances on exploring new application domain knowledge and leveraging existing marketing knowledge. Also other alliances were added as controls, those of manufacturing and licensing. Results are robust at t-1 where cumulated alliance counts are lagged by a year for allow for learning effects (see Table 7 and Table 8).

Table 7. Logistic Regression of Alliances on Cross-Application

(Dependent variable is binary, coded 1 if the firm had TYPE 2 innovation that year)

Intercept	-1.054* (0.3983)
Marketing	-0.7315* (0.4807)
R&D	-0.2101 (0.1646)
Licensing	-0.2993 (0.3529)
Manufact.	-0.7315 (0.4807)
Patents	0.0344 (0.0072)
Age	0.0045 (0.0185)
Size	-0.1204 (0.1882)
State	-0.3023 (0.2990)

*p<0.05

Table 8. Robustness Check with Lagged Alliance Data

(R^2=0.5094 for Tolerance and VIF Tests for Lagged Data)

Category (TYPE 2 is the reference group)	**TYPE 1**	**TYPE 3**	**TYPE 4**
Intercept	-0.8462** (0.3268)	-0.2602 (0.2818)	0.7572* (0.2172)
Marketing	-0.1852 (0.1189)	-0.3216* (0.1203)	-0.2042* (0.0761)
R&D	0.0351 (0.0841)	0.1269 (0.0760)	0.1945* (0.0622)
Patents	0.0007 (0.0006)	-0.0030* (0.0007)	-0.0008 (0.0005)
Age	-0.0149 (0.2823)	-0.0167* (0.0082)	-0.0198* (0.0067)
Size	0.1807 (0.1416)	0.03219* (0.1274)	0.2763* (0.0084)
State	0.6091* (0.2824)	0.2870* (0.2307)	0.0292 (0.1946)

*p<0.05

DISCUSSION

This paper identifies a missed opportunity for entrepreneurial firms in innovation, if they adopt the traditional prescription for continued innovation. While R&D alliances help explore new technology, they do not help leverage technology into new applications. Marketing alliances are essential to leveraging technology and exploring new application domain knowledge.

Why should marketing alliances increase cross-application innovation events? The type of knowledge that is being shared in marketing alliances seems to be about new application domains and developing existing technological knowledge for these new domains. Besides the ability to overcome technological myopia and technological dependence by moving scientists into a new context for problemistic search (Von Hippel and Tyre, 1994), marketing alliances also seem to offer: 1) resource complementarity; 2) less hierarchical controls; and 3) the sharing of firm routines that become interfirm routines for discovery and development. First, alliance formulation is positively affected by complementary resource bases (Chung, Singh and Lee, 2000). Thus, it might become a subsequent incentive to utilize those complementary assets in innovation, which leads to greater cross-application. Second, anticipated coordination costs and expected appropriation concerns govern the magnitude of hierarchical controls on in the contractual relationship underlying alliance formulation (Gulati and Singh, 1998). As marketing alliances do not seem to present as much coordination costs or appropriation concerns, hierarchical controls should be less. Thus, it might create a less restricted environment for innovation resulting in greater opportunity for cross-application. Third, alliances provide opportunities to share and develop routines around the partnership leading to relational rents (Dyer and Singh, 1998). Thus, it could be the sharing of routines in marketing alliances that create interfirm routines resulting in greater cross-application.

Thus, this paper begins to integrate the realms of marketing and innovation strategy. Instead of using developed innovations to set marketing alliances strategy; firms could use marketing alliances to develop a commercially-driven innovation strategy. While this study focuses on entrepreneurial firms and the use of cross-application to continue growth, established firms will also undertake cross-application. However, in such firms, resources might allow marketing teams to be developed in stead of using marketing alliances. Integrating marketing and innovation has been a strong empirical trend in large pharmaceutical companies where commercially-driven product development groups are being built to promote entrepreneurship within the larger R&D organization, as evidenced in Pfizer, Merck, and Novartis.

This is an important insight as hi-tech entrepreneurial firms are often headed by founding entrepreneurs who are first and foremost "engineers" or "scientists," and only second consider themselves "marketers" (Doherty, 1990; Roy, 2004). As a result, knowledge creation is not tied to application domain knowledge. When it comes to clarifying what the application domain comprises, technical orientation focuses narrowly on technology and thus disregards the distinction between application issues versus marketing or manufacturing issues (Doherty, 1990). Scientists and engineers can move away from current narrow functionality of existing technology. Marketing alliances between firms can allow for a more comprehensive understanding of the application domain and help entrepreneurial firms understand where to place existing technology to leverage expensive knowledge networks or alliances. Especially for entrepreneurial firms that do not have marketing initiatives, marketing alliances are critical.

The concept of cross-application merges the "technology push" versus "demand pull" arguments (Mowery and Rosenberg, 1979; Dosi, 1982). Innovation is a mixture of meeting application domain needs and utilizing firm resources. This paper sheds some light on the overarching question of what motivates innovation and channels its direction (Mowery and Rosenberg, 1979). As Mowery and Rosenberg state: "Both demand and supply side influences are crucial to understanding the innovation process." As Adner and Levinthal elaborate:

> "Discussions (on managing technology) pay little attention to the market contexts in which innovations are exploited and the impact these market interactions may have on exploration

activity. Because of the belief that technological revolutions occur in the lab, manager sometimes undervalue the importance of applications. While 'supply side' considerations are important, it is critical to consider constraints and thresholds on the demand side as well."

This paper also positions entrepreneurial firms as the agents behind transformative technological change, such as creating speciation events (Levinthal, 1998; Adner and Levinthal, 2000). By doing so, this paper adds to the entrepreneurship literature by clarifying the role of entrepreneurial firms in technology development in the transitional stage after initial innovation and inception (Gartner, 1985; VanderWerf, 1993; Bhave, 1994; Shane, 2001). The entrepreneurial firm becomes as important in its discovery of a novel opportunity as it does in its continuing role of recognizing new application domains in which to leverage initial innovation.

LIMITATIONS AND EXTENSIONS

The entrepreneurial firm's preliminary innovation in which an initial application area is chosen is not examined as extensive research has looked as this issue, including those of the founding conditions (Stinchcombe, 1965) and initial venture creation (Gartner, 1985; VanderWerf, 1993; Bhave, 1994; Shane, 2001). However, it is hoped that future work will link the selection of the initial application to subsequent application choices to find out what drives application domain knowledge exploration.

As this paper characterizes the physiology of the firm in aggregate, this paper may lead to further questions that are more reductionist in nature (e.g., identifying key success factors). This analysis examines a firm profile across time to investigate how different firm profiles trigger a set of outcomes. There is a mix of outcomes as patenting is not mutually exclusive. As there exist a set of outcomes, there is no mapping to a single outcome. Such a mapping may be desirable. Finding a method to include more discrete analysis could provide interesting additional information about cross-application and an untapped yet significant source of value for entrepreneurial firms.

Currently this paper does not distinguish between types of alliances partners (Ahuja, 2000; Chung, Singh and Lee, 2000; Sampson, 2004). There may be different characteristics that drive alliance formation between two specific firms (Ahuja, 2000; Chung, Singh, and Lee, 2000). There also may be different characteristics that affect the ability of firms to learn from each other (Sampson, 2004). These characteristics can influence the relationship of the strategic alliance and its outcomes in leveraging technological and application domain knowledge. Technologically diverse marketing partners might increase the likelihood of exploring new application domain knowledge. Future research could incorporate measures of technological diversity (Sampson, 2004) and or complementarity (Chung, Singh, and Lee, 2000) to understand the potential effects of cross-application.

This paper also does not address whether firms can develop a capability to utilize alliances in innovation. Evolutionary economics reasoning has been applied to the strategic alliance context (Zollo, Reuer, and Singh, 2002) to find that inter-firm coordination and cooperation routines enhance effectiveness of collaboration agreements. This logic could be applied to cross-application and the benefits of marketing alliances. Future research can investigate how the routinization process can affect the results of partnering to explore application domain knowledge. The focal firm may be able to determine a method by which marketing alliances can drive cross-application, and utilize this method to efficiently produce more cross-application innovations with subsequent marketing alliances. This paper does not distinguish typologies of marketing alliances. There is a broader theoretical question regarding whether all marketing alliances are the same.

Another question not addressed in this paper but suggested for future research would be investigation of how cross-application impacts firm success. Leveraging existing technological knowledge and exploration of application domain knowledge has been shown to have an impact on the economy at large (Diamond, 1999), however it is still not understood what the specific impact is to the entrepreneurial firm. As Adner and Levinthal (2000) illustrate, firms such as Sanyo, Sharp and Casio were able to introduce profitably existing technology into new application domains.

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