MNE KNOWLEDGE NETWORKS IN THE PHARMACEUTICAL INDUSTRY: THE INTERNATIONAL GEOGRAPHY AND STRATEGY OF KNOWLEDGE SOURCING AND DIFFUSION

by

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ABSTRACT OF THE DISSERTATION

MNE knowledge networks in the pharmaceutical industry:
The international geography and strategy of knowledge sourcing and diffusion

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This dissertation examines the evolution of the international knowledge network of leading MNEs in the pharmaceutical industry from 1976 to 2016. It is organized into eight chapters, including three novel empirical studies on the geography and strategy of knowledge sourcing for technology creation, the subsequent use of new applications, and the reciprocal exchange of knowledge. We begin with a literature review on a line of work which can be traced back to an earlier question, 'under what conditions do MNEs source technology internationally through a network of geographically dispersed affiliates?'. We then provide an analytical structure for which the histories of the pharmaceutical industry are told in Chapter 3. We elaborate on a set of potential research questions arising from this reflective presentation of the historical background of the industry, and describe the organization of the data used in our empirical studies in Chapter 4. We use patents granted between 1976 and 2016 by the US Patent and Trademark Office (USTPO) to examine the sources or antecedents of technological knowledge over time, arranged by the originating organization and its sector of activity as well as the location of inventors. Using these data, we aim to answer questions related to the geographic and strategic dimension of MNE knowledge structures in three studies. In chapter 5 (Study 1), we examine how sourcing patterns may differ depending on the extent to which foreign subunits focus on competence creating (CC) vs competence exploiting (CE) types of inventive activities. In chapter 6,

(Study 2), we investigate patterns of intra-MNE diffusion of CC innovations to the home and within the host country settings. In chapter 7 (Study 3), we examine the degree to which geographic profiles of MNEs regulate their interaction with other firms in the industry. Our dissertation offers a neglected way to examine the sourcing activities of contemporary MNEs and provides new insights on patterns of technological knowledge building within and between organizational and spatial boundaries, and their consequences.

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CHAPTER ONE: INTRODUCTION

The more open international environment has been a stimulus to expanding the range of geographic and organizational knowledge sourcing activities of multinational enterprises (MNEs). In this dissertation, we leverage network ideas in international business, economic geography, and innovation studies to explain how the structure of knowledge networks have been evolving, given that increasingly aspects of technological change are organized across borders (Cantwell, 2017). We begin with a brief literature review on a line of work which can be traced back to an earlier question 'under what conditions do MNEs source technology internationally?' (e.g. Dunning, 1998). To guide our investigation of the evolution of knowledge networks for innovation or technology creation, we highlight theoretical mechanisms and functions of a typology of ties, i.e. external vs internal knowledge sourcing, and local and global knowledge connectivity. We focus on knowledge networks for different types of inventive activities (competence-creating vs competence-exploiting), the subsequent use of new capabilities, and the reciprocal exchange of knowledge.

We follow this review with a comprehensive historical examination of the creation and evolution of the pharmaceutical industry, which is the context of our research. We explain the specificities of three consecutive paradigms in its development. The first paradigm begins in the mid-19th century, when the influence of chemistry on medicinal research had reached a degree of maturity and ends with the outbreak of WWII. The second paradigm requires a better understanding of organizational features that differ from the old-line pharmaceutical companies that emerged in the 19th century. These companies were largely influenced by legislative and institutional improvements (including fiscal incentives for firm innovative activities), as well as restrictive environments, and turbulent decades. The third paradigm reflects geographic shifts of specialization in pharmaceuticals and changes in the composition of organizations involved due to scientific and technological breakthroughs; its setting is more collaborative (with mergers and acquisitions playing a decisive role) and networked than previous paradigms. We conclude this chapter by summarizing the institutional and organizational elements of these changes, the network dynamics between firms, and the political and macroeconomic trends that date back to the mid-19th century.

We provide a set of potential research questions arising from the reflective presentation of the historical background of the pharmaceutical industry. We explore these questions by adopting a network perspective, e.g. networks within and between firms, and other organizations (universities, hospitals, etc.). We infer the organizational and geographic knowledge structure of MNEs using patents extracted from USPTO websites from 1976-2016. We describe the organization of the data employed and provide a revised interpretation of citation-based knowledge networks. Our essential analytical scheme is grounded upon a conceptualization of technological knowledge accumulation over time, i.e. each dyad or connection between an earlier cited patent A and a subsequent citing patent B represents a recognition of knowledge relevancy, or a step in a knowledge building process. Our basic question is thus, drawing upon a knowledge building perspective, how does the structure of knowledge sources or origins evolve over time, within and between organizations and across space?

The objective of our first study (chapter 5) is to consider how sourcing patterns may differ depending on the extent to which foreign-located MNE subunits focus on competence creating (CC) vs competence exploiting (CE) types of inventive activities. While recent studies have explored the relationship between the use of internal and external knowledge sources in innovation (Phene and Almeida, 2008; Rosenkopf and Padula, 2008; Hagedoorn and Wang 2012; Monteiro and Birkinshaw, 2017), and the evolving structure of knowledge development in MNEs within and across national boundaries (Ambos and Ambos, 2011; Berry, 2014; Monteiro, 2015; Cano-Kollmann *et al.*, 2016; Turkina and Assche, 2018; Cantwell *et al*. 2019), less attention has been given to the influence of different types of organizational networks on the geography of knowledge sourcing by the activities of foreign MNE subunits. This leaves a gap in our understanding of the conditions under which foreign subunits source technological knowledge locally or globally, and the impact different types of organizational ties have on these trends. We therefore examine the effects on international knowledge sourcing of drawing upon different types of knowledge ties. We argue that drawing on specialized knowledge may increase international search efforts for CE inventions since the probability of acquiring excellence in core technical fields, or the best university science-based knowledge for exploitative efforts is greater. We qualify this argument by noting that sourcing internationally requires a clear understanding of how new knowledge is relevant and can be recombined with firm capabilities. On the other hand, explorative types of knowledge sourcing may be locally bound, i.e. exploring into new areas of expertise or developing CC inventions is dependent on the subjective character associated with local knowledge-based interactions, where organizational processes and knowledge building efforts can be more easily observed. We test hypotheses that distinguish between explorative and exploitative activities, and suggest an association between the type of organizational linkage and international knowledge search efforts. We compliment the empirical analysis by applying techniques from SNA to provide a descriptive investigation of the changing structure of foreign-subunit's knowledge networks for CC vs CE activities over time, and compare the change in composition of sources. This allows us to go beyond traditional indicators to understand the landscape of knowledge building using patent citations, which, by allowing us to construct nodes (organizations) from patents and the links between them, reveals the overall knowledge network of foreign located subunits. We find a greater importance of local, diverse knowledge sourcing for CC activities, and an international, application focus for CE activities.

The objective of our second study (chapter 6) is to focus on the extent new areas of expertise diffuse within MNEs. We explore HQ-subsidiary or inter-subsidiary knowledge transmission (Andersson *et al.*, 2007; Ambos *et al.*, 2011), given their importance for the affiliates concerned. We focus on the relevance and transmission of new areas of expertise to the home country and within the host country setting, not merely the creation of capabilities in MNE foreign subunits, or the specific roles of the subunits in the MNE network. Through the process of reviewing work that investigates the advantages of intra-MNE network connectedness, the following mechanisms have been forwarded as possible explanations for the diffusion of new capabilities. First, the development of new combinations around the core business expertise of the MNE group requires a more reciprocal international knowledge exchange relationship with the parent company (Berry, 2014; Cantwell and Piscitello, 2014; 2015), through which the corporate group knowledge is accessed and possibly combined with the new knowledge generated by the foreign subunit's competence-creating activity. The reciprocal exchange of knowledge therefore increases the parent firm's awareness of how new capabilities developed in the host country may be relevant to subsequent developments. In turn, foreign subunits may attract the attention of their parents when engaged in competence creative types of activity that relate to the core knowledge base of the MNE. Second, while on average, difficulties associated with achieving embeddedness in international and local networks may negatively impact knowledge diffusion in the host countries, higher technological performers can manage to achieve dual embeddedness despite its typical drawbacks; i.e. without simultaneous consideration of the subunit's network position and creative activity, a subunit is unlikely to transmit locally the knowledge it identifies. We estimate how much of the empirical pattern of knowledge diffusion can be explained by the subunit's ability to create new knowledge, identify the relevance of new developments, as well as the extent to which its centrality accelerates the diffusion of new areas of expertise. Our results reveal the reciprocal exchange of knowledge and the degree of relatedness of competence creating inventions to the developments undertaken by the parent firm are important determinants of diffusion to the home country. However, we find that the diffusion within the host country is driven by subunits that can achieve dual embeddedness more successfully.

The objective of our third study (chapter 7) is to examine two types of geographic leverage that relate to the sources of knowledge and recombination potential in affecting inter-MNE knowledge reciprocation – the *geographic profiles of innovations*, i.e. the sites of origin of inventions, given that learning processes may be influenced by the context within which activities were undertaken, and the *geographic overlaps of external sourcing* in the form of cited inventions. We emphasize the idea that reciprocation is influenced by the firm's proximity to its competitors as well as the spatial distribution of its knowledge sources in relation to the sourcing behavior of other firms. We build on arguments from the knowledge spillovers perspective, which focuses on externalities that arise from siting activities in a particular location (Shaver and Flyer, 2000; Arino et al., 2004; Ghemawat 2005, Rugman 2005, Khanna et al. 2006; Nachum et al., 2008; Cantwell and Mudambi, 2011), and the knowledge building perspective, in which technological knowledge is cumulatively developed within and between organizations and across space. We consider how the strategic and geographic positioning of MNE knowledge arrangements may increase the knowledge exchange between them. Results confirm that the reciprocal exchange of knowledge between leading MNEs in the pharmaceutical industry is influenced by the degree to which these firms co-locate their technological activities as well as the degree to which the geographic profile of their knowledge sources of basic science and clinical applications overlap. While the overall relationship between co-location and reciprocation is negative, closer analysis reveals an inverted U-shaped relationship, essentially showing that firms at a certain geographic distance are more likely to exchange knowledge in order to access complementary areas of specialization that they lack, i.e. at a certain distance, but not too far away, as that would lead to a lack of connection between profiles. Findings also indicate MNEs that source external knowledge from a similar profile of city-regions increase their knowledge exchange. Taken together, we discuss how the sites of origin of inventions, proximity to competitors, and commonalities in sourcing knowledge beyond a geographically bounded context influence inter-firm knowledge reciprocity. We offer a richer conceptualization of geographic profiles. Chapter 8 concludes the dissertation.

CHAPTER TWO: THE SPREAD OF MNE KNOWLEDGE NETWORKS FOR INNOVATION

The objective of this chapter is to provide a brief overview of the literature on the changing nature of the MNE and its knowledge networks for innovation. While early international business theories focused on the evidence of in-house activity in large firms, and accordingly, the role of foreign located subunits, more recent research has paid attention to changes in MNE knowledge structures, accompanied by an acceptance of a wider array of strategic and geographic positioning of foreign subunits (Cantwell and Piscitello, 2000). We therefore adopt the view of an evolution of international business networks that incorporate the MNE, but are not necessarily restricted to it; and try to explain what a network perspective has to offer to the analysis of the knowledge sourcing activities of MNEs, given that increasingly aspects of technological change are organized in their foreign subunits (Cantwell, 2017). We draw on the technological accumulation approach (Cantwell, 1989), in which technological knowledge is understood as being cumulatively developed through international networks, and new technologies rely on novel combinations of prior knowledge (Arthur, 2009). We also make use of a line of work in innovation studies which has argued that open innovation systems are supplementing formal MNE structures since they spread wider and aren't limited by contractual relationships (Chesbrough, 2003, 2006; Laursen and Salter, 2006; Gassmann, Enkel and Chesbrough, 2010; Pénin, Hussler and Burger-Helmchen, 2011). We limit our attention to research on external vs internal knowledge sourcing, and the geographic profile of knowledge sources and innovation. This allows us to make connections across research areas that have appeared in international business and provide a sense of some of the ongoing themes and potential research directions that make use of network related arguments.

Organizational sources of innovation

The essential premise of the received explanation of the existence of the MNE is that the MNE is primarily a connector of different innovative locations (Dunning, 1998). It is further argued that technological knowledge tends to be built cumulatively over time (Nelson and Winter, 1982; Rosenberg, 1982). This starting point for the analysis of the MNE as a technology creator across national boundaries (Cantwell, 1989) has led to greater interest in the competence-based approach to the firm in the analysis of the MNE and its network for innovation. Historically, technological knowledge that related to the MNE's core field of specialization was primarily created in the parent company, upon which subunits and external partners relied (Vernon, 1966; Buckley and Casson, 1976; Porter, 1990). In this traditional model, new competency creation typically occurred in selected subunits in foreign markets. While the parent firm still plays an important role as a source of competence creation through the existence of foreign subunits of the MNE (Berry, 2018), aiding the transfer of parent-generated knowledge that would then be adapted to local conditions, the increased interaction between other subunits within the MNE and external affiliates suggests a steady evolution of international knowledge networks that incorporate the knowledge developed by the parent firm, but is not necessarily restricted to it.

An earlier line of writings has drawn attention to the intimate connections in intra-corporate group networks, and how these have enabled foreign subunits to identify the relevance of new areas of expertise (Patel and Pavitt 1991; Kogut and Zander, 1992; Gupta and Govindarajan, 2000; Hansen, 2002). Within their host country environment, these subunits engage in greater knowledge-based interactions with local actors (Andersson and Forsgren, 2000; Andersson *et al.*, 2002; Almeida and Phene, 2004; Alcacer and Chung, 2007; Singh, 2008). Their ability to develop external ties in the host-country network, through which technical knowledge is located and accessed is critical for the development of new competencies, and continued participation in local communities, e.g. important clusters of knowledge, sophisticated suppliers, universities, and other local firms in the knowledge network (Porter, 1990; Furman *et al.*, 2002). Because the greater access to knowledge and resources of other organizations in the local innovation system has led foreign located subunits to behave more autonomously, a major theme in international business has therefore converged around the subsidiary's influence and autonomy (Andersson et al., 2007) and the knowledge ties within MNEs (Mudambi and Navarra, 2004). Gaining access to new knowledge requires networking efforts that determine the subunit's ability to successfully apply new applications (Tsai, 2001).

An influential line of research in the innovation studies literature has therefore highlighted the importance of external knowledge search (Chesbrough, 2006; Phene and Almeida, 2008; Rosenkopf and Padula, 2008; Hagedoorn and Wang, 2012; Laursen and Salter, 2014; Monteiro and Birkinshaw, 2017), suggesting that technological progress is a function of combining internal and external knowledge sources of innovation (Dosi, 1988; Cohen and Levinthal, 1990; Veugelers and Cassiman, 1999; Cantwell *et al*., 2019). For example, in the context of science-based industries, where the search-facilitating knowledge is partially held in-house and partially by external sources to the firm, e.g.

"public science", one determinant of how successfully firms further exploit their competencies is their ability to access and incorporate relevant research areas from those sources outside the firm, i.e. R&D performed in universities and research institutes, or clinical applications from hospitals. Interestingly, with the exception of a few studies that provide some insight on sourcing university knowledge internationally (D'Este and Iammarino, 2010; D'Este, Guy, and Iammarino, 2013), extant studies have suggested that university-industry linkages tend to be geographically localized (Jaffe, Trajtenberg, and Henderson, 1993), lacking insight about the type of knowledge being sourced internationally, and for the purposes of different kinds of knowledge building efforts – explorative or exploitative. Prior literature has also tended to treat hospitals as part of universities, since patient contact is needed in training new doctors, and so indeed, many hospitals are attached to universities. However, the close associations between hospitals and universities does not mean that they are universities (Hicks and Katz, 1996), and so little is known about connections to clinical or medical practices, particularly from the perspective of MNE affiliates in generating new technologies of an either specialized or creative kind. While prior literature might expect that sourcing hospital knowledge isn't necessarily bound to the local context in the development of knowledge for medical practice (Bignami *et al.* 2019), given the codifiable nature of clinical science, the purpose and nature of established hospital knowledge ties may differ for explorative vs exploitative types of activities (see chapter 5).

Geographic sources of innovation

Research in the economic geography and innovation studies offers some guidance about the innovative outcomes of local vs global sourcing. On the one hand is the embeddedness perspective (Almeida and Phene, 2004), which argues that firms are embedded in the environment they are situated in, and so source knowledge locally (Cantwell and Iammarino, 2000), since researchers in a particular region are surrounded by a plethora of knowledge, i.e. any actor who participates in that region's economic sphere may benefit from its local 'buzz' (Bathelt et al. 2004; Stroper and Venables, 2004). The extent of embeddedness in a cluster therefore influences a firm's likelihood of generating competence-creating types of inventions. The kind of tacit knowledge that is essential for exploratory tasks may transfer more readily through embedded ties between actors that share a mutual understanding of new research and applications within the constraints of some established institutional arrangements. Localized networks are also characterized by repeated interactions based on trust and cooperation (Granovetter, 1973; Uzzi, 1996, 1997; Hansen, 1999; Obstfeld, 2005), which may discourage opportunistic behavior, since these may be associated with adverse reputational consequences (Coleman, 1988). Especially when experimenting into new areas of competencies, which implies a greater variance in the quality of output, it may be easier to draw on local sources of knowledge when there is no contract to regulate or control partner inputs. Recent writings have therefore asked whether firms benefit from different types of clusters (Cantwell and Mudambi, 2011), or how they may be able to contribute to a local business network (Cantwell, 2009). For example, Cantwell and Mudambi (2011) argue that MNEs benefit from sourcing locally in clusters which offer a diverse base from which an MNE is able to construct an external network of knowledge linkages; a higher degree of local industrial concentration would inhibit local knowledge sourcing by outsiders.

By way of contrast, international connectivity can benefit firms to a greater extent in further exploiting existing competencies (Scalera *et al.*, 2018), because the probability of acquiring the right specialized knowledge is greater, particularly when searching for excellence, e.g. in core technical fields, or the best university science-based knowledge. An important dimension of exploitative search efforts is that subunits may have explicit objectives when searching internationally for activities that are closely aligned to the existing knowledge base of the firm. In such cases, the locus of innovative search is likely to reside within external networks that are not necessarily where the MNE or its affiliates are sited. The basic assumption is that the impact of participating in external technical communities on international search efforts depends on specific properties of such networks. For example, sourcing knowledge from universities located abroad entail higher transaction costs, since such linkages lack the subjective character associated with local knowledge sourcing, e.g. a mutual understanding of new knowledge and applications within the constraints of the local network. Searching for knowledge internationally is rarely subjective and requires a clear understanding of how this new knowledge is relevant and can be recombined with firm capabilities [by implication, high levels of absorptive capacity]. Put differently, even though sourcing knowledge from abroad entails higher transaction costs, MNEs rely on specialized knowledge to complement internal research, which may be located elsewhere in the world, but nonetheless provide clear prospects of returns on innovation.

Moreover, while economic geographers have explored the kinds of technological knowledge transmitted within a city-region (Florida, 2005; Bathelt and Glückler, 2011, 2017), the motivation to establish a knowledge tie within- or across-locations is also partly determined by the networks that characterize areas that host relevant research activities (Cantwell and Piscitello, 2002), as opposed to location advantages that are fixed within them (Derudder, Witlox, and Taylor, 2007). MNEs with dispersed technological activities may be able to exploit more effectively established competencies in a particular location when moving into new technological areas; however the international business literature has yet to fully incorporate the diversity of ties entailed in cross-border geography of networks for different types of inventive activities, as opposed to organizational aspects of the MNE's network, i.e. parent-subsidiary relationships, and thus home-host country associations (Cuypers *et al.*, 2020).

Research setting

In the context of the recent evolution of the MNE a good example is the pharmaceutical/bio-technology industry. This provides us with an ideal archetype of the evolution towards an international business network theme, since until quite recently it was regarded as one industry in which a successful MNE must be tightly vertically integrated from basic R&D through to distribution. Now instead basic drug ideas can be picked up and licensed from smaller biotech firms, and clinical trials are outsourced. Basic technological capability relies increasingly on the capacity of the pharma major (MNE) to be an effective knowledge integrator across a network of technologically proficient organizations, which may include universities and public research institutes as potential sources, as well as other firms. Related portfolios of drugs can then be in-licensed (where they've not been generated in-house), but then distributed through subsidiaries in dispersed locations. For locations not covered by a given MNE, out-licensing of drugs is increasingly also considered, perhaps sometimes in return for strategic cross-licensing agreements with selected partners. Yet when dealing with technological trajectories, it's important to take account of pressures that seem to be leading some pharma firms away from one location towards another. Especially in recent times, firm-specific advantages have evolved to increasingly become network-specific; internalization advantages increasingly relate to certain kinds of knowledge or selected components of knowledge that can be transferred effectively across borders to other parts of a corporate group or a closely coordinated international business network; while location advantages may have come to comprise some endogenous local network-specific advantages, as well as developments that lie beyond any given business network. In the course of this evolution, we wish to focus on the improvement and transformation of the knowledge base of this industry, which is partially common within the MNE and partially common with other organizations in the overall network.

CHAPTER THREE: PARADIGM CHANGE IN THE HISTORY OF THE PHARMACEUTICAL INDUSTRY

The history of the pharmaceutical industry as told in this chapter is focused on the limits to growth of the sciences upon which the industry relies on, the changes in the nature and structure of the largest companies active in the industry, and the knowledge networks between those companies and various organizations. It also makes the connection between organization-level developments and macroeconomic trends as well as with the institutional structure that affect or encourage knowledge-based relationships. I maintain that paradigm change can only arise through a continuous interaction between science, technology, business organizations, national institutions, and the wider growth of economic and social developments. I demonstrate that the technological progress in pharmaceuticals cannot be fully understood where any of these are taken in isolation.

I build on several strands of research to identify and conceptualize paradigm change in the pharmaceutical industry. The first parallels the historical development theorized by Freeman and Louca (2001). This work has directed attention to the interdependencies of economic and social movements, which include technological and scientific innovations, within the framework of institutional settings. The second adopts the three epochs, or major paradigms suggested by Henderson et al. (2000), and implicitly recognized in the specialist literature on pharmaceuticals. The third builds upon the systemic perspective suggested by Cantwell et al. (2010), who proposed that international business co-evolves with its institutional environment. The objective is to connect the three major paradigms in the history of the pharmaceutical industry to global developments, since in the evolutionary process of substantial change that has characterized this sector, firm behavior and institutions related to both science and public policy have strongly interacted with one another.

The pharmaceutical industry is driven by advances made in science, high research and development (R&D) investments and long development cycles. It has produced the majority of new medicine, and in many ways, changed the character of the medical community. The evolution of the industry has also been significantly shaped by the environment for which it has taken part. To understand the continuous historical transformation of the industry, I analyze the leading area of interaction between science and technology with the external environment, differentiating contexts within which different views about modes of organizing business activity have taken place.

While theoretical and empirical studies have paid attention to the structure of the health care system, the institutional arrangements surrounding health-related research, and the role of intellectual property protection in affecting the processes of innovation, scant attention has been paid to the interaction between the shift in the technological paradigm in this industry from chemistry to the life sciences, the changes in organizational composition over time, as well as the context within which the interactions between various organizations have taken place. I examine the changes in corporate structure which reflect paradigm change in the industry, the varying types of investments, and increasing cooperation of the major companies with various types of organizations, and within the wider context of shifting paradigms. The history that lies behind the term ‘paradigm change’ in the industry under study is therefore an intriguing mix of accounts of science, technology, institutions, political and social trends, and conceptions of chance and history.

The chapter is structured as follows. First, I conceptualize the nature of paradigm change as a shift from preceding patterns of commercializing pharmaceutical technologies by relating scientific advances to organization-level developments as well as macroeconomic trends. This provides the analytical structure for which the histories of the pharmaceutical industry are told in section 3: Paradigm 1 (1850 to 1939), Paradigm 2 (1940 to 1989), and Paradigm 3 (1990 to date). I then summarize the major developments in science, technology, types of business organization, national institutions, and political and economic trends since the mid-19th century. Finally, I elaborate on a set of potential research questions arising from this reflective presentation of the historical background of the industry

Understanding the nature of paradigm change in the pharmaceutical industry

Paradigm change in the pharmaceutical industry can be perceived broadly, dating back to Ancient Egyptian prescription records, or narrowly, to the first specialized pharmaceutical plant in Germany. A broad lens would include all efforts of drug discoveries over time, much of which took place in isolated societies that progressed at much slower speed with simpler forms of technology. Paradigm change in the pharmaceutical industry as seen through a narrow lens focuses on activities that necessarily entail a strong interaction between technological efforts and scientific advances, each of which have been influenced by the tighter and more complex form of interdependencies of recent history. From this dichotomy, industry specialists, business historians, as well as scientists in the field of biology, have taken a narrow perspective of development in the pharmaceutical industry, where the science and technology linkages are central. Within such narrow perspective, the relative autonomy of evolutionary developments in science and technology justifies independent consideration.

Over the last few decades, economists have paid attention to Schumpeter's claims, particularly that technological innovation revolutionizes the economic structure from within, destroying old formations of markets and incumbent advantages (Christensen, 1993; Tripsas, 1997), allowing for new entrants unencumbered by firm history; though the modern evolutionary literature on technological change has tended to follow the Penrosean tradition (Cantwell, 2002), which accounts for the cumulative nature of corporate learning (Helfat and Raubitschek, 2000; Zollo and Winter, 2002), i.e. deeply entrenched capabilities that accumulate and coevolve with products and markets, as well as the complexities that arise in different institutional contexts.

The parallel observation made in technology holds for science; the most discussed account of scientific revolutions is Thomas Kuhn's. In his work, scientific paradigms displace the old, and are so radically different that they can no longer be compared with the preceding paradigms in guiding future research. Nelson and Winter (1977, 1982) had drew attention to the relative autonomy of developments along a technological trajectory, and the possibility of noncumulative, conceptual and practical changes in subsequent epochs. Dosi (1982) further developed this work by drawing analogies to Kuhn's paradigms in science for technology; though, unlike Kuhn, Dosi's ideas didn't speak to a particular community, and for this reason, can be seen cited in the wider social sciences (Tunzelmann et al. 2008), as well as higher levels of analysis, such as the evolution of an industry. Nonetheless, there is evidence that suggests, as the sciences upon which technological knowledge relies on shifts, so does the locational specialization of the technological knowledge; and though science and technology may have their paradigms, more needs to be understood about the extent to which patterns of science have affected technological developments, and the limits to growth science has to offer for commercializing new drugs.

While developments in technology and science can be seen as relatively independent, as is reflected in their social reorganization, methodological standards, content and goals, it is essential to take into account their interdependencies, and their reliance on institutional and economic developments for the purpose of understanding paradigm change, emergence, and evolution in the pharmaceutical industry. Freeman and Louca (2001) have suggested a coevolution of social subsystems (science, technology, politics, economics, culture) to provide insight into the process of paradigmatic shifts. This work builds on earlier theorizing by Derek De Solla Price (1984), Nathan Rosenberg (1969, 1974, 1976, 1982), Keith Pavitt (1995), which demonstrated the way in which systemic features of scientific and technological developments have interacted, and with the wider economic and institutional environment. Recent traditions in management and economic geography already reflect the perspective of technological change as an evolutionary process, and take into account the wide range of institutions that coevolve with technology at the micro-level of the firm. A long discussion in the international business literature has, in many ways, rethought what is meant by 'evolutionary' processes, drawing attention to sociological, wider ranged approaches of technological accumulation, the interaction between production, institutions, and governance structures, as well as the influences the expansion of the firm has itself had in helping to stimulate change in the environment (Cantwell et al. 2010). There is also work in the strategy and organizational theory literature, which has also begun to suggest that organizational analysis should be more about how individuals aggregate to the collective level, capturing a more complex social interaction and interdependence with institutional entities.

In what follows, I assume the definition of paradigm change as put forth by Dosi (1982): discontinuous change is associated with the emergence of a new technological paradigm, defined as a pattern of solutions selected and established by the interplay between scientific advances, various economic and institutional variables. Once a technological paradigm has been selected among new, competing paradigms, in relation to the long-run patterns of social development, the path selected and established shows a momentum of its own (Nelson and Winter 1982; Rosenberg, 1969), which is consistent with classical theories of social evolution, most notably Hegel and his contemporaries. Furthermore, technological knowledge is cumulatively developed (Cantwell, 1989), and new technologies rely on novel combinations of prior knowledge, product portfolios and adaptive organizational capabilities (Arthur, 2009; Zott and Amit, 2008; Helfat and Raubitschek, 2000; Teece, et al, 1997). In this way, while a discontinuity reflects a break with the past, the past is necessarily synthesized in subsequent paradigms. To be sure, a trajectory is defined as the direction of advance within the boundaries of an established paradigm (Dosi, 1982), whereas the existence and nature of paradigm change is induced at the crossing between science, technology, institutions, political and economic trends, and for this reason, needs to be explained historically.

As previously mentioned, I also parallel the co-evolutionary developments presented in Freeman and Louça (2001) with adjustments to the subsystems as would be applicable to the process of paradigmatic shifts in the context of the pharmaceutical industry. Revised definitions of these subsystems are the following. In particular, I've replaced culture with institutions, since I regard culture as a partial feature of what is meant by institutions in the relevant literature, (Cantwell et al. 2010; North, 2005) and is consistent with prior work on institutional change and social and physical technologies (North, 2005; Nelson and Sampat, 2001). Furthermore, developments which occur within each paradigm require understanding and reviewing the feature of subsystems which, taken together, are profoundly different in subsequent paradigms.

(1) **Science** is the generalizable and replicable knowledge of nature, usually resulting from basic research and represented by refereed and published papers. The science involved in drug discovery, through which potential new medicines are identified, include biology, chemistry, and pharmacology.

(2) **Technology** is a collective capability or knowledge of production (products, processes and services), which is not easily replicable. The technologies involved in drug discovery in the current paradigm include various computational tools.

(3) **Business organization** is a form within which application of science to production and practitioner knowledge of technology take place in pursuit of commercial interest. Firms in the pharmaceutical industry were historically integrated. The industry now relies on networked based structures.

(4) **National institutions** are such things as laws, scientific regulations, educational institutions, national innovation policies, culture, etc., which mold and differentiate the nature of innovative activity across countries.

(5) **Economic, political, and social trends** reflect the wider economic and social growth and demand, political developments, or industry-related crises.

In summary, although each of these subsystems have distinctive features and have their own paradigms, their interdependencies and interaction express the process of paradigmatic shifts of the industry. First, for a coherent paradigm to take hold, each of the aforementioned subsystems need to be harmoniously connected. Thus: a paradigm is a social system with interconnected parts. Changing one part cannot be done without changing others. There may be paradigms within each of the sub-systems identified: e.g. as argued by Kuhn for science. However, in a science-based industry where the developments of science and technology are well connected, the reciprocal influence of the developments that occur within each of the aforementioned subsystems need to be taken into account (Price,1984; Rosenberg, 1969, 1974, 1976, 1982; Pavitt,1995). Moreover, while the emergence of a new paradigm causes conflict with older paradigms, as reflected in the nature of linkages between scientific, business and government institutions, old paradigms can be seen as retained and embedded in a subsequent paradigm. Science and technologies are cumulatively developed, new institutions embody old formations, and political, economic and social contradictions are ultimately resolved and integrated in practice.

Histories of the pharmaceutical industry

The history of the pharmaceutical industry is told within the three major paradigms implicitly recognized in the specialist literature, and explicitly, though roughly divided in Henderson et al. (2000), due to its' usefulness for examining the evolution of the pharmaceutical industry. The shift between each paradigm is due to a number of key features that are so profoundly different and merit descriptions. The first paradigm receives a longer period of time through which prescriptions were customized and formulated at local laboratories in various societies. It begins in the mid-19th century, when the influence of dye chemistry and analytical chemistry on medicinal research had reached a degree of maturity, and ends with the outbreak of WWII. The second paradigm requires a better understanding of organizational features that differ from the old-line pharmaceutical companies that emerged in the 19th century. These companies were largely influenced by new institutions, restrictive environments, and turbulent decades. The third paradigm reflects geographic shifts of specialization in pharmaceuticals and changes in the composition of organizations involved; its' setting is more collaborative and networked than previous paradigms. Needless to say, the ability to link the research concerns of markets, and the interaction with the emergence of external research institutes as well as connection to university science and engineering for background knowledge and training has been critical, and so much of the focus will therefore be on the current paradigm.

First Paradigm (1850 to 1939)

In the mid-19th century, the science of chemistry was providing new learning and generating new product opportunities. During this time, Germany and Switzerland were leaders in the science of chemistry and in the synthetic dye industry. It was thus initially Swiss and German chemical producing enterprises, such as Roche, Ciba, Sandoz, BASF, Bayer, and Hoechst that exploited their technical competencies and knowledge accumulated in organic chemicals and dyestuff to commercialize drugs based on synthetic dyes. A number of British and American firms, such as Wyeth (later, American Home Products), Eli Lilly, Squibb, Upjohn, Pfizer, Merck, Abbott, SmithKline, Warner-Lambert, and Brothers-Wellcome emerged as specialized in pharmaceuticals in the later part of the 19th century. These firms would eventually become old line pharmaceutical companies which grew internally then via merger and acquisitions to overcome barriers to entry, and pioneer technical capabilities needed to produce and market prescription drugs for national and international markets.

In the US, the industry evolved largely in response to the advent of modern transportation and communication (Chandler, 2009). The major US core companies were rather wholesaler/producer enterprises with strong marketing capabilities and distribution channels—e.g. use of new radio networks to reach mass markets—operating in commercial cities (Liebenau, 1987). They relied on German and Swiss firms to supply new prescription drugs based on revolutionary organic chemical technologies, and merely processed, packaged, and marketed a variety of existing over-the-counter drugs derived from natural resources. In general, large firms tended to grow in the most technologically advanced and dynamic centers, and so the new transport and communication technologies of the 19th century was a precondition for the administrative coordination of production decisions, and were therefore regulated by the potential for economies of scale and scope. In fact, up until the end of the second paradigm, scale and scope were closely linked. Achieving scale depended upon bringing together the production of related products and common distribution networks.

However, strategies of diversification and internationalization required an evolution in the organizational structure that would later support the new sciences, and capture returns on new technologies. First, an evolution from the hierarchical to a managerial structure (Chandler 1986) was required to provide the institutional support for in-house corporate R&D, which would become essential for large firm survival in the second paradigm. This evolution can be traced back to the early years of the 20th century, when three major

German companies had begun to integrate upstream into the production of essential raw materials, expanding into other areas of chemistry, pharmaceuticals, nitrogenous fertilizers, plastics, photographic products and synthetic materials (fibers), by extension from organic chemistry (Cantwell, 2004). Following the formation of IG Farben in 1925, intensification of research was in the hands of professional managers than it was influenced by top-level decision-makers, thus becoming the "world's first truly managerial industrial enterprise (Chandler)". Likewise, corporate R&D needed to be divisionalized, with a central facility that commanded a strategic overview function led by technically trained managers. It was therefore the central labs which were likely to incorporate some basic research activities with the more localized support of divisions, which had their own R&D facilities. In this way, the firm was not only narrowly focused on the demands and narrowing research agendas of each division, but with the wider firm and industry within which these demands belong.

Second, the more restricted environment that took hold toward the end of the first paradigm and through to the second paradigm obliged firms to jump barriers by investing in markets abroad. Thus, German chemical firms, such as Merck and Schering, established subsidiaries in the US, whereas firms whose innovative diffusion of home markets led them to replicate their activities abroad included companies like Roche, which would later become a world leader in genetic engineering. The openness which characterized the first paradigm allowed American firms to effectively incorporate European, largely Swiss and German, development capabilities, and build research laboratories to create the necessary production facilities, and commercialize new prescription drugs on their own. This cumulative experience would have great implications for large firm survival in subsequent paradigms.

The science of chemistry began to peter out by the early 20th century, as the science of biology created new learning and opportunities for commercialization. In addition, the institutions that supported the efforts that were driven by chemistry did not represent suitable platforms for the newly emerging drug research that had become increasingly guided by pharmacology and clinical sciences. During this time, the US was relatively specialized in biology, becoming more sensitive and aware to public health concerns, and the need the contents and sale of pharmaceutical products (the history of the FDA requires a chapter in its own right). But it wasn't until the US ceased importing German products during WWI that American firms began to investigate throughout the interwar years how to develop the technical capabilities needed to commercialize prescription drugs based on newer pharmaceutical technologies. After the discovery of penicillin and other antibiotics, pharmaceutical companies either established departments of microbiology and fermentation units, or exploited their microbiological capabilities to find drugs.

Second Paradigm (1940 to 1989)

The institutions created for drug research and development in the second paradigm, which has its' roots during WWII, led to the formation of the pharmaceutical industry as we know it, where mass production required greater linkages with universities, medical schools, hospitals, research institutes, and/or national laboratories, depending on the way in which funding is administered nationally, and the nature of the linkages between research and practice locally. In the US, government-sponsored crash programs provided the financing required to build research labs and the necessary production facilities focused on commercial production techniques and chemical structure analysis. The increasing dialogue between microbiologists, biochemists, pharmacologists, and chemists resulted in substantial advances in physiology, pharmacology, enzymology, and cell biology, as well as a revolution in prescription drugs, in antibiotic drugs and then in other therapeutic areas. In addition, the industry's transition to an R&D intensive business increased the likelihood of large firm survival by increasing the capacity to learn and adapt to changing environments. Though not all German firms adopted the managerial form structure, they did have centralized science based strategies, benefited from research institutes, and pioneered industry-university cooperative relationships, which would later become critical in the third paradigm.

With the outbreak of the second world war, pharmaceutical companies were faced with a "target rich" environment, but had very little detailed knowledge about the causes, much less of the biological underpinnings of specific diseases. These companies relied on what has become known as "random screening", a method for finding new drugs, by which the specific biochemical and molecular roots of many diseases were not well understood. The advances made in traditional biology (physiology, pharmacology, enzymology, and microbiology) and use of enzyme systems as screens led to enormous progress in the medical understanding of both, the chemical reactions of existing drugs, as well as diseases for which no drug therapy existed (Gambardella 1995; Henderson 1994). Several companies in the US, UK, and Switzerland were among the first to design significantly more sophisticated and sensitive screens to screen a wider range of compounds that were previously available in either small quantities or difficult to evaluate due to the complex mixture of reactions in living animals (Henderson and Cockburn, 1994; Scannell, et al, 2012; Lipinski and Hopkins 2004). French, Italian, other European, and Japanese firms were slower in absorbing the concepts introduced by biochemistry, such as enzymes and receptors. This is partially due to a number of factors, including a comparative weakness in scientific research functions in addition to absence from the global industry (with the exception of Takeda). These differences would have significant implications for firm response to the advent of molecular biology as well as the technological specialization of countries in pharmaceuticals.

The introduction of genomic sciences, rapid DNA sequencing, combinatorial chemistry in the 1970s required specially trained scientists, innovative approaches to drug discoveries, and a fresh set of ingredients and services – that is to say, the institutional and organizational support that distinguishes the US environment and explains the success of biotech in the US. First, the Diamond vs Chakrabarty Supreme Court patent decision, allowing the patenting of novel living organisms and their DNA in 1980, removed barriers to biotechnology. Second, a federal statute enacted in 1983, known as the Orphan Drug Act, gave tax benefits and granted a 7-year monopoly to enterprises that commercialized drugs to treat relatively uncommon life-threatening conditions, which would otherwise be uneconomic to discover and bring to market. Major pharmaceutical firms had been investing their efforts on best-selling drugs (with sales of $1 billion or more), and neglected marketing efforts behind smaller, existing products, many of which could have become best sellers, and benefit a wider array of patients than originally anticipated (as was the case with AIDs, asthma, etc.). Third, changed social relationships within universities attracted the entrepreneurial interest of numerous professors who knew how to use advances made in genetic engineering to enhance the productivity of discovery in addition to benefiting from niche drugs large pharmaceutical firms neglected in favor for those in demand. Inevitably, a number of startups emerged in the late 1980s, quickly built integrated learning bases, and created from scratch the functional capabilities needed to, and succeed in commercializing products from new technology based on the new discipline of molecular biology (Chandler 2009). Together, the new startups created the infrastructure of a new industry—biotechnology, that marked the transition to the third paradigm.

However, the evolution of biotechnology, and ultimate success of the biotech industry was unclear for some time, so the use of molecular biology hadn't yet been adopted as a research tool until the third paradigm. Moreover, the 1970s was an instable decade, characterized by stagnation, recession and high unemployment, in addition to high prices, decreasing rate of successful new product introduction, and the breakdown of the postwar system of international monetary exchange (Chandler, 2009). During this period, pharmaceutical companies were merely investigating the transition to guided discovery, and what it would take to incorporate the new technical knowledge and procedures with the advent of molecular biology. However, no momentum appeared in light of the new technology and no successful biotech firm emerged until the late 80s, with the exception of Genentech, founded in 1976, now a subsidiary of Roche as of 2009.

Following the chemical crisis between 1979 and 1982, chemical firms had also begun to redefine product lines to commercialize, mostly by buying and selling business units from one another (Chandler, 2009). The coming of new pharmaceutical technologies based on a new science (molecular genetics) presented a dramatically different pattern of growth to which pharmaceutical firms had no inherent advantage over chemical firms (Kenney, 1986). To increase profits, there was a trend among US pharmaceutical companies to diversify into related consumer chemicals (household and personal goods), food and drink, as well as medical instruments and devices—an industry related in terms of markets, but not technology. However, these firms quickly realized that the less diversified their company the better their financial performance, and the stronger positioned they were to recognize the importance of biotech in addition to exploiting the new learning in traditional biology, especially microbiology.

In the meantime, chemical companies began a large-scale restructuring of their product portfolios, first by strengthening their core competencies followed by the drive into pharmaceuticals – that is, developing products based on the new science of biology than chemistry. For example, Monsanto was the first to successfully grow capabilities in traditional biology and biotechnology, and in trying to commercialize chemically based and genetically engineered agricultural products. However, not all chemical firms were particularly successful. Du Pont's response to the crisis was to diversify into pharmaceuticals by acquiring a small drug company, Endo, then by forming a joint venture with Merck, through which Du Pont would learn how to develop the necessary functional capabilities. Unable to compete with industry rivals, Du Point sold its' pharmaceutical division to Bristol-Meyers Squibb in 2001. Dow had also quickly failed, abandoning its attempt to enter through acquisitions, including its' 1989 Marion Laboratories, which it later sold to Hoechst 5 years later. While these companies had strong marketing capabilities, they failed to build ties with startups, universities, and research institutes, which would later become especially important in the third paradigm. European chemical firms were more successful in shifting their focus from chemicals to pharmaceuticals by quickly selling or spinning off their chemical businesses: e.g. following the merger of Ciba-Geigy and Sandoz in 1995 that formed Novartis, the firm quickly sold off its' chemical businesses to focus on pharmaceuticals; Hoechst merger with Rhone-Poulenc Rorer to form Aventis, led the firm to spin off its chemical businesses; Britain's ICI spun off its' pharmaceutical division as a separate enterprise (Zeneca).

In sum, large pharmaceutical firms were fully integrated from drug discovery through clinical development, regulations, manufacturing, and marketing. Within this paradigm, these firms produced a range of drugs, prescription and over-the-counter, relying on a few best sellers, each with annual sales in excess of $1 billion. Drug discovery had been conducted in-house, where large random-screening programs were used with, as mentioned earlier, limited knowledge about the underlying physiological processes. However, this in-house capacity had begun to rely upon collaborations with other organizations, including universities, research institutes, and government-funded institutes.

Third Paradigm (1990 to date)

The advent of molecular biology attracted a number of firms from different technological traditions and had a great impact on a number of other fields, including chemicals, diagnostics and agriculture. Needless to say, the new science had its greatest impact on human therapeutics, and the organizational structure of the pharmaceutical industry. First, the potential to understand disease processes at the molecular (genetic) level and to determine optimal molecular targets for drug intervention presented new concepts of drug discovery. In the current paradigm, the search for a new drug begins with a therapeutic area of interest, and analysis of existing drugs and patents. Scientists mine the scientific literature to identify a drug target—a protein (e.g. enzymes, receptors) or nucleic acid (e.g. DNA, RNA) involved in a disease to which a drug is directed to change its' behavior or function. With information on drug targets, genes, and the biological mechanisms responsible for the disease, medicinal chemists comb through a what is known as a "chemical space" to design and synthesize compounds that can bind to the target. Leading candidate compounds are then selected for advancement into clinical trials. This approach to drug discovery is known as reverse pharmacology or target-based drug discovery (Drews, 2000).

By the mid-1990s, firms were quick to adopt a novel technique called "combinatorial chemistry" and replaced synthetic and medicinal chemists with powerful computation tools. These tools lowered the cost per molecule achieved, by allowing chemists to create millions of related compounds in a single step, and model 3-dimensional structures of gene targets with those chemical structures. Around the same time, the first draft of the human genome was introduced by the Human Genome Project, which enhanced coordinated search efforts in drug discovery by providing a clearer picture of the target landscape. The availability of the human genome map was a complementary innovation for target-based drug discovery (Hoang and Rothaermel, 2010); the map was therefore mainly beneficial to firms experienced in target-based strategies, which were either large, diversified, and research intensive firms or smaller specialized biotech firms with unique intellectual properties (Zucker, et al, 1994).

The challenge for long-established core pharmaceutical companies—which had continued to rely on the support of the existing nexus that had been so enlarged by the post-WWII therapeutic revolution (Chandler, 2009)—was to incorporate new technical knowledge and procedures and transition to the "drug discovery by design" (from a process of trial and error). In addition, these companies had to maintain the new sub disciplines of biology (including microbiology, enzymology, and biochemistry). Pharmaceutical companies were the first to shift towards the biotech model for R&D, and develop strong ties to various scientific institutions (universities and government research laboratories) which were heavily supported by governments with funding for research in the new science that could aid the private sector's R&D. Countries therefore sought to create the optimal financial arrangements for public-private partnerships. In the US, funds are administered through the government-owned National Institute of Health (NIH), funding more than one-third of biomedical research. The Foundation of the NIH (FNIH) was an additional government agency that supported research and educational programs as well as foster collaborative relationships between the NIH, firms active in pharmaceuticals, universities, and non-profit organizations. The nature of these collaborations were specified in formal contracts (including cost sharing and rights to patents). In the UK, biomedical research is funded by the Department of Health, the Medical Research Council, and private foundations such as the Wellcome Trust (UK); France and Germany, biomedical research is performed directly in government research laboratories, such as CNRS, INSERM, Deutsche Forschungsgemeinschaft and the Max Plank Gesellschaft.

Pharmaceutical companies gained advantage in becoming the first industrial group to learn and recognize the importance of molecular biology, rDNA, and biotech through a number of intangible benefits, including membership to scientific networks, where interactions improve the learning activities of participants, i.e. company scientists (Kenney 1986; Pavitt 1991). And so were also the first to redefine their strategic boundaries and acquire the research tools and production technology the new sciences had to offer. However, the maturing of biotechnology as a research and manufacturing technique brought an increasing number of MNCs into the industry and increased competition. As discussed previously, chemical firms sought to reverse stagnation, using the products of biotech as a tool to create new products for agriculture.

The synergies between the skills developed in applications of biotech to agriculture and medicine meant that pharmaceutical companies had no inherent advantages over chemical firms in producing drugs (Kenney, 1986), and so the technical barriers between chemical and pharmaceuticals, both producers and marketers of molecules, eroded – the use of molecular biology as a production tool was a competence destroying innovation (Henderson et al. 1999), particularly for firms that had little experience with target-based strategies. While pharmaceutical companies had the advantage in becoming the first industrial group to recognize the importance of biotech, and take the lead in their investments, chemical firms were larger financial entities and increasingly research-oriented (Kenney, 1986). Thus, chemical executives saw pharmaceuticals as an ideal area to expand into, given the technical similarities (e.g. strong screening programs), and especially due to the relative importance of owning propriety rights to molecules in the new era; whereas pharmaceutical companies met the competitive entry of the leading chemical companies, resulting in a decade of international mergers. The purpose of these mergers was to enter markets where the barriers to entry were too high due to an increase in patenting new disease related genes. The only way to combine strengths in different geographical markets, capture economies of scale and scope, and expand potential products in the pipeline was through a merger (Chandler 2009). By the 1990s, every large chemical and pharmaceutical firm had adopted more than one strategy to ensure a strong position in the bio-revolution. Investments have ranged from the development of in-house research capacity, linkages with universities (which provide basic science) and hospitals (which undertake basic and applied research) to compensate internal resources and infrastructure for conducting R&D, capital investments in biotech start-ups, to a combination of strategies in accordance with the particular market position of the firms.

The environment within which the major pharmaceutical, biotech, and chemical firms operate in the current paradigm has become more focused and business networked, where various organizations interact more directly, and within which the gap between academia and large pharmaceutical companies has bridged and strengthened. Finding, characterizing, and developing medicines has become so complex that new technical and institutional instruments are being generated to apply new scientific advances to the solution of societal problems. While areas like cancer have benefited from strong academic and corporate research (several anti-cancer drugs achieved blockbuster status by the early 2000s, including MabThera, Gilvec, Eloxatine, Gemzar, Casodex, Taxotere and Zometa), other areas, like neurology and neuroscience have not benefited from target-based research to the same extent. Health issues in less developed countries have also received less attention than the US, Western Europe and Japan, which consumed most of the world's total production of pharmaceuticals. Advances made in technology, artificial intelligence in particular, is continuing to change drug discovery science, and appropriate strategies, i.e. developing optimal research relationships across countries.

Summary

The received structure of the pharmaceutical industry is best represented in summary of the three paradigms. Table 1. depicts the major developments in science, technology, types of business organization, national institutions, and political and economic trends since the mid-19th century.

Insert table 3.1 here

The predominant drug discovery strategy in the earlier paradigm was non-target based, or phenotypic drug discovery (Scannell, et al, 2012; Lipinski and Hopkins 2004), a method of modifying bioactive compounds without a clear understanding of the drug target or underlying disease, and testing them for efficacy in animals. This method is also known as non-target based, or trial and error learning approach, which had been long established in pharmaceutical firms (Gittelman, 2016). Target-based strategies were resource intensive and required deep background knowledge of gene targets, and the adoption of computational tools and screening capabilities. The historical coincidence between World War II crash programs, the introduction of new organizational routines, and the relative strength of American and British positions in the science of biology differentiated the pattern of development of pharmaceutical activities in the English-speaking world. These countries witnessed the birth of specialized pharmaceutical producers who leveraged on the technical experience and organizational capabilities accumulated through wartime efforts to develop antibiotic drugs. By contrast, German and Swiss companies, which had previously dominated the world's prescription drug markets, as well as French producers, were preoccupied with wartime pressures. The advent of molecular biology in the 1970s and entry of chemical firms following the crisis in the chemical industry created many challenges and increased competition. Drug discovery in the current paradigm is an inter-disciplinary endeavor (Fleming and Sorenson, 2004); it involves the recombination of new and existing component technologies (Henderson and Clark, 1990; Fleming and Sorenson, 2001) as well as scientific knowledge to explore the technological landscape and work with smaller sets of possible combinations without full experimentation. In addition, the organization of drug discovery involves more actors and requires new firm capabilities (genomics, combinatorial chemistry, computational sciences), and so the setting of the third paradigm is more collaborative and networked than previous paradigms. The strong university-industry interactions in the US, for example, specifically the openness of American universities to entrepreneurial activity on the part of their researchers (Mazzoleni and Neslon, 2007), further encouraged the developments that opened up a new route for the American pharmaceutical industry, and in gaining a leading position in the new biotech sector. With several thousand biotech firms launching by the end of the second to the beginning of the third paradigm, drug discovery became more science-intensive, and the importance of firm-university relations, and relations with publicly funded institutes increased.

The paradigms identified herein exhibit a change that is subsequently synthesized in light of new interconnections between scientific, business and government institutions. As argued in Section 2, old paradigms can be seen as retained and embedded in subsequent paradigms due to the cumulative nature of its subsystems. Science and technology are cumulatively developed, new institutions embody old formations, and political, economic and social contradictions are ultimately resolved and integrated in practice. The implication for large pharmaceutical companies developing new strategies to deal with new challenges and opportunities is to take into consideration various differences between countries, long governmental approval processes, R&D projects and collaborative research efforts, and participation in supporting a biotech sector that appears to be in financial disarray. Various new technologies, including AI, also seem to be changing patterns of drug discovery science, and so pharmaceutical companies will need to adopt the new developments in technologies.

Conclusion

In this chapter, I tell the history of the pharmaceutical industry by focusing on the relationship between science and technology, the changes in the nature and structure of the largest companies active in the industry, the connection between organizational level developments and macroeconomic trends, and the institutional structure that affect the organizational and locational character of the industry's knowledge network. I conceptualize the nature of paradigm change as a shift from preceding patterns of commercializing pharmaceutical technologies by relating scientific advances to organization-level developments and macroeconomic trends. This provides the analytical structure for which the histories of the pharmaceutical industry are told: Paradigm 1 (1850 to 1939), Paradigm 2 (1940 to 1989), and Paradigm 3 (1990 to date), within which the reciprocal influence of the developments that occur within each of the aforementioned subsystems are harmoniously connected. However, this chapter is not without its limits. The accounts of the three paradigms told herein, and the shifts between them, are brief, as it was not my immediate intention to synthesize all events for event sake. I merely distinguish three paradigms to conceptualize the way in which path-dependent and mainly incremental changes to previous patterns of development led to a qualitative transformation that induced a movement from one epoch to another.

I used this chapter as a starting point for understanding when new paradigms emerge, and how, in terms of the processes discussed herein. In the process, a series of questions have been raised. First, what is the structure of the knowledge networks on which a population of firms in the pharmaceutical, biotechnology, and chemical firms have relied internationally? What are the preferred sources of knowledge in the pharmaceutical industry in leading countries for innovation? What is the organizational and geographic composition, and the relationship between localized geographic proximity and global excellence at a distance? How should internal and external knowledge sources be combined, how important are hospitals compared to universities as knowledge sources for the industry, and to what extent are these relationships geographically localized? Third, what is the role of cross-border networks in the transmission of knowledge within the firm? Fourth, what are the pressures that seem to lead pharmaceutical firms to relocate their activities from one city to another within countries? How does the composition of innovation, and the linkages between science and technology in particular be responsible for an evolution in the geographic profile and nature of investments? How does the geographic profile of large firms regulate their interaction?

To explore these questions, we adopt a network perspective, e.g. networks within and between firms, and other organizations (universities, hospitals, etc.). We infer the organizational and geographic knowledge structure of firms using patents extracted from USPTO websites from 1976-2016. We describe the organization of the data employed and provide a revised interpretation of citation-based knowledge networks in the following chapter.

CHAPTER FOUR: DATA

Given the difficulty and secrecy involved in obtaining firm R&D investments, patents of large firms and corporate groups active in the pharmaceutical industry provide an interesting empirical setting. US data offer a disaggregation by cross-country, cross-firm, structural and historical dimensions on a scale that is not achievable through other sources.

Dimensions covered for the use of patent statistics

In fields like chemicals and pharmaceuticals, a large part of the inventions is codified in patents, because they provide firms with key, inimitable resources (Gambardella, 1992), the ability to "patent block" their rivals from entering product markets or disease areas, as well as forcing those rivals into negotiations (Cohen, Nelson and Walsh, 2000; Ziedonis, 2004; McGrath and Nerkar, 2004). A patent is a legal document and a set of exclusionary rights granted by an authorized governmental agency (Griliches, 1990). The right embedded in the patent can be assigned by the inventor to somebody else, usually a corporation, and/or sold to or licensed for use by somebody else. In the past, inventors contracted with firms. But in view of the changing organizational structure, this relationship became adapted within the firm, as specified in the employment contract, where the inventor is an employee of a firm, and assigns the invention to a firm, if such was invented in a corporate lab. In this way, the patent is granted to the inventor (inventor-team). And at the time of grant, the inventor then assigns the patent to an organization. The dimensions covered for the use of patent statistics include: (i) the year of grant and application; (ii) type of technological activity, derived from historically consistent patent class system; (iii) city or town and country of the inventor's residence (host country); (iv) references (citations), essentially knowledge building, because of the dependence on earlier (interdependent) increments of knowledge; and (v) the organization to which the patent has been assigned. In turn, the assignee organization can be identified with an owner, such as a corporate group (corporate consolidation requires an extensive search into the history of those firms), along with its' sectoral and home country code (derived from external sources), as well as the nature of the background context. The referenced patents can also be extracted and consolidated at the level of the organization, e.g. other firms in other industries, universities, hospitals, research institutes.

Organization of the data

Table 4.1 provides a listing of the top patenting corporate groups and private companies in pharmaceutical technologies. We examined the ownership structure and identified the subsidiaries of each of these firms by conducting an extensive search into their history (including merger and acquisition activity) using the D&B Who Owns Whom directories, Bloomberg, public announcements made by those companies, company websites, and via informal interviews with contacts employed at those companies. These firms reflect recent consolidation, including Pfizer's acquisition of Pharmacia, the merger of Sanofi and Aventis, and so on. We consolidated patenting assignees associated with each of these corporate groups and identified the organizational affiliation of assignees that are cited parts of the knowledge network (knowledge sources). To examine the organizational character of the firm's knowledge network (using SNA methods), further consolidation of the knowledge sources is required.

Insert table 4.1 here

We extracted from USPTO websites all patents granted from 1976-2016 belonging to the corporate groups identified (769 subunits; 196,000 patents), and all the earlier patents referenced by these (839 organizations; 823,000 patents). The citing patents of the major groups included all the patents from their worldwide research facilities. The record for each patent included the ultimate ownership (the affiliation of the assignee) and the location of inventors, as well as the year in which the patent was granted and the technological field of activity (derived from the patent class and sub-class). We also recorded the sector of activity of each organization; the home or headquarter country of each firm; and coded the locations from which the patents originate. The cited organizations include other corporate groups, as well as smaller firms, universities, research institutes, hospitals or health care providers, and government institutes. We grouped all pairs of citing and cited patents (1.5 million citations) according to whether the implied knowledge flow was intra- vs inter-organizational, and whether it was localized vs global, etc., depending on the research question. Thus, the network nodes are organizations in a specific geographical location. This allows us to trace from which organizational setting each sub-unit sources knowledge and to investigate the effect of relying on different combinations of this (i.e. knowledge developed by pharmaceutical firms, non-pharmaceutical firms, hospitals and basic science organizations). The term ‘knowledge networks’ is used in the literature to denote a set of nodes and their knowledge relationships (Carnabuci and Bruggeman, 2009; Yayavaram and Ahuja, 2008). In a knowledge network, the nodes represent the knowledge generating, transmitting and receiving units; the link between them indicates the knowledge-based relations between these nodes.

Patent citations and social network analysis

A network is a set of actors, called "nodes" (e.g. persons, teams, organizations), connected by a set of ties. These ties connect pairs of actors and can be directed (i.e. an organization sourcing knowledge from another), or undirected (i.e. as being collocated in the same geographic area), and can be dichotomous or valued. A binary social relation defines different networks, e.g., the network of a subunit's CC inventive activity is distinct from its CE activity (see chapter 5), since the different ties are typically assumed to function differently: the centrality in the CC network has different implications for the actor than centrality in the CE network. Network data are fundamentally dyadic, meaning that we observe a value for each pair of nodes, and hypotheses can be formalized at the dyadic level. Dyadic hypotheses essentially predict the ties of one social relation with the ties of another relation measured for the same actor, e.g. an inventor, an organization, or a geographic area. While in network research, the distinction between the individual and organization is subtle, in the sense that both are indeed an actor or a node, the implications take on very different meanings, and tell very different stories. We adopt a perspective of networks within and between firms, and other organizations, which share information, recombine ideas, and generate outcomes that result in innovation using patents granted in the US. The key feature of these patents is that each patent record includes its citations. Prior work has found that these citations provide a suitable proxy for organizational networks, since they indicate an organizational, geographic, and technical link for the purpose of knowledge building (Frost, 2001; Almeida 1996; Jaffe et al. 1993).

Our essential analytical scheme is grounded upon a conceptualization of technological knowledge accumulation over time, as an evolutionary process. Each dyad or connection between an earlier cited patent A and a subsequent citing patent B represents a recognition of knowledge relevancy, or a step in a knowledge building process. In Jaffe *et al.*'s (1993) words, 'a citation of Patent X by Patent Y means that X represents a piece of previously existing knowledge upon which Y builds.' Citation data therefore allow us to examine two complementary elements or to two stages in the process of constructing knowledge relevancy or knowledge building: (i) some citations represent component knowledge, which is recombined to generate some new application; and (ii) some citations depict the achievement in a new artifact or device of a further differentiation in knowledge or technology space, which serves to delineate the novelty of an invention compared to what had come before. Our basic question is thus, drawing upon a knowledge building perspective, how does the structure of knowledge sources or origins evolve over time, within and between organizations and across space?

Our motivation for adopting a networked approach is our interest in studying the wider system among actors or overall structure of the knowledge network compared to the more atomistic or reductionist perspective adopted in the strategy literature. The traditional meaning of 'networks' (whether in innovation studies or even more so in IB) which stresses some form of agency and often the particular kind of governance structure that is associated with that agency (as in transaction cost economics, or sociological discussions of organizational groups with shared values and trust, or social capital, etc.). Thus e.g. co-inventor networks link inventors on the basis of their co-involvement in research projects, which entails their active cooperation. MNE corporate internal networks are bound together by managerial hierarchy. Formal alliance networks depend on legally negotiated contracts, etc. Instead, we propose the language knowledge 'relevancy' or 'building'. For this much wider meaning of a knowledge network it is sufficient that there are a variety of transmission and diffusion processes that characterize a knowledge-based community. In epistemic communities, knowledge is shared informally through a variety of channels, not merely via person-to-person ties – i.e. inventor A knows inventor B personally and learned about the knowledge through a person-to-person conversation, and so there is an account of their mutual experience or co-involvement. Instead, in Marshall's terminology, knowledge is 'in the air' in a community of practice. Such knowledge circulates in a community before scientists publish a paper or apply for a patent, but is nonetheless absorbed by the process, progressing one piece of knowledge to the next.

CHAPTER FIVE: STUDY 1: Knowledge sourcing by foreign MNE subunit's innovation

INTRODUCTION

The environment in which MNE subunits operate has become more open and networked, allowing greater access to international markets, and an increase in intra-firm and inter-organizational knowledge exchange. While recent studies have explored the relationship between the use of internal and external knowledge sources in innovation (Phene and Almeida, 2008; Rosenkopf and Padula, 2008; Hagedoorn and Wang 2012; Monteiro and Birkinshaw, 2017), and the evolving structure of knowledge development in MNEs within and across national boundaries (Ambos and Ambos, 2011; Berry, 2014; Monteiro, 2015; Cano-Kollmann *et al.*, 2016; Turkina and Assche, 2018; Cantwell *et al*. 2019), less attention has been given to the influence of different types of organizational networks on the geography of knowledge sourcing by the foreign subunits of MNEs. This leaves a gap in our understanding of the conditions under which foreign subunits source technological knowledge locally or globally, and the impact different types of organizational ties have on these trends. In this paper, we examine how sourcing patterns may differ depending on the extent to which foreign subunits focus on competence creating (CC) vs competence exploiting (CE) types of inventive activities.

The main theme in the conventional literature has been the relevance of local knowledge search for new areas of expertise (Birkinshaw and Hood, 1998; Chini, 2004; Cantwell and Mudambi, 2011), or has related the CC vs CE typology of subunits to their overall mandates (Cantwell and Mudambi, 2005). However, there may be elements of both

CC and CE types of technological efforts in any given subunit (Cantwell and Piscitello, 2014); and so CC vs. CE activities in our context implies a distribution of activities within each subunit rather than a subunit level classification. Put differently, MNE subunits are not only creating new capabilities, which is what a subunit-level CC classification suggests, they're also relying on different types of knowledge-based connections to further exploit existing competencies, and vice versa. Extant studies have shown that the greater access to knowledge assets and resources has led foreign located subunits to behave autonomously in generating innovations (Andersson *et al.*, 2007; Ambos *et al.*, 2011) to accommodate location-specific demand, though less is known about the extent to which foreign subunits rely on internal (parent firm or other subunits) vs external sources (e.g. firms in the same or other industries, and scientific institutes) for different types of technological activities (CC or CE), and the impact on the geography of sourcing. We therefore ask, under which conditions do subunits source knowledge from anywhere in the world, and how has international sourcing been affected relative to sourcing knowledge from the host country environment?

With these considerations in mind, we adopt an international business interpretation of social network analysis (SNA) to further examine the structural changes of networked relationships for the purpose of knowledge building and make suggestions as to how the nature of CC and CE organizational knowledge building impact international sourcing. We argue that drawing on specialized knowledge may increase international search efforts since the probability of acquiring excellence in core technical fields, or the best university science-based knowledge for exploitative efforts is greater. We qualify this argument by noting that sourcing internationally requires a clear understanding of how new knowledge is relevant and can be recombined with firm capabilities. On the other hand, explorative types of knowledge sourcing may be locally bound, i.e. exploring into new areas of expertise is dependent on the subjective character associated with local knowledge-based interactions, where organizational processes and knowledge building efforts can be more easily observed.

We use a unique and novel dataset of organizational knowledge ties created by patents granted by the US Patent and Trademark Office (USTPO) to the foreign located subunits of the largest corporate groups active in the pharmaceutical industry. We test hypotheses that distinguish between creative and exploitative activities and suggest an association between the type of organizational linkage and international knowledge search efforts. We compliment the empirical analysis by applying techniques from SNA to provide a descriptive investigation of the changing structure of foreign-subunit's knowledge networks for CC vs CE activities over time and compare the change in composition of sources. This allows us to go beyond traditional indicators to understand the landscape of knowledge building using patent citations, which, by allowing us to construct nodes (organizations) from patents and the links between them, reveals the overall knowledge network of foreign located subunits. The timespan for our analysis covers the period 1976 to 2015 to represent a historical outlook of knowledge building across technological fields and geographic space. Compared to recent studies adopting patent-based network approaches, which focus on actor linkages, agency, and the channels of knowledge transmission, thereby enhancing our knowledge on the role of individual inventor networks on innovation, we trace knowledge sources or antecedents over time, within or between nodes represented by MNE subunits that conduct research leading to patentable inventions, and examine the ties entailed in the structure of knowledge building. Thus, we pay attention to the evolving structures of geographic, organizational, and cross-technological field knowledge development over time to address the remaining gap in our understanding of the performance of MNE foreign-located subunits as a whole as opposed to the performance of a focal actor within the MNE.

The paper is structured as follows. First, we review the literature and hypothesize the effect of internal vs external organizational sources of knowledge that foreign subunits have relied in developing CC vs CE technological innovations, and the impact these trends have on sourcing knowledge beyond a locally bounded context. Next, we describe the empirical research methodology and the data employed; and compare the evolution of CC vs CE networks. We then specify our models and report the results. Finally, we discuss our findings, the implications for future research, and draw some conclusions.

THEORETICAL BACKGROUND

The original received internalization explanation of the existence of the MNE is based on the supposition that the MNE is merely a vehicle for technology transfer; technology is first developed in the parent company, then disseminated to subsidiaries as a central resource (Buckley and Casson, 1976); its knowledge may then spill over to the local environment in the place where it is sited. The early question in the IB field was therefore "under what conditions does the firm transfer technology internally within the MNE or externally to other firms (e.g. through licensing)?" (see e.g. Buckley and Casson, 1976, for an analysis that was grounded within transaction cost economics). When technology transfer occurs within the MNE, according to the conventional account this is because the primary concern of the firm is fear of knowledge leakage. In this view, technology is typically treated as a form of public good, as being analogous to information that is fully tradable, and can be transmitted at low marginal cost. However, tacit capability is also a part of technology, and this private good element is not easily traded or exchanged. Thus, an alternative line of work can be traced back to another question, "under what conditions do MNEs source technology internationally through a network of geographically dispersed affiliates?" (e.g. Dunning, 1998). This supposes instead that the MNE is primarily a vehicle for innovation or technology creation, of which technology transfer becomes then part of a wider story. This research stream derived from innovation studies led to a greater interest in the competence-based or capabilities-based approach to the firm in the analysis of the MNE (Cantwell and Piscitello, 2000; Teece, 2014), and in the role of inter-company knowledge networks through which MNEs may be able to capture returns on their innovation (Mowery, Oxley, and Silverman, 1998).

Technological knowledge tends to be built cumulatively over time (Nelson and Winter, 1982; Rosenberg, 1982), and so creating new knowledge entails drawing on a variety of sources. MNEs in particular are distinguished by deployment of international networks for innovation, since these networks reinforce the local specialization of spatially dispersed but connected learning processes (Cantwell, 2017). However, because technology is actually difficult to transfer across different geographic contexts (Teece, 1997), prior work has not only investigated how technological change is localized, but the conditions under which subunits of firms continue to innovate in their own local subsidiary environment (Rugman and Verbeke, 2001). A later study finds that they may do so to tap into the local innovation system and discover new ways of innovating in that environment, in what has been termed competence creating types of subsidiaries (Cantwell and

Mudambi, 2005), and in such cases they become more locally embedded in the local innovation system. It therefore follows that especially once it has a subsidiary network in which at least some subsidiaries are locally competence creating, the MNE is not just an agent of technology transfer but more generally a vehicle for international innovation or distributed knowledge creation through a geographically dispersed yet connected network.

The literature which has shown that typically only some selected subsidiaries are highly innovative contributors and central to their knowledge networks of relationships within the corporate group (Birkinshaw and Hood, 1998; Chini, 2004), reinforced the significance of the conceptual distinction between competence creating (CC) and competence exploiting (CE) types of subsidiary or subsidiary activity. Cantwell and Mudambi (2005) in particular related the typology of subsidiary technological development to the overall mandates of subsidiaries using survey evidence, although it seems reasonable to suppose that there may be elements of both CC and CE types of technological efforts in any given foreign-owned subsidiary, i.e. CC subsidiaries are likely to perform at least some CE efforts, and vice versa (Cantwell and Piscitello, 2014). In our view, CE activity is akin to public good element of technology, which is then more readily available, is more common with other subunits of the corporate group and can be more easily shared and circulated across different parts of the enterprise. This ease with which technology is transferred within the MNE network may be attributed to the establishment of a common social community with shared values across its differentiated subunits (Kogut and Zander, 1993; Nohria and Ghoshal, 1997), and the networked pattern of inter-unit knowledge exchange (Chini, 2004; Monteiro, Arvidsson, and Birkinshaw, 2008). CC activity, on the other hand, is more akin to novelty of private element of technology that depends on the distinctiveness of a subunit's network, or what's different about the subunit as opposed to what's shared within the subunit as a group, where the more central subunits in the internal MNE network tend to engage in greater knowledge-based interactions with both their parent firm, and their own local environment. Our line of reasoning is similar to March's (1991) distinction between exploitation and exploration, since he characterized exploitation by "the refinement and extension of existing competencies" whereas exploration is characterized by "experimentation with new alternatives" (March, 1991: 85); though we examine these processes with referents from the MNE literature on location.

HYPOTHESES

An influential part of the innovation studies and strategy literature highlights the positive effect of knowledge search (Cohen and Levinthal, 1989; Chesbrough, 2006; Laursen and Salter, 2014), and provides many suggestions about the importance of international knowledge sourcing, i.e. technological progress is a function of combining internal and external knowledge sources (Dosi, 1988; Cohen and Levinthal, 1990; Veugelers and Cassiman, 1999; Cantwell *et al*., 2019), where the locus of innovation resides in "the interstices between firms, universities, and research laboratories" (Powell, Koput, Smith-Doerr, 1996:118). However, little is known about the role of intra- and inter-organizational knowledge linkages in a relational system, and how these roles function internationally, and for which technical purpose. While the strategy literature seems to suggest that most of the benefits of inter- and intra- organizational networks are features of some network configuration or structure, the geographic characteristics of these networks has generally been overlooked in this literature. Moreover, prior empirical work has also tended to focus primarily on a focal inventor as an actor within the firm, and the immediate inventor network of that actor, rather than the overall network structure of the MNE or its affiliates. Guler and Nerkar (2012) have tested the benefits that accrue to the overall organization as opposed to the actor, yet the local vs global distinction featured in their work is driven by the network, and not the geographical contexts of which the MNE subunits are a part. Important underlying conceptual issues seem therefore missing, e.g. a more general explanation of the conditions under which MNEs source knowledge internationally, the impact organizational ties have on this trend, and how sourcing patterns differ for CC vs CE subunits' innovation.

Internal knowledge sources

Historically, technological knowledge related to the MNC's core field of specialization was primarily created in the parent company, upon which subunits and external partners relied (Vernon, 1966; Buckley and Casson, 1976; Porter, 1990). In this traditional model, new competency creation typically occurred in selected subunits, but the increased interaction between local creativity (e.g. adapting to local conditions or establishing relationships with other firms or scientific institutes) and knowledge availability elsewhere in the world, has led us to think in terms of a steady evolution of international subsidiary networks that incorporate the knowledge developed by the parent company, but are not necessarily restricted to it. Sourcing knowledge from other subunits within the MNE, and across different geographic boundaries, has become more critical in the creation of new competencies (CC and CE) within the subunit. This is in line with earlier writings which have shown that the intimate connection in intra-corporate group networks have enabled units to identify the relevance of new areas of expertise that contribute to innovation (Patel and Pavitt 1991; Kogut and Zander, 1992; Gupta & Govindarajan, 2000; Hansen, 2002).

While we know that sourcing knowledge from the local environment increases knowledge sharing with other subunits which happen to be located there (Phene and Almeida, 2003), it's unclear for which type of technological search efforts this occurs. Moreover, very few studies have explicitly investigated the effect of intra-MNE knowledge building on the international sourcing by foreign subsidiaries (Asakawa et al., 2018).

We propose that the internal knowledge building has different significantly for CC activities, which may rely on the subjective character associated with local knowledge sourcing, and CE activities, since the probability of acquiring technological excellence for exploitative efforts is greater when searching internationally. Foreign subunits may be able to draw on CC developments internally from their host country environment since the more tacit elements of exploratory tasks may be more easily transmitted through local ties. At the same time, prior work has argued that increased connectivity among actors within a local network can homogenize knowledge stocks (Zhang *et al.,* 2019). However, since CE activities are more relevant to the efforts of other subunits, these developments may be more likely to attract the interest of units located abroad. We expect that foreign subunits are not only relying on knowledge from their parent firm for exploitative innovations, they're also relying on internal knowledge that may increase search for new CE inventions wherever it is in the world. Put differently, foreign subunits are more likely to source knowledge internationally that is relevant, closely aligned to the existing knowledge base of the subunit and can be recombined with its existing capabilities. We therefore hypothesize that ties with other subunits within the corporate group are related to international sourcing for CE activity, but local sourcing for CC activity. Thus:

Hypothesis 1a: For foreign-located competence exploiting subunit activities, when building on intra-MNE knowledge, international knowledge sourcing rises relative to local knowledge sourcing.

Hypothesis 1b: For foreign-located competence creating subunit activities, when building on intra-MNE knowledge, international knowledge sourcing falls relative to local knowledge sourcing.

External knowledge sources

There is a stream of research in the international business and economic geography literature which offer some guidance about the organizational innovative outcomes of local vs global sourcing. On the one hand is the embeddedness perspective (Almeida and Phene, 2004), which argues that subunits are embedded in the environment they are situated in, and so source knowledge from their local, inter-organizational networks (Cantwell and Iammarino, 2000), since information is more readily transmitted via face-to-face interactions, due to a mutual understanding of new knowledge and applications within the constraints of some established institutional arrangement (Stroper and Venables, 2002; Bathelt, Malmberg, and Maskell, 2004). The primary function of a competence creating subunit in particular is to tap into the local knowledge base to augment the MNE group's overall strength (Cantwell and Mudambi, 2005). However, while the locus of innovation for subunits developing CC activities resides within local, external and diverse networks, we might expect that for CE activities, subunits draw on specialized competencies wherever it is in the world. To be sure, our distinction between creative and exploitative activities suggests a basic association between the type of organizational linkage and international knowledge sourcing strategies that underpin those activities. While the opportunities for finding important sources of complementary knowledge through inter-sectoral linkages have indeed increased the extent of international dispersion of innovations, little is known on how drawing on specific organizational ties affect the geographic sourcing of CC vs CE activity.

Put differently, foreign-located subunits may draw on the knowledge of diverse organizational networks for explorative efforts locally, since these are qualitatively different from linkages established with the home country. At the same time, novel recombination requires a detailed level of understanding components that are tacit and difficult to source elsewhere in the world. This is because experimenting into new areas of competencies implies a greater variance in the quality of output in subunit's CC innovations. These types of innovative efforts may be more easily observed via frequent face-to-face knowledge-based interactions in the subunit's local environment, where there is no contract to regulate or control partner inputs. Moreover, prior literature has found that localized structures are not only characterized by repeated interactions based on trust and cooperation (Granovetter, 1973; Uzzi, 1996, 1997; Hansen, 1999; Obstfeld, 2005); they also discourage opportunistic behavior, since they may be associated with adverse reputational consequences (Coleman, 1988). The kind of tacit knowledge that is essential for exploratory tasks may therefore transfer more readily through embedded ties between actors that share a common understanding due in part to similarities in interests and motives (Uzzi, 1997; Hansen, 1999; Obstfeld, 2005). Subunits developing CC inventions in particular need to be able to migrate from an outsider to an insider status (Cantwell and Mudambi, 2011) to benefit from knowledge-sourcing activities in their local environment.

We therefore hypothesize that ties with inter-industry sources are related to local search for CC activity. Thus:

Hypothesis 2: For foreign-located competence creating subunit activities, when building on the knowledge of diverse organizations, international knowledge sourcing falls relative to local knowledge sourcing.

Conversely, international connectivity can benefit firms to a greater extent in further exploiting existing competencies (Scalera *et al.*, 2018), because the probability of acquiring the right specialized knowledge is greater, particularly when searching for excellence, e.g. in core technical fields, or the best university science-based knowledge. An important dimension of exploitative search efforts is that subunits may have explicit objectives when searching internationally for activities that are closely aligned to the existing knowledge base of the firm. In such cases, the locus of innovative search is likely to reside within external networks that are not necessarily where the subunit is sited. This in turn increases international search, because these specific organizational ties provide clearer prospects of returns to innovations. The basic assumption of our perspective is that the impact of participating in external technical communities on international search efforts depends on specific properties of such networks. For example, sourcing knowledge from universities located abroad entail higher transaction costs, since such linkages lack the subjective character associated with local knowledge sourcing, e.g. a mutual understanding of new knowledge and applications within the constraints of the local network. Searching for knowledge internationally is rarely this subjective and requires a clear understanding of how this new knowledge is relevant and can be recombined with firm capabilities [by implication, high levels of absorptive capacity]. We therefore hypothesize that ties with specialized organizations are related to international sourcing for CE activity. Thus:

Hypothesis 3: For foreign-located competence exploiting subunit activities, when building on the knowledge of specialized organizations, international knowledge sourcing rises relative to local knowledge sourcing.

To recap, prior literature on the typology of subsidiary roles (competence creating vs. competence exploiting) has focused on the characteristics of the location in which the subunit is cited as well as the determination of innovation in each type of subsidiary (Cantwell and Mudambi, 2005). What can be seen missing from this literature is the diverging patterns of organizational knowledge building of foreign-located subunits, particularly in terms of the conditions for international search efforts of CC vs CE inventions. We argue that for CC activities, subunits depend on knowledge diversity, whereas for CE activities, subunits rely on specific organizational ties to further exploit existing capabilities. Drawing on specialized knowledge may increase international search efforts since the probability of acquiring excellence for exploitative efforts is greater. We qualify this argument by noting that sourcing internationally requires a clear understanding of how new knowledge is relevant and can be recombined with firm capabilities, i.e. drawing on specialized knowledge increase international sourcing for CE, whereas drawing on diverse knowledge sourcing decrease international sourcing for CC. This is because experimenting into new areas of expertise implies a greater variance in the quality of innovations subunits undertake. Explorative types of knowledge sourcing may therefore be locally bound, where organizational processes and knowledge building can be more easily observed.

DATA

Empirical setting

To test our hypotheses, we needed a research setting that allows us to compare and contrast the network of foreign-located subunit's innovations in order to detect systemic differences in the organizational and geographic patterns of knowledge sourcing. In the context of the evolution of MNC foreign-located subunits toward network formations, a good example is the pharmaceutical industry, since basic technological capability relies increasingly on the capacity to integrate knowledge across a network of technologically proficient organizations, which may include universities as potential sources, as well as other firms. A rich pool of relevant shared private or public knowledge among various actors increases the awareness of the properties of a wide range of incremental and novel applications across a variety of geographic contexts. We therefore focus on the improvement and transformation of the knowledge base of subunits in this industry, which is partially common within specific organizations (e.g. other subunits within the same corporate group), inherited from the past, and partially common with other organizations in the public domain (e.g. public science). We adopt a network perspective, e.g. networks within and between firms, and other organizations (universities, hospitals, etc.). We infer the organizational and geographic knowledge structure within foreign-located subunits of MNEs using patents, since the key feature of these patents is that each record includes its references to other patents (i.e. citations).

Organization of data

The right embedded in a patent can be assigned by the inventor(s) to an organization at the time of grant. In turn, the assignee organization can be identified with an owner, e.g. a corporate group, university, hospital, etc. We first identified the major corporate groups engaged in US patenting in the pharmaceutical field. These groups are either pharmaceutical/biotech firms or firms in related industries with a substantial interest in pharma. For example, we include Bayer, which has a major pharmaceutical business, and Novartis, which quickly sold off its' chemical businesses following its creation through the merger of Ciba-Geigy and Sandoz to focus on pharmaceuticals. We do not include firms such as Du Pont, a firm that responded to the chemical crisis by diversifying into pharmaceuticals. Even though it had strong marketing capabilities, it failed to build ties with scientific institutes, which is critical to success in developing pharmaceutical technologies in the current era. Du Pont eventually sold its' drug division to Bristol-Meyers-Squibb, a large pharmaceutical company in our sample. To identify the subsidiaries of these firms, an historical examination of the ownership structure of each pharmaceutical corporate group was conducted through an extensive search into their history using the D&B Who Owns Whom directories.

We extracted from USPTO websites all patents granted from 1976-2016 belonging to the 45 groups identified in Table 1 and their subsidiaries. These included all the patents from their worldwide research facilities. The record for each patent included the ultimate ownership (the affiliation of the assignee) and the location of the inventors, as well as the year in which the patent was granted and the technological field of activity (derived from the patent class and sub-class). We also recorded the sector of activity of each organization and the home or headquarter country of each firm. We then extracted all patents that were cited by the patents that belonged to our 45 corporate groups. The organizational affiliation of assignees of these cited patents (the knowledge sources) were also identified and consolidated. The cited organizations include other corporate groups or smaller firms (in the same or other industries), universities, research institutes, and hospitals or health care providers. Consolidating the assignees of the citing and cited patents is critical to analyzing the knowledge sourced within and between organizations and across geographic boundaries (using SNA methods, each cited to citing patent is a knowledge dyad). Thus, knowledge-based linkages are represented by citations to other organizations in geographic space. We grouped citations according to whether the implied knowledge sourced from cited to citing patent was from other subunits within the MNE, other pharmaceutical or non-pharmaceutical firms, universities, or hospitals, and whether it was local (within the same country of invention) or international.

Insert table 5.1 here

The analysis was conducted on the foreign-located subunits of these corporate groups. We disaggregated the citing subunit's activity to distinguish between CC and CE components, following Cantwell and Piscitello (2014). CC activity represents exploratory search efforts into new scientific and technological areas, whereas CE activity represents an extension of search efforts undertaken by the parent firm in the home country. To classify patents in this way, we first constructed a measure of parent firm specialization, i.e. a Revealed Technological Advantage (RTA) index equal to, or greater than one in a field. An RTA index allows us to control for inter-field and inter-firm differences in the propensity to patent (Cantwell, 1989). Specifically, RTA is defined as follows: RTA = $(P_{ij} / \sum_i P_{wj}) / (\sum_j P_{ij} / \sum_{ij} P_{wj})$, where P_{ij} is the number of patents in technological field j, by a parent firm i, and P_{wj} is the number of all patents in the same sector by all firms. We then constructed a measure of a foreign-located subunit's specialization, i.e. an RTA equal to, or greater than one in a field. We classified patents as CC search efforts if the citing patent is in the same field and in which the citing foreign-located subunit has an RTA equal to, or greater than one, but the parent firm has an RTA less than one in that field; all other patents of these subunits were classified as CE, which include those that are merely imitating the parent firm, or that aren't bringing in new areas of specialization into the group knowledge. We therefore proxy the foreign-located subunit's innovative activity by the number of patents granted in the US to the MNE for research carried out in another country than the MNE's home country. In other words, we exclude parent firms from this study, which, by definition, are the benchmark for which subunits are defined. For example, we exclude all Pfizer in the US, Glaxo in the UK, etc. Empirically, this is an improvement on Frost (2001), since the data constructed was able to delineate what is CE activity for the subunits, which is more readily available to flow around the enterprise.

Table 2a includes descriptive statistics about the foreign-located subunits in our sample. As can be seen in that table, the MNE's innovative activity is increasingly conducted abroad, i.e. the total number of patents in foreign-located subunits rose from 7,510 in period one to 15,656 in period eight. We identified and observed 297 foreign-located subunits developing CC technologies and 579 foreign-located subunits developing CE technologies, and ran separate regressions for these from 1976 to 2015 (broken into five-year intervals) because the USPTO has not updated its classification system from which we are able to construct our RTAs and determine the CC and CE patents for our analysis.

It is worth noting, while there is a rise in the number of foreign-located subunits, the number of subunits with CC activity have not increased, implying there is a partially offsetting trend of a rise in the number of subunits with no CC activity. In other words, since knowledge in the pharmaceutical industry has reached a certain level of maturity (Edris, 2019), the number of subunits engaged in pure CE activity is increasing. However, while the number of CC subunits have not increased over the period, we find that the share of CC patents has doubled, which is consistent with the Cantwell and Mudambi (2005) evolutionary argument, i.e. that inter-subunit diversity and differentiation within corporate groups tends to increase the capacity for exploration. Indeed, as can be seen in Table 2b, in earlier periods, most subunits with CC activity either had <20% or >80% CC patents. In later periods, the distribution is far more evenly dispersed, so there are far more subunits with a balanced portfolio of CC and CE patents, and this is pushing up their average CC share.

Insert tables 5.2a and 5.2b here

KNOWLEDGE NETWORKS

The term "knowledge network" is used in the literature to denote a set of actors, called "nodes" (e.g. persons, teams, organizations), connected by a set of ties, i.e. their knowledge relationships (Yayavaram and Ahuja, 2008; Carnabuci and Bruggeman, 2009). In a knowledge network, the nodes represent the knowledge generating, transmitting and receiving units; the link between them indicates the knowledge-based relations between these nodes. These ties connect pairs of actors and can be directed (i.e. an organization sourcing knowledge from another), or undirected (i.e. as being collocated in the same geographic area), and can be dichotomous or valued. A binary social relation defines different networks, e.g., we claim the network of a subunit's CC activity is distinct from its CE activity, since the different ties are typically assumed to function differently. Frost

(2001) in particular has argued, if local innovative activity of subunits is exploitative, subsidiaries are more likely to cite the parent company, with the added qualification that the technology of the parent is adapted to the local environment; whereas competence creating subunits are more likely to cite local actors (Kogut and Zander, 1993; Almeida, 1996; Frost 2001) and leverage potential benefits of local differentiation compared to what would have been received from the parent firm.

Our essential analytical scheme is grounded upon a conceptualization of technological knowledge accumulation over time, i.e. each dyad or connection between an earlier cited patent A and a subsequent citing patent B represents a recognition of knowledge relevancy, or a step in a knowledge building process. In Jaffe Trajtenberg, and Henderson's (1993) words, "a citation of Patent X by Patent Y means that X represents a piece of previously existing knowledge upon which Y builds." Citations provide a suitable proxy for organizational networks, since they indicate an organizational, geographic, and technical link for the purpose of knowledge building (Jaffe *et al*., 1993; Almeida, 1996; Jaffe and Trajtenberg, 1999; Frost, 2001). They are also distinct in certain respects from inventor networks in allowing us to trace knowledge sources or antecedents over time within or between nodes represented by organizational subunits that conduct research leading to patentable inventions. Our basic question is thus, drawing upon a knowledge building perspective, how does the structure of knowledge sources or origins evolve over time, within and between organizations and across space?

We employ network visualization techniques to provide a first assessment of the evolution of the structure of foreign-located subunit networks (Powell and Grodal, 2005; Rosenkopf and Padula, 2008; Tomasello *et al*., 2016). We constructed the structure of CC vs CE knowledge networks between 1976 and 2015, broken down in five-year periods, by forming a matrix of knowledge ties between organizations using citations on patents. Since we were interested in comparing structural features of the network, we dichotomized the network matrix before calculating our measures. Figure 1 illustrates the network of foreign-located subunits for the development of CE technologies. Figure 2 illustrates the network of foreign-located subunits for the development of CC technologies. We further subdivide these networks into eight periods to derive network measures for the analysis.

Insert figure 5.1 and 5.2 here

We are specifically interested in observing the organizational links foreign-located subunits have relied in developing innovations over time; in this way, we not only observe where knowledge is sourced, but for what purpose, i.e. CC vs CE. Using a social network analysis over time (across periods) as illustrated in Figures 1 and 2, we can observe that the size of the networks increases in terms of nodes (organizations) and intensity of ties (number of citations between organizations); this also means, because new nodes tend to be less connected to central existing nodes, the density of the networks decrease over time (Albert and Barabasi, 2002). In other words, the knowledge network of these subunits has become far more widespread and interconnected across actors (our network nodes) since the 1970s: the overall network connectivity in terms of the existence of knowledge ties (as measured by the average weighted degree) rose over time, while connectivity in terms of the average intensity of ties (as measured by graph density) fell over time. We can also observe the difference in the structure of the networks. Indeed, the presence of ties are not stable over time, e.g. Novartis and Sanofi subunits were identified as one of the most central in first period of the CC networks, but other subunits have become more central in later periods. Another interesting feature of the network is its strength. The strength of the CC networks have been increasing consistently over time (an increase in the number of interactions), whereas the strength of the CE network decreased in the sixth and seventh periods, suggesting shifts in firm strategy, but also a change in the composition of network ties over time.

Overall, we find increasing trends in citations along various sources of knowledge. Not only are local and international sources being used with increasing frequency, inter-organizational knowledge sourcing show an increasing trend. First, we find that for both, CC and CE innovations, subunits' reliance on intra-firm knowledge sourcing have declined substantially over the period (from the first to the eighth period, the share of intra-firm citations decreased by 31.89 percentage points for CE inventions, 17.25 percentage points for CC inventions). Foreign subunits have increasingly relied on pharmaceutical and biotech firm knowledge for CE inventions. University sourcing also grew more than previously, with a substantial increase in citation shares in the sixth period, when share of university citations accounted for 9.15 percent. While the presence of ties with subunits for CC inventions were mainly geographically localized (local citation shares were about 60.94 percent in the eighth period), subunits have seen relative increases in international knowledge sources for CE inventions (the sharpest acceleration from the fourth to fifth period, by 12.88 percentage points). As expected, subunits rely primarily on diverse, inter-industry knowledge sources for CC activities; in the eighth period, these account for 27.44 percent, the greatest share of organizational sourcing. There has also been modest increases in hospital knowledge sourcing by both, CC and CE innovations over time. Our predictions are broadly consistent with our findings, which show that for CC activities, subunits have relied on local and diverse knowledge sources, whereas for CE activities, subunits have relied on organizational sources which increase the potential for specialized knowledge building. The geographic spread of these patterns is depicted in figure 3.

Insert figure 5.3 here

STATISTICAL ANALYSIS

Model estimation

To justify our decision to estimate separate models for the sub-samples and make comparisons between the estimates of factors that influence the share of international knowledge sourcing by foreign-located subunits, we calculated the Chow test (Chow, 1960). We reject the null hypothesis that the dataset can be represented with a single regression line, since our calculated F-value was greater than the F-critical value. The effects of the factors we estimate would have been otherwise ignored if only a pooled sample model were used. Based on this finding, the statistical analysis is conducted on a cross-section at the level of foreign-located subunit's CC vs CE innovations of our 45 corporate groups between 1976 and 2015 (broken into 5-year intervals). Thus, the fundamental unit of analysis in the models pertaining to these hypotheses is a foreign-located subunit in a given period (297 subunits developing CC technologies; 579 subunits developing CE technologies).

To explore our hypothesis in the pharmaceutical industry, we developed dependent variables from the two datasets, which are derived from the geographic information contained on citing and cited patents. We constructed the dependent variables as an indicator of whether a patent citation was developed by inventors in the local environment, or elsewhere in the world. The dependent variable is therefore the share of international citations of foreign-located subunit's CC vs CE inventions. We test hypotheses by running separate regressions, one with the dependent variable from the CC sample, and the other from the CE sample. Our hypotheses relate the international knowledge sourcing to the type of organizational link foreign-located subunit have relied in developing their inventions. In the context of the pharmaceutical industry, R&D and basic research are considered the main sources of technology, and developing related products, exploiting basic science and clinical research are central strategic management tasks. We therefore identified biotech firms, universities, and hospitals. To test hypotheses related to CC inventions, we also created a category for inter-industry sources. Measures to operationalize these were constructed from the citing and cited patent. To test our hypotheses, we calculated the share of cites to subunits within the firm, to biotech firms, inter-industry sources, universities, and hospitals. We also control for the subunit's knowledge portfolio (types of organizational sources) and eigencentrality (position or influence in the knowledge network), as well as cross-country differences, i.e. economic, political, and geographic distance between the host country the subunit is situated in and its home country. Table 3 below summarizes the variables used in the analysis. The model is the following: $\text{International}_{ip} = f(\text{Intra-MNE}_{ip}; \text{Biotech}_{ip}; \text{Inter-industry}_{ip}; \text{University}_{ip}; \text{Hospital}_{ip}; \text{controls}_{ip})$, where i=foreign-located subunits, p=time periods.

Insert table 5.3 here

Results

Table 4a provides descriptive statistics of the variables and Table 4b provides a correlation matrix. Results are reported in Table 5, which is divided into two sections by geographic dependent variables of the search effort implied. Numbers in parentheses represent standard errors. Interpretation of the regression coefficient follows a normal pattern: positive, significant values indicate that an increase in that variable increases the share of international citations for CE search efforts in model 1, CC search efforts in model 2, *ceteris paribus*.

Insert table 5.4a, table 5.4b, and table 5.5 here

Overall, the data provide support for our hypotheses, suggesting that international search efforts by foreign-located subunits are influenced by the organizational characteristics of the knowledge network. First, we find that building on intra-MNE knowledge is strictly negatively (95% CI=[-0.157 to -0.064]) associated with international sourcing by subunits for CE innovations in model 1, indicating that subunits' CE innovations that build directly on prior technologies of other subunits within the corporate group decrease their search for knowledge internationally ($p<.001$). While we also find that building on intra-MNE knowledge is negatively (95% CI=[-0.394 to -0.215]) associated with international sourcing by subunits' CC innovations ($p<0.001$) in model 2, the effect size is much smaller in model 1. Specifically, building on intra-MNE knowledge decreases international sourcing by subunits' CE innovations by 11.1 percent compared with a 30.5 percent decrease of international sourcing by subunits' CC innovations. This is because CE activity represents the area of commonality across different parts of the enterprise, and so this finding confirms the relevance of CE activity as the organizational knowledge glue that can flow around the network more readily. At the same time, even CE technological efforts need adapting to the local environment. We don't find a strictly positive or negative association between ties with pharmaceutical firms and international sourcing, suggesting an increased reliance on other types of organizational knowledge sources.

We find that building on inter-industry knowledge is strictly negatively (95% CI=[-0.200 to -0.041]) associated with international sourcing by subunit's CC innovations in model 2. In other words, foreign-located subunit's CC innovation that build directly on prior technologies developed by firms in different industry settings locally (p=0.024), decrease international sourcing by 12.1 percent, since they're embedded locally by necessity. These types of subunits are more likely to tap into the local innovation system, especially when they've gained a more insider status in their local environment (Cantwell and Mudambi, 2011). We also find that both, centrality (p=0.035) and knowledge portfolio (p<0.001) negatively impact sourcing knowledge internationally, suggesting differentiation in research conducted locally, and reliance on the innovative traditions of diverse organizations in the local environment.

We also find that building on biotech firm knowledge is strictly positively (95% CI=[0.014 to 0.196]) associated with international sourcing by subunits' CE activity in model 1 (p=0.089). In other words, foreign-located subunits' CE innovation that build directly on prior, specialized technology developed by biotech firms increase international sourcing by 9.1 percent. This is partially due to the more open and collaborative setting that took hold of the industry, as well as the maturing of biotech, which attracted the attention of an increasing number of large pharmaceutical MNEs (Edris, 2019). The increased reliance on the research tools and innovative contributions made by specialized biotech firms are particularly important for continued innovations and further exploitation of firm-capabilities. Foreign-located subunits have therefore begun to draw on a more international network for specialized technical knowledge to exploit firm capabilities. At the same time, we find that both, centrality ($p<0.001$) and knowledge portfolio ($p<0.001$) negatively impact sourcing knowledge internationally.

Moreover, we find that building on university knowledge is strictly positively (95% CI=[0.060 to 0.245]) associated with international sourcing by subunits' CE innovations in model 1 ($p=0.001$). In other words, foreign-located subunit's CE innovation that build on prior technologies developed by universities increase international sourcing by 15.3 percent. This is because for CE activities, subunits will search internationally for specialized knowledge external to the MNE, particularly when searching for the best university science-based knowledge, where that knowledge is not necessarily located where the subunit is situated. However, building on university knowledge is not strictly positively or negatively (95% CI=[-0.220 to 0.100]) associated with international sourcing by subunits' CC activities in model 2. Perhaps, because no centralized authority commands their development, scientific institutes may be able to generate and transmit their knowledge internationally more quickly through their ability to establish personal ties (Perri, Scalera, and Mudambi, 2017). In other words, for CC activities, subunits may establish linkages with the local science base, which is itself internationally connected. Future research should examine scientific specialization of these universities, as well as the transmission of knowledge from universities to the industry.

In the context of the pharmaceutical industry, the firm's ability to access and incorporate relevant scientific research conducted in universities is particularly useful for guiding the search for innovations (Fleming and Sorenson, 2004), and complement internal R&D. While a line of research has documented the degree of industry reliance on academic research contributions (Mansfield, 1991, 1995, 1998; McMillan, Narin, and Deeds, 2000;

Cockburn and Henderson, 2001; Grossman, Reid, and Morgan, 2001; Cohen, Nelson, and Walsh, 2002), we find little evidence on university sourcing internationally. Our findings suggest that foreign subunits source scientific research from universities for exploitative innovations wherever it is in the world, but that the benefits associated with explorative efforts may be confined to local actors, since the subjective element of local knowledge search makes it easier to absorb new, and distant knowledge.

Finally, hospital knowledge is not positively or negatively associated with international sourcing by subunits' CE activities in model 1 (95% CI=[-0.148 to 0.496]) or with international sourcing by subunits' CC activities in model 2 (95% CI=[-0.509 to 0.852]). We find a high standard error for these effects (0.164 in model 1, 0.347 in model 2), suggesting foreign-located subunits' reliance on hospital knowledge sources varies greatly across firms. Future research should not only explore causes of this heterogeneity, and issues that relate to downstream practical applications of knowledge around the core knowledge base of the firm, but also the geography of these linkages at the subnational level, e.g. whether hospitals that are collocated with universities are likely to drive international sourcing for specific types of knowledge. To be sure, prior literature has tended to treat hospitals as part of universities, since patient contact is needed in training new doctors, and so indeed, many hospitals are attached to universities. However, the close associations between hospitals and universities does not mean that they are universities (Hicks and Katz, 1996; Bignami, Mattsson, Hoekman, 2019); connections to clinical or medical practices, particularly from the perspective of MNE affiliates in generating new technologies of an either specialized or creative kind needs further attention.

Taken together, what we find is that accessing relevant and specialized knowledge is critical for the further development of exploitative activities, whereas drawing on the knowledge of diverse knowledge bases is critical for novelty, but may be locally bound.

DISCUSSION AND CONCLUSION

Where MNEs and their affiliates draw their knowledge from is a central question in international business, particularly in examining the evolution of MNE knowledge networks. This study sought to address this question by examining the organizational and geographic characteristics of the knowledge network of CC vs CE innovations by foreign-located subunits. We contribute to the discussion on these subunit's desire to gain knowledge from diverse sources, which may include other subunits within the corporate group, other firms within the same or other industries, universities and hospitals. We adopt a perspective of networks within and between firms, and other organizations (Kuhn, 1962; Jackson, 2008; Guler and Nerkar, 2012; Graham, 2015), that generate outcomes that result in inventions using patents granted in the US. Our motivation for adopting a networked approach is our interest in studying the wider system among actors or overall structure of the knowledge network as opposed to the more atomistic or reductionist perspective adopted in the strategy literature. Using backward patent citations, we collected and compared network data from multiple organizations as a whole (the consolidated assignees), e.g. the major corporate groups and other firms (in the same, or in other industries), with hospitals, universities, research or government institutes, as opposed to individual inventors within organizations.

We discuss the organizational affiliations and differentiated networks within which foreign-located subunits source knowledge to develop innovative activity. We find that building on intra-MNE knowledge decrease international sourcing to a greater extent by subunits CC relative to CE activities. This is an improvement on Frost (2001), since the data constructed was able to delineate what is CE activity for the subunits, which is more readily available to flow around the enterprise, and the conditions these subunits rely on building on intrafirm knowledge. We also find that CC and CE subunit's innovations rely on different types of knowledge-based connections to build on their competencies, reflecting the emergence of knowledge-seeking (Doz, Santos, and Williamson, 2001; Thursby and Thursby, 2006) as opposed to traditionally local market-seeking or resource-seeking strategies. Specifically, subunit's CE innovations that build directly on prior specialized (technical or scientific) sources increase international search efforts (suggesting a more application focus), whereas subunit's CC innovations that build on diverse, inter-industry sources decrease searching for knowledge building activities internationally. In other words, the knowledge sources that increase international knowledge search for CE activity is a combination of internal, biotech firm, and university innovations wherever this relevant knowledge to the industry is in the world. At the same time, our results highlight the role of subunit centrality and the diversity of knowledge sourcing. One key contribution of this study is therefore to ask though which organizational link do CC and CE subunit's innovations rely in their knowledge sourcing strategies in an international business context by investigating the evolution of their networks and estimating the effects of intra-MNE, pharmaceutical and biotech firm, inter-industry, university, and hospital knowledge building on the firm's global search efforts. Future studies can complement the insights and findings from our work by examining the types of organizational ties for innovation which may be relevant to other industries, and how these linkages may impact the geography of knowledge sourcing for CC vs CE developments.

In the conventional literature, the main theme has been the relevance of local knowledge search for CC activity. While the empirical literature has shown that subunit performance involves external and geographically distant sourcing (Venaik, Midgley, and Devinney, 2005; Phene and Almeida, 2008; Cantwell and Piscitello, 2014), scant attention has been given to how international knowledge sourcing has been affected by the activities of foreign-located subunits in a relational system. This paper makes several specific contributions that distinguish it from prior research. Theoretically, we combine international business, innovation, and strategic management strands of literature which dichotomize explorative and exploitative search efforts. Empirically, we link organizational characteristics of knowledge networks to geographic sourcing for knowledge building dating back to the mid-1970s. Key factors that emerged from the analysis include the characteristics of the MNEs innovative efforts that suggested an association with a logic of competence creating or competence exploiting; and discerning which types of organizational linkages impact international knowledge sourcing, including subunits within the corporate group, other subunits in the pharma and biotech industries, as well as in other industries, universities, and hospitals.

Because of the richness of the data used to conduct the analysis, we were able to detect the links between organizations by aggregating their patent citations to other organizations. The empirical analysis here spanned organizational and geographic levels, not merely the focal actor within a specific firm. The first step is to show the evolution of the CC and CE networks and provide a descriptive investigation of the changing structure of networks over time. We observe that the networks change in the composition for each type of search effort. We then examined the sources of knowledge over time and the ties entailed in the structure of the MNEs knowledge network. Thus, we pay attention to the evolving structures of geographic, organizational, and cross-technological field knowledge development over time to address the remaining gap in our understanding of the performance of MNE foreign-located subunits as a whole as opposed to the performance of a focal actor within the MNE, i.e. co-inventor networks link inventors on the basis of their co-involvement in research projects, which entails their active cooperation.

However, the study is not without its limitations. Given the positive significant effect of university linkages on international sourcing for CE types of activity, future research should examine the scientific specialization of the universities where a link is established to better understand which scientific disciplines are relevant for the industry, and how they impact international sourcing. We expect that only some kinds of university science is accessed internationally, while others are accessed locally. While universities may be responsible for the country for which they are situated, contributing to national science and technological availability, the nature of science has itself become more global, e.g. Harvard is not just a national institution, because the nature of science itself has changed. This is due in part to the internationalization of professional and epistemic communities (Thomson, 1993), the increase in ties between international scientific networks and technological practice (Mazzoleni and Nelson, 2007), and the increase in scope of knowledge dissemination within and between organizations (Dunning, 1995). This may also partially explain why we don’t find a strictly positive or negative effect of building on university knowledge on international sourcing by CC activities in foreign subunits. Though we weren't able to find support for firm-hospital linkages, we believe this is an opportunity for future research, since little is known about the connections between drug discovery search efforts and downstream knowledge of hospitals. With the exception of a few studies which have separately identified basic science, which involve the discovery of mechanisms and processes that underlie specific diseases, and clinical science, which involve development processes which are thoroughly documented and heavily regulated. While prior literature might expect that sourcing hospital knowledge isn't necessarily bound to the local context in the development of knowledge for medical practice (Bignami *et al.* 2019), given the codifiable nature of clinical science, it's reasonable to argue that the purpose and nature of established hospital knowledge ties may differ for CC and CE activities. Future research might also benefit from revealing the direction of causality between types of organizational (inter- vs intra-organizational) and geographic (local vs global) knowledge ties. We expect that the MNE network contributes to the development of MNE innovativeness in a self-reinforcing way, i.e. firms that draw on their own intra-MNE knowledge networks are more likely to use international inter-organizational networks for their innovations. Exploring the dynamics of such linkages holds promise in future research.

The results of this study also have potentially important implications for issues and debates in international business, innovation, and economic geography. The extent to which foreign-located subunits search for CC and CE innovative activities internationally is driven by their engagement in both intra-corporate and ties to various types of organizations (Venaik *et al*., 2005; Meyer, Mudambi, and Narula, 2011). Foreign-located subunits' CC innovations benefit from both external embeddedness in their local environment (Andersson and Forsgren, 2000; Andersson, Forsgren, and Holm, 2002), which allow these subunits to access wider internationally dispersed knowledge networks (e.g. of other MNE competitors) and internal embeddedness within their MNE group (Chung and Alcacer, 2002; Cantwell and Piscitello, 2014). On the other hand, foreign-located subunits have increasingly relied on international connections external to the MNE (e.g. of biotech firms and universities) for CE activities. Results also have important policy implications, given the openness and cross-border integration of business networks of the current era, firms have increasingly relied on international organizational sources of knowledge, and so the availability of wider knowledge sources have become steadily more important (Cantwell and Piscitello, 2014).

CHAPTER SIX: STUDY 2: Home vs host country diffusion of competence creating innovations in MNEs

INTRODUCTION

The innovativeness of multinational enterprises (MNEs) is largely driven by their ability to orchestrate and connect international networks, combine dispersed sources of knowledge, and develop new knowledge globally (Doz *et al.*, 2001; Turkina and Assche, 2018; Scalera *et al.*, 2018; Cano-Kollmann *et al.*, 2016). While the international business literature has been dealing with patterns of competence building and sourcing within the MNE across locations, and the creation of new areas of expertise in overseas subunits in particular, the determinants of the subsequent use of new applications (competence creating relative to competence exploiting inventions) by other parts of the corporate group have received less attention. This paper argues that the diffusion of new competencies to the home country vs host country is driven by specific characteristics of the relationship with the parent or sister-affiliates. We leverage a network perspective in international business research to examine the degree of HQ-subsidiary or inter-subsidiary knowledge transmission (Andersson *et al.*, 2007; Ambos *et al.*, 2011; Blomkvist *et al.*, 2018; Beugelsdijk and Jindra 2018), given their importance for the affiliates concerned and the impact on the overall MNE's innovative efforts.

We focus on the transmission of new areas of expertise to the home country and within the host country setting, not merely the creation of innovations in MNE foreign subunits, or the specific roles of the subunits in the MNE network. To this end, we identified several strands of literature to form the context of our research on competence building and intra-MNE knowledge diffusion. One line of work claims that knowledge is more easily transmitted from within the corporate group, from the parent company to its foreign subunits (Kogut and Zander, 1992; Almeida, 1996; Frost, 2001; Andersson *et al.*, 2002; Phene and Almeida, 2008; Chen *et al.*, 2012), and integrated by the MNE (Rosenkopf & Almeida, 2003; Berry 2014). A second perspective maintains that knowledge is geographically localized (Jaffe et al. 1993), and can be transmitted from subunits that have acquired a competence creating mandate (Cantwell and Mudambi, 2005) – though there may be elements of both, competence creating and competence exploiting types of activities in any given subunit (Cantwell and Piscitello, 2014), and so the distinction between competence creating and competence exploiting in our context implies a distribution of activities within each subunit rather than a subunit level classification. We also draw on the literature which has suggested that a higher degree of competence creating types of inventions in foreign subunits benefit from their autonomy (Andersson et al., 2007; Ambos *et al.*, 2011; Beugelsdijk and Jindra 2018); however, we suggest that a greater autonomy requires at least a greater exchange of knowledge with the parent firm to obviate tensions associated with organizational disconnectedness. Finally, we draw on recent work which has contrasted the effects of internal and external embeddedness on global knowledge sourcing by foreign subunits (Asakawa *et al.*, 2018), building on an earlier set of writings that took a social network perspective to international business (Granovetter 1985; Ghoshal and Noharia, 1989, 1993; Bartlett and Ghoshal, 1989; Ghoshal and Bartlett, 1990; Uzzi 1997).

Through the process of reviewing the literature that investigates the advantages of intra-MNE network connectedness, the following mechanisms have been forwarded as possible explanations for the diffusion of new inventions. First, the development of new combinations around the core business expertise of the MNE group requires a more reciprocal international knowledge exchange relationship with the parent company (Berry, 2014; Cantwell & Piscitello, 2014; 2015), through which the corporate group knowledge is accessed and possibly combined with the new knowledge generated by the foreign subunit's competence creating inventions. The reciprocal exchange of knowledge increases the parent firm's awareness of how new capabilities developed in the host country may be relevant to subsequent developments. In turn, foreign subunits may attract the attention of their parents when engaged in competence creative types of activity that relate to the core knowledge base of the MNE. Second, while on average, difficulties associated with achieving embeddedness in international and local networks may negatively impact knowledge diffusion in the host countries, higher technological performers can manage to achieve dual embeddedness despite its typical drawbacks. Put differently, subunits are more likely to gain a central position for their exploitative inventions, since these are more common to the activities other subunits already perform. For this reason – without simultaneous consideration of the subunit's network position and creative activity – a subunit is unlikely to transmit locally the knowledge it identifies, given that creative competencies are more difficult to diffuse.

We estimate how much of the empirical pattern of knowledge diffusion can be explained by the subunit's ability to create new knowledge, identify the relevance of new developments, as well as the extent to which its centrality accelerates the diffusion of new areas of expertise. Though it can be difficult to obtain systemic data on the relations between all firms in the industry, we can infer such relations by making use of the organizational and geographic information in patents registered with the Unites States Patent and Trademark office (USPTO). We construct a rich and longitudinal database of the overall knowledge structure of the largest corporate groups active in the pharmaceutical industry. To examine the features of foreign subunits that explain the extent to which new areas of expertise are used in subsequent development of technology in the home country and host country setting, we analyze the forward citations that patents classified as competence creating received from future patents within the MNE. The timespan for network analysis covered the period 1976 to 2015 to represent a historical outlook of the determinants of knowledge transmitted across space and time. We find that the diffusion to the home country is driven by the reciprocal exchange of knowledge with the parent firm and the degree of relatedness of the subunit's competence creating inventions to the parent company knowledge base. We also show, intra-MNE knowledge diffusion in the host country is driven by the subunit's ability to develop competence creating inventions from a central position in the knowledge network.

The paper is structured as follows. First, we review the literature and hypothesize the effects on intra-MNE diffusion of new competences to the home country and within the host country. Next, we describe the data employed and specifications of our model. We then report the results and discuss our findings. The final section concludes our study and proposes new direction for future research.

CONCEPTUAL BACKGROUND AND HYPOTHESES

Foreign located subunits' competence creating inventions build on the technological efforts of diverse organizational networks locally, since these are qualitatively different from linkages established with the home country. Extant literature on the typology of subsidiary activity has focused on the relevance of local knowledge sourcing for innovation (Birkinshaw and Hood, 1998; Chini, 2004; Cantwell and Mudambi, 2011), the characteristics of the location in which the subunit is sited (Cantwell and Mudambi, 2005), and the conditions for tapping into the subsidiary network in which at least some subsidiaries have acquired a competence creating mandate, and can provide access to diverse host-country knowledge and know-how (Kogut and Zander, 1992; Almeida, 1996; Frost, 2001; Andersson *et al.*, 2002; Phene and Almeida, 2008). Recent literature has also suggested that a higher degree of novelty in overseas subsidiaries benefit from their decision-making autonomy (Beugelsdijk and Jindra 2018); that subunits located in rich developed markets exhibit stronger technological capabilities at home (Chen *et al.*, 2012); and examined the effects of inter-subsidiary differentiation on intra-MNE knowledge diffusion (Blomkvist *et al.*, 2018). However, little is known about the extent to which new areas of expertise resulting from the competence creating types of inventions (as opposed to the mere exploitative types of activities) of any given subunit within the corporate group is transmitted to other affiliates within the MNE. In this paper, we focus on the intra-MNE diffusion patterns to the home and within the host country settings.

Home country diffusion

Historically, new competence creation occurred in selected subunits in foreign markets and related to the MNE's core field of specialization (Vernon, 1966; Porter, 1990). In this traditional model, foreign located subunits relied on the knowledge assets that were generated by the parent company; these assets would then be adapted to local conditions (Buckley and Casson, 1976). To some degree, the majority of MNEs centralize their R&D activities in their home country (Berry, 2014), and so the parent firm continues to play an important role as a source of competence creation throughout the existence of the foreign located subunit (Berry, 2018), since the parent firm aids the transfer of parent-generated knowledge to foreign operations to benefit the overall group competitiveness across markets (Berry, 2015). Extant studies have shown that parent firm knowledge is a valuable source for foreign located subunits (Phene and Almeida, 2008; Berry, 2014), and that the transmission of such knowledge allows for the more tacit and more complex aspects of the parent firm's knowledge to transfer there (Hansen, 1999; Szulanski and Jensen, 2006).

However, the greater access to knowledge and resources of other firms or scientific institutes in the local innovation system has led foreign located subunits to behave more autonomously in generating capabilities that may detach them from their parent firm's agenda, i.e. the competence creating activities foreign-located subunits perform are embedded in countries (Rugman & Verbeke, 2001), shaped by systemic elements – policies, educational institutions, innovation systems, and business and nonbusiness networks (Cantwell 1989; Dosi et al., 1990; Nelson, 1993) that are difficult to transfer elsewhere in the world. A major theme in international business has therefore converged around the subsidiary's influence and autonomy (Andersson et al., 2007) and the knowledge ties within MNEs as important factors of bargaining power of and rent appropriation by subsidiaries (Mudambi and Navarra, 2004). While prior work has shown that a greater autonomy is associated with a higher probability of performing novel types of innovations (Beugelsdijk & Jindra 2018), little is known about the extent to which this type of invention diffuses back to the home country, where headquarters may be interested merely in those areas of knowledge which may be useful from their own perspective (Gupta and Govindarajan, 2000).

Since the primary function of a foreign located subunit is to tap into the local knowledge base to augment the MNE group's overall strength (Cantwell and Mudambi, 2005), the reciprocal exchange of knowledge between the subunit and the parent firm is critical for subunits with higher levels of competence creating types of inventions – not only because of the increased internal and external complexity of the parent and foreign located subunit's environment (Ibarra-Caton *et al.*, 2018) but also because of inter-unit competition for resources and attention from the parent for risky types of activities (Bouquet and Birkinshaw, 2008; Luo, 2005). All else being equal, the parent firm tends to resist external technologies that do not fit the dominant logic of the overall MNE (Bettis & Prahald, 1995; Prahalad & Bettis, 1986). Knowledge reciprocity is therefore vital in sustaining the relationship of subunits with the parent firm upon which the subunit depends in further developing competence creating types of inventions. When foreign located subunits are highly embedded in the parent knowledge network, subunits develop a deep understanding of how the knowledge they're generating is relevant to the dominant technologies of the MNE. At the same time, the parent firm is more likely to take interest and make use of the new areas of competence developed by a foreign subunit that is consistently exchanging relevant knowledge. Knowledge reciprocity – i.e. the degree to which new applications have the potential to connect to the developments of the parent firm – may therefore allow these subunits to benefit from both, their external embeddedness in their local environment (Andersson and Forsgren, 2000; Andersson, Forsgren, and Holm, 2002) – e.g. accessing wider internationally dispersed knowledge networks (of other MNE competitors or universities which are themselves internationally connected) – and internal embeddedness within their MNE group (Chung and Alcacer, 2002; Cantwell and Piscitello, 2014), in which the foreign located subunit's relationship with the parent firm is the most representative form of internal embeddedness.

By relating creative competencies or local expertise to the parent's knowledge stock, the subunit is more likely to be recognized by the parent firm (Cohen and Levinthal, 1990; Yang *et al.*, 2010), decreasing uncertainties associated with the quality of its output (Schulz, 2001). This encourages foreign located subunits to develop technologies that can be reconciled with the existing knowledge base of the firm (Rosenkopf & Almeida, 2003: 753). Indeed, the benefit of knowledge relevancy has more to do with attracting the attention of the headquartered or parent firm, which may add value in improving the subunit's knowledge generations and filtering those opportunities that may not fit the overall objective of the MNE (Monteiro, 2015). We therefore expect that the diffusion of new areas of expertise to the home country is driven by reciprocity between the foreign subunit and the parent firm, as well as the ability of the parent firm to develop relevant new knowledge combinations deriving from the competence creating developments of its subunits. Subunits that are more engaged in competence creative types of activity that relate to the core knowledge base of the MNE, and hence of the parent company, are more likely to be attractive to their MNE parents. Within the intra-corporate network, subunits are able to draw upon the knowledge and resources of their parent (Phene & Almeida, 2003; Bartholomew, 1997; Phene *et al.*, 2006), combine local learning with the knowledge absorbed from the parent firm, and distribute new competencies back to their home country (Cantwell, 1995). In this way, foreign located subunits with increased levels of knowledge reciprocity with their home country and when their competence creating inventions relate to their parent firm's knowledge ensure their new competence creating efforts are relevant to the MNE's overall strategic goals (Zhang *et al.*, 2019). Thus:

Hypothesis 1a: When the level of the reciprocal exchange of knowledge with the home country is high, so is the extent of intra-MNE diffusion of competence creating inventions to the home country.

Hypothesis 1b: When the degree of relatedness of a subunit's competence creating inventions to the parent company knowledge base is high, so is the extent of intra-MNE diffusion of competence creating inventions to the home country.

Host country diffusion

An influential line of work has shown that some selected foreign located subunits are central and innovative contributors in the internal MNE network (Birkinshaw and Hood, 1998; Chini, 2004; Cantwell and Mudambi, 2005; Cantwell and Piscitello, 2014). Within their host country environment, these subunits engage in greater knowledge-based interactions with local actors (Andersson and Forsgren, 2000; Andersson *et al.*, 2002; Almeida and Phene, 2004; Alcacer and Chung, 2007; Singh, 2008). Their ability to develop external ties in the host-country network, through which technical knowledge is located and accessed is critical for the development of new competencies, and continued participation in local communities, e.g. important clusters of knowledge, sophisticated suppliers, universities, and other local firms in the local knowledge network (Porter, 1990; Furman *et al.*, 2002). At the same time, competence creating types of activities are characterized by experimentation and differentiation from intra-MNE knowledge. While they can potentially create competitive advantages, the knowledge generated may be difficult to transfer, i.e. an increase in creative endeavor essentially means the subunit's activity is removed from the overall group agenda and disconnected from the intra-firm network. This tension may be associated with a decrease in knowledge relevancy and organizational connection, making it difficult to build on the new knowledge these subunits generate.

Gaining access to new knowledge requires networking efforts that determine the subunit's ability to successfully apply and diffuse new applications (Tsai, 2001). Subsidiary knowledge networks reinforce their learning processes and cooperation, which may involve the transfer of knowledge in a shared context in which subunits are linked to other units within the firm, and other organizations. A subunit's influence in the knowledge network may help create the conditions necessary for knowledge diffusion, since the newness of creative types of activity require intensive interactions with diverse organizational sources for the generation of innovative recombination (Zander, 1998), and successful transfer of the new knowledge within the MNE (Zhang *et al.*, 2019). However, while network embeddedness can be looked upon as influencing the subsequent diffusion of the subunit's innovations, this process may vary between firms depending on the type of activity being generated from its network position.

Prior work has maintained, increased connectivity among actors within a local network can homogenize knowledge stocks (Zhang *et al.*, 2019). Because competence exploiting types of activities are more common with intra-MNE knowledge generation, and can be more easily transferred within the MNE network, due to the establishment of a common social community (Kogut and Zander, 1993; Nohria and Ghoshal, 1997), and the networked pattern of inter-unit knowledge exchange within the enterprise (Chini, 2004; Monteiro, Arvidsson, and Birkinshaw, 2008), the subunit is more able to attract the interest of other parts of the group generating competence exploiting relative to competence creating types of activity. Foreign subunits are more likely to gain a central position for their competence exploiting efforts, which are more relevant to the activities subunits perform, than creative competencies, which are subsequently more difficult to diffuse.

Recent work has not only contrasted the effects of internal and external embeddedness in a geographically local context (Asakawa *et al.*, 2018), it has also explored the effects these may have on subsidiary autonomy, suggesting that internal and external embeddedness have, at times, opposite effects (Ambos et al., 2011). However, we have reason to believe that higher technological performers can manage to achieve dual embeddedness despite its typical drawbacks. Earlier writings in particular have investigated foreign subsidiaries' entry into technological areas that were new to the MNE, but find these contributions were made by a select number of advanced subsidiaries (Blomkvist *et al.*, 2010; Kappen, 2009). These subunits are embedded in both, the intra-corporate group network, which coordinates internal processes of knowledge transfer, and an external network that involves resource sharing (Galbraith, 1977; Gresov and Stephens, 1993; Gupta and Govindarajan, 1984, 1986), enabling units to identify the relevance of new areas of competencies that contribute to their subsequent inventions. This intimate connection between different organizational units is critical in facilitating the creation of capabilities (Kogut and Zander, 1992; Tsai, 2000) and the ability to obtain and use new knowledge (Huber, 1991).

We therefore expect, while network centrality initially reduces the diffusion of competence creating inventions in the host country – given the difficulty of achieving dual embeddedness in both international and local networks – past some point it turns upwards.

These most central subunits with high levels of competence (in terms of their competence creating output) manage to achieve dual embeddedness more successfully. Thus, one of the main advantages with higher technological performing subunits is the possibility to transfer new competences between subunits in the host country. We would therefore expect that, within an MNE, knowledge would diffuse from subunits occupying a central position with high levels of competence. Generating competence creating relative to competence exploiting activities from a more influential position in the knowledge network impacts the subsequent diffusion of these competencies in the local environment. Without a simultaneous consideration of its network position and relative increase in competence creating activity, a subunit is unlikely to be attractive for these types of endeavors, and it may even be unable to transfer the new opportunities for knowledge building. This is consistent with Phene and Almeida (2003), who find that knowledge sourcing from the local environment increases knowledge sharing with other subsidiaries, but not the parent firm; suggesting that the mechanism that influences diffusion in the host country differs from knowledge reciprocation and relevancy discussed previously. We therefore formulate the following hypothesis:

Hypothesis 2: The subunit's network centrality is curvilinearly (taking a U-shape) related to the extent of intra-firm diffusion of competence creating inventions in the host country.

METHODS

Data

We explore our hypotheses in the context of the pharmaceutical industry using patents registered with the USPTO. To construct our sample, we identified 45 major corporate groups engaged in US patenting in the pharmaceutical field and identified subsidiaries of these firms by conducting an historical examination of the ownership structure of each group using D&B Who Owns Whom directories. Second, we extracted from the USPTO websites all patents granted from 1976-2015 belonging to the 45 groups identified, which included all the patents from their worldwide research facilities. The patent records included the affiliation of the assignee, the address of the inventors, as well as the year in which the patent was granted and the technological field of activity (derived from the patent class and sub-class, which were themselves used to classify patents as competence creating vs competence exploiting types of activity). We also recorded the sector, and the home or headquarter country of each firm. All patents that were cited by the patents that belonged to our 45 corporate groups were then extracted and the organizational affiliation of assignees of these cited patents were consolidated; the cited organizations include other pharmaceutical or non-pharmaceutical firms, universities, hospitals, etc.

Third, and most important, we disaggregated the foreign subunit's activity to distinguish between competence creating and competence exploiting components. Competence creating inventions represents exploratory search efforts into new scientific and technological areas, whereas competence exploiting inventions represents an extension of search efforts undertaken by the parent firm in the home country. To classify patents in this way, a measure of parent firm specialization was first constructed, i.e. a Revealed Technological Advantage (RTA) index[1], to control for inter-field and inter-firm differences in the propensity to patent (Cantwell 1989). Patents of foreign located subunits were classified as competence creating if the foreign subunit had an RTA equal to, or greater

[1] RTA is defined as follows: RTA = $(P_{ij} / \sum_i P_{wj}) / (\sum_j P_{ij} / \sum_{ij} P_{wj})$, where P_{ij} is the number of patents in technological field j by a parent firm i, and P_{wj} is the number of all patents in the same sector by all firms. We then constructed a measure of a foreign subunit's specialization, i.e. an RTA equal to, or greater than 1 in a field. Parent firms were excluded, since they were the benchmark for which foreign subunit's were defined.

than 1, but the parent firm has an RTA less than 1 in that field (Cantwell and Piscitello, 2014). All other patents of these subunits were classified as competence exploiting, since this was interpreted to meaning the subunit was either merely imitating the parent firm, or not bringing in new areas of specialization to the MNE. We identified 579 foreign subunits developing competence exploiting types of technologies and 297 foreign subunits developing competence creating types of technologies.

Table 1 includes descriptive statistics about the 297 foreign subunits developing some distribution of patents that were classified as competence creating; the geographic spread of these subunits are depicted in Figure 1. While our current study only observes the foreign subunits developing competence creating technologies, it is worth noting, while the number of subunits engaged in competence exploiting types of activity have increased, the number of subunits engaged with creative endeavors have not. On the one hand, inter-subunit differentiation within MNEs increase the capacity for exploration, but the output of such endeavors are more difficult to diffuse. Our final dataset included 10,108 competence creating patents. We grouped citations according to whether the implied knowledge used is by subunits within the MNE, and whether it was diffused to the home or within the host country setting. Home country is defined as the country for which the foreign subunit's parent company is located (source: D&B). Host country is defined as the country for which the foreign subunit is sited (source: USPTO).

Insert table 6.1 here

Insert figure 6.1 here

Statistical analysis

Since we are interested in knowing the extent of subsequent citations by other parts of the corporate group – the degree of diffusion from the user's, as opposed to the creator's perspective – we modeled the number of cites foreign located subunit's competence creating patents received between 1980 and 2015 (broken into 5-year intervals) using negative binomial regressions, which produce correct standard errors for count data that exhibit a great deal of over dispersion (Cameron and Trivedi, 1998). The diffusion effect is therefore cumulative and properly captures the absolute number of subsequent cites.

Variables

Our analysis focuses on the knowledge diffusion patterns within multinational corporations at the geographic levels of the home or within the host country settings. We developed dependent variables from the geographic information contained on the citing and cited patents, i.e. an indicator of whether a patent citation was by inventors located in the foreign subunit's home country or host country. The dependent variables are therefore the number of times a focal patent is cited in any subsequent period, where the citing patent is the parent company, or originating from the focal subunit's host country.

To test our hypotheses, we constructed a variable to examine the extent of the reciprocal exchange of knowledge between the foreign subunit and its home country, i.e. the number of times the focal subunit cites the parent, as well as the degree of relatedness of a subunit's competence creating inventions to the core knowledge base of the MNE, i.e. the number of times the focal subunit's competence creating inventions were cited by the parent firm, where the citing (parent firm) patent and cited (subunit) patent were in the same technological field. We also calculated the share of the foreign subunit's competence creating patents, as well as the subunit's centrality in the overall knowledge network using citation data. Each cited to citing patent is a knowledge dyad; knowledge-based linkages are represented by citations to other organizations, which include other pharmaceutical or non-pharmaceutical firms, universities, hospitals, etc., locally or globally. We controlled for the diversity of knowledge sources (or the variety of knowledge sources a subunit has access to) since an increase in the types of knowledge ties increases the potential for exploratory innovation (Wang et al. 2014; Rodan & Galunic, 2004). We controlled for the subunit's size, and whether the subunit's cited patent is in the pharmaceutical field.

Moreover, for patents in our sample, we tracked all future patents that cite them in subsequent periods: the end of 1980, 1985, 1990, 1995, 2000, 2005, 2010, and the end of 2015. Since the significance of new competence creating inventions rises over time, then dies out pretty quickly, we include a variable *patent age* to control for the truncation effect. To parse out the different effects of age and recency bias, we calculate the total number of citations a subunit receives by its competence creating patents in the ten years after grant, i.e. the window within which a patent would receive most of its citations. We expect recency to be inversely related to age, since recent patents are likely capturing prior inventions without citing those that have been cited by them. Finally, we made use of distance calculations developed by Berry et al. (2010) to control for national differences, i.e. economic, political, and geographic distance between the foreign subunit's home and host countries. These measures have been updated in 2017 and are made available on the author's website. Table 2 summarizes the variables used in the analysis.

Insert table 6.2 here

RESULTS

Table 3 shows the mean values and standard deviations, and Tables 4 provides a correlation matrix of all the measured variables. Results of negative binomial models are shown in Table 5.

Insert table 6.3 here

Insert table 6.4 here

Insert table 6.5 here

We find support for hypothesis 1a. In model 1 the reciprocation measure is positive and highly significant ($p<0.01$), suggesting that citing the parent firm on patents that are classified as competence creating is associated with highly cited competence creating patents in subsequent developments at home. The reciprocal exchange of knowledge increases the parent firm's awareness of how complex technical knowledge from overseas subunits may be relevant and recombined, increasing the likelihood the parent firm takes interest and makes use of the subunit's competence creating inventions. We also find support for hypothesis 1b. In model 2, the degree of relatedness of a subunit's competence creating inventions to the knowledge base of the MNE, and hence the parent company, is also positive and highly significant ($p<0.01$), suggesting the ability of the corporate HQ to develop relevant new knowledge combinations deriving from the competence creating inventions of its subunits influences the transmission of these inventions to the home country. Indeed, while foreign located subunits draw on complex and diverse pools of knowledge from the local environment more effectively, experimenting various recombination of knowledge elements independently may result in tensions associated with organizational disconnectedness. Taken together, the reciprocal exchange of knowledge as well as the relatedness of a subunit's inventions to the technological developments undertaken by the parent firm enables the parent to identify the relevance of, and build on the knowledge generated by the foreign subunit; in turn, this is likely to aid the subunit with additional resources.

We also find support for hypothesis 2. In model 3, the network centrality measure is negative and highly significant ($p<0.01$), suggesting that, on average, subunits occupying a more central position in the overall knowledge network are less likely to see their competence creating types of inventions diffuse in the host country, particularly if they've gained a more central position for their exploitative developments, since these types of inventions are more familiar to the activities undertaken by their recipients. Competence creating types of inventions are characterized by experimentation and differentiation from intra-MNE knowledge. While they can potentially create competitive advantages, the knowledge generated may be difficult to transfer. This is partially confirmed by the negative, significant coefficient of the increase of the subunit's competence creating relative to competence exploiting types of activity (CCshare) on diffusion in the host country. This tension may be associated with a decrease in knowledge relevancy and organizational connection, making it difficult for the recipients to build on the new knowledge these subunits generate.

While foreign subunits can transmit more readily in a shared local context, they are more likely to attract the attention of other subunits within the MNE for their competence exploiting – which are more common to the activities others perform – relative to their competence creating types of activities. However, as can be seen in model 4, we find a nonlinear effect of centrality in the knowledge network ($p<0.01$) on the diffusion of new innovations in the host country, i.e. while network centrality initially reduces the diffusion of competence creating inventions to the host country, past some point it turns upwards. The subset of subunits that can transmit new areas of expertise resulting from their competence creating inventions in the local environment would be higher technological performers who have managed to achieve dual embeddedness more successfully.

CONCLUSION AND FUTURE RESEARCH

This paper offers a neglected way to examine competence creating activities of contemporary, geographically dispersed MNEs, by disaggregating the activities of all its subunits. While prior work has made clear contributions to theories about intra-MNE knowledge integration and the MNEs' role in international knowledge transmission (Beugelsdijk & Jindra 2018; Blomkvist et al. 2018; Chen et al. 2012), this paper sought to examine the extent of intra-MNE diffusion of competence creating types of inventions to the home country and within host country settings. We complement prior literature which has suggested that novel innovations in overseas subunits benefit from greater autonomy (Andersson et al., 2007; Ambos *et al.*, 2011; Beugelsdijk and Jindra 2018). We find that the reciprocal exchange of knowledge and the degree of relatedness to the parent firm developments are important in determining diffusion patterns to the home country, suggesting an increase in the parent firm's awareness of the activities undertaken by the subunit, and hence its ability to develop relevant new knowledge combinations deriving from their competence creating inventions. Our contributions parallel the discussions on the subunit's desire to attract the attention of its parent company, especially since an increase in creative types of endeavors is associated with the risk that the activities the subunits perform are removed from the overall group agenda. We also emphasize that embeddedness of exchange within knowledge networks across organizational and geographic space provide opportunities and constraints that may affect subsequent use of new applications. We find that developing competence creating types of activities from a central position influences the transmission of knowledge in the host country, since these links provide combinatorial opportunities, mutual learning and cooperation, stimulating the subsequent use of new areas of expertise; without simultaneous consideration of the subunit's network position and creative activity, a subunit is unlikely to transmit locally the new areas of expertise it identifies, especially if it gained its central position for competence exploiting relative to competence creating types of inventions, which are difficult to diffuse. The more central the unit, and the more creative its knowledge base, the more the subunit's attractiveness influences the subsequent diffusion in its local environment.

The deliberate efforts of the MNE to integrate sub-unit activity and to direct some division of labor in tasks that require inter-unit coordination ensures that the technological activities of the different parts of an MNE network tend to be related. However, new areas of competences are not easily transferrable across units (Teece, 1981), since these are often sticky to spread. After risky and expensive new competence creation, managers of foreign subunits should ensure that the new knowledge is readily available to other units, and relevant to the parent firm in particular. Managers should therefore rethink the role of knowledge management within their overseas subunits with the aim of identifying new areas of expertise or generating competence creating innovations that relate to the core developments of their parent firm, as well as the way in which their position in the knowledge network may impact the subsequent use of the new applications in the local environment. Our findings also have important policy implications. MNEs are distinguished by their deployment of international networks for innovation, since networks reinforce learning processes and coordination within the firm and can increase cooperation and learning processes with others in the host country environment. The pharmaceutical industry in particular relies heavily on inter-sectoral knowledge networks in absorbing complementary areas of knowledge, and generating new knowledge combinations (Edris, 2019). These knowledge-based networks increase the awareness of each firm about the knowledge repositories available from external sources, and how they may potentially fit with the firm's own efforts. However, the greater openness of the macroeconomic environment – which has contributed to the increase in the scope for discovering new knowledge combinations (Cantwell and Piscitello, 2014) as well as being held together by more reciprocal knowledge exchanges within and across organizations and geographic boundaries (Held *et al.*, 1999; Morgan, 2001; Karlsson *et al.*, 2010) – should not be taken for granted. Policy makers should encourage MNE arrangements that promote knowledge management and networked relationships, since being exposed to diverse knowledge sources can enable combinatory opportunities that benefit the host country environment, i.e. lead to a higher number of innovative outputs, and increased success in knowledge diffusion.

The focus of this paper has been to enrich prior streams of research of the extent of intra-MNE diffusion patterns of competence creating activities as opposed to the creation and sourcing of it. In the process, we noted research directions that can continue to expand and deepen the integration of international business and knowledge management research. First, studies that consider knowledge diffusion to third country settings can complement the insights and findings from our work, since the increased interaction between local creativity and knowledge availability elsewhere in the world has strengthened the connections across subunits within the MNE. While prior literature has suggested that subunits might resist transferring knowledge to other units from within the firm (Fleming *et al.*, 2007; Gupta and Govindarajan, 2000; Reagans and McEvily, 2003), given the difficulties associated with understanding specialized or tacit knowledge (Frost, 2001; Zhang *et al.* 2019), we have reason to believe diffusing knowledge to other intra-MNE units may increase efficiency (Hansen, 2002). To the extent the reciprocal exchange of knowledge reduces redundant effort, it ensures the efficiency of activities and that the knowledge is relevant to the technological information produced in third country settings (Patel and Pavitt 1991), i.e., when discovering potentially competence creating types of activity by chance, instead of changing trajectory, subunits may transmit this capacity to other units that can continue working on such developments. However, while inter-unit connections increase the potential for information sharing and visibility, technological advancements and globalized competition have accelerated the speed of knowledge dissemination (Katila and Ahuja, 2002). This means the ability to access new knowledge originated in geographically distant locations via external linkages may offset intra-firm transmission channels (Zhang *et al.*, 2019). MNEs may therefore compel subunits to disseminate new competencies to those subunits that can exploit them and discourage hoarding knowledge for private gain, particularly if the subunit perceives that new knowledge as a source of competitive advantage. It would be interesting to know the conditions under which foreign subunits are incentivized to diffuse newly absorbed knowledge internationally, and how to resulted recombination impacts the performance and long-term competitiveness of the MNE.

Moreover, further research exploring cooperative vs competitive effects would be useful to expand our knowledge on inter-MNE, as opposed to intra-MNE knowledge transmission. While problems of appropriability might arise, the increase in inter-firm agreements over the last decades suggest that the difficulty of appropriating a full return on particular knowledge elements is not the main concern of a firm (Cohen & Levinthal, 1990). The growing significance of basic science within technological knowledge, rising technological interrelatedness and technology fusion, emergence of broader technological systems, and rising costs of R&D are only some of the reasons motivating these agreements, which result in a more focused profile of technological specialization. The reciprocal exchange of knowledge between MNEs can therefore increase subsequent cooperation and formal learning processes, e.g. utilize overlaps between complementary paths of technological development that are strongly influenced by spatial proximity mechanisms that favor cumulativeness. Knowledge transfer among organizations provides opportunities for mutual learning and cooperation that stimulate the creation and subsequent use of new areas of expertise (Tsai & Ghoshal, 1998). At the same time, the transmission of knowledge is influenced by the ability to identify the relevance of the knowledge generated, which may be limited due to absorptive capacity or reciprocal exchanges with potential recipients located elsewhere in the world. Finally, there are some theoretical gaps regarding the degree to which the geographic structure of MNEs promote knowledge management. While the relationship between a subunit and its parent firm, as well as the subunit and its local environment remain relevant, describing and examining the locational composition of international networks for knowledge sourcing and diffusion can be an interesting starting point for future research, particularly for cases of MNEs that have a selection of subunits that occupy central positions in more than one location. International business researchers are very well placed to examine how MNE geographic portfolios regulate the interaction between MNEs.

CHAPTER SEVEN: STUDY 3: How location portfolios and geographic overlaps of external sourcing regulate the reciprocal exchange of knowledge

INTRODUCTION

Inter-firm knowledge exchange is vital in promoting networks for innovation within and across organizational boundaries and international space. The reciprocal exchange of knowledge sustains membership structures between those that hold or have access to complementary bodies of knowledge (Cantwell and Salmon, 2019). MNEs are especially well positioned to search, extract, and exchange knowledge across geographic areas in which any facility in their network is situated (Lorenzen and Mudambi, 2013), though a fundamental issue concerns the sharing of firm knowledge, and how the geography of MNE inventive activities and external sources affect inter-MNE knowledge reciprocity. In our paper, we examine these two types of geographic leverage that relate to the sources of knowledge and recombination potential in affecting inter-MNE knowledge reciprocation – the *geographic profiles of innovations*, i.e. the sites of origin of inventions, given that learning processes may be influenced by the context within which activities were undertaken, and the *geographic overlaps of external sourcing* in the form of cited inventions, given that spillovers can take place over longer distances (Ponds *et al.*, 2010).

We scanned an established literature on the factors that influence the location choice of MNEs. The most common reason in economics refers to externalities that occur as a result of agglomeration and proximity to other firms in an industry (Marshall, 1920; Head et al., 1995; Nachum and Zaheer, 2005), though conceptual disagreements on what attracts or deter MNEs from moving to such locations can be found in the international business literature (Shaver and Flyer, 2000; Arino et al., 2004; Ghemawat 2005, Rugman 2005, Khanna et al. 2006; Nachum et al., 2008; Cantwell and Mudambi, 2011). We adopt the view of the MNE as a portfolio of diverse locations (Johanson & Vahlne, 1977; Chang, 1995, 1996; Cantwell, 2005; Barkema & Drogendijk, 2007), which shapes it's experience and capacity to absorb new areas of expertise (Cohen and Levinthal, 1990), and determines its location moves (Belderbos & Zou, 2009). Our first question is thus: given that MNEs construct coherent portfolios of locational assets (Ghemawat, 2001; Ricart et al. 2004), to what extent does the location profile of innovation of firm pairs influence the reciprocal exchange of knowledge between them?

Another stream of research has examined the greater complementarity between internal and external knowledge sourcing (Phene and Almeida, 2008; Rosenkopf and Padula, 2008; Hagedoorn and Wang, 2012; Monteiro and Birkinshaw, 2017). One line of work in particular has argued that open innovation systems are supplementing formal governing structures (Chesbrough, 2003, 2006; Laursen & Salter, 2006; Gassmann, Enkel & Chesbrough, 2010; Pénin, Hussler & Burger-Helmchen, 2011), since these spread wider, are comparatively more open, and are not limited by contractual relationships. While economic geographers have made a significant contribution to understanding the systemic interdependencies between firms and places over geographic distances (Breschi & Malerba, 2001; Florida, 2005; Bathelt & Glückler, 2011, 2017), how MNE interactions relate to the geographic profile of their sourcing behavior has been overlooked in the literature (Beugelsdijk *et al.* 2010), especially since MNEs rely on knowledge sources outside their location. Our second question is thus: given that MNEs have reconfigured their international connections (Mudambi, 2008; Lorenzen et al., 2020), relying especially on external sources of knowledge to complement internal research, to what extent does the geographic overlap of knowledge sourcing of firm pairs influence the reciprocal exchange of knowledge between them?

By examining both, the *geographic profile of innovations* and the *geographic overlaps of external knowledge sources* of firm pairs, we emphasize the idea that reciprocation is influenced by the firm's proximity to its competitors as well as the spatial distribution of its knowledge sources in relation to the sourcing behavior of other firms. We build on arguments from the knowledge spillovers perspective, which focuses on externalities that arise from siting activities in a particular location, and the knowledge building perspective, in which technological knowledge is cumulatively developed within and between organizations and across space. We consider how the strategic and geographic positioning of MNE knowledge arrangements may increase the knowledge exchange between them. We argue that the geography of inventions and sources of knowledge is necessary for inter-firm knowledge transfer and reciprocity.

We advance our hypotheses on MNE knowledge and location structures, and inter-firm knowledge reciprocation in the pharmaceutical industry between 1976 and 2016. The pharmaceutical industry is the context of our research, since around 1980, there has been a rapid growth of inter-firm knowledge exchanges, due to the rise of technological interrelatedness, and more open innovation strategies. It is also an industry in which a firm's ability to access and incorporate relevant external research, i.e. scientific and clinical knowledge, is especially useful for guiding the search for innovations (Fleming and Sorenson, 2004). We use a unique dataset of knowledge ties created by patents granted by the US patent and Trademark Office (USTPO) to examine the degree to which the geographic profile of inventive activity and geographic overlaps of external knowledge sources of MNEs in the pharmaceutical industry regulate their knowledge reciprocity with other firms in the industry. We expect that inter-firm reciprocation of knowledge has been affected by co-location of innovations and knowledge sources and connections that are not necessarily restricted to a geographic scale.

The paper is structured as follows. First, we review the literature on location and sourcing strategies and hypothesize the effects on interfirm reciprocation. Next, we describe the data employed and specify our models. We then report our results, discuss our findings, and draw some conclusions. The reciprocal exchange of knowledge is of great relevance for the development of theory in international business, economic geography, and innovation studies, but also for MNE executives making location decisions and establishing external linkages, as well as policy makers in an increasingly uncertain environment.

THEORETICAL BACKGROUND AND HYPOTHESES

Geographic profiles of innovation

The importance of an MNE's position in geographic space is recognized in a number of theoretical strands, at different levels of analysis, e.g. cities, countries, and regions, though conceptual disagreements on MNE location moves remain. For example, an earlier explanation of knowledge spillovers in the strategy and regional science literature is based on the supposition that MNEs are attracted to clusters, where access to the total stock of knowledge accumulated in the area may be available to MNEs that locate there (e.g. Porter, 1994, 1996, 2000). However, the international business literature countered this argument, suggesting a possible deterrent to location in knowledge-based clusters, i.e. the problem of adverse selection, since laggards have more to gain from knowledge spillovers, whereas technology leaders would have more to lose from knowledge or technology leakage to potential future competitors (e.g. Shaver and Flyer, 2000). A stream of literature continued to focus on MNE concerns about locating in knowledge clusters, including effects on its competitive advantage, e.g. its ability to profit from its innovation efforts through leakage of its intellectual property (Shaver and Flyer, 2000; Chung and Kalnins, 2001; Alcácer, 2006; Alcácer and Chung, 2007; Aharonson *et al.*, 2007), as emphasized in the original received internalization explanation that was grounded within transaction cost economics (Buckley and Casson, 1976). Cantwell and Mudambi (2011) provided some clarity to these opposing lines of work. They argue, so long as a cluster is not characterized by a highly concentrated local industry, and instead offers a diverse base from which an MNE is able to construct an external network of knowledge linkages, MNEs would indeed benefit from locating in such a cluster, since they would have more scope to become locally embedded insiders in this environment. A higher degree of local industrial concentration tends to inhibit local knowledge sourcing by outsiders, since they might discourage the transfer of local resources to new entrants, and might also impede other possibilities, such as recruiting technical personnel. On the other hand, an increase in the diversity of available potential connections to other actors in a cluster is associated with better access to channels for knowledge discovery, which may contribute to the building of new capabilities based on new knowledge combinations (Caves and Porter, 1977; Cantwell & Mudambi, 2011).

Traditional theories in international business however hold that MNE location moves are either determined by the comparative advantages of country in the world economy (Wheeler & Mody, 1992; Caves, 1996; Arino et al., 2004; Ghemawat 2005, Rugman 2005, Khanna et al. 2006), the location choices of their competitors (Knickerbocker, 1973; Johanson and Vahlne, 1977), or firm-specific characteristic or advantage (Cantwell, 1989; Alcacer, 2006). Recent studies have instead conceptualized the MNE as a portfolio of locations (Cantwell, 2005; Nachum and Song, 2011), rather than MNE developments in relation to individual subunits. Nachum et al. (2008) in particular have shown that a country's proximity to the global distribution of knowledge, markets, and resources may drive or deter MNEs from locating there. In a macro-level context of incomplete integration (Ghemawat 2003), MNEs may design location portfolios to strategically leverage large sophisticated markets and knowledge bundles in the form of learning capabilities across national boundaries (Bartlett and Ghoshal, 1989; Rugman Verbeke, 2001). At the same time, MNEs tend to expand into areas which resemble the locations they currently operate in, since the potential for new opportunities are likely to be within the domain of firms' existing knowledge (Cantwell, 1989; Belderbos & Zou, 2009), reducing uncertainties associated with international expansion and risks that result from operating in new, and unfamiliar environments. It is therefore reasonable to argue that location choice is determined by internal fit as well as the relative character of alternative locations, i.e. based on an evaluation of the benefits and costs that alternative moves are likely to yield.

A portfolio approach views MNE moves as a series of inter-connected choices carried out within the context of their existing portfolios (Johanson & Vahlne, 1977; Chang, 1995, 1996; Barkema & Drogendijk, 2007). It provides a basis for examining the effect of the location portfolio of firm pairs, and the extent of inter-MNE reciprocation of technological capabilities, some of which is across borders to other firms in the industry, which remain expensive and difficult (Rugman and Verbek, 2003). The diversity of a location portfolio, in terms of levels of economic development, resource abundance, institutional environment, etc., shapes a firm's experience and capacity to absorb new areas of expertise (Cohen and Levinthal, 1990). Put differently, a firm's technological activities may be dispersed across different types of geographic space to exploit more effectively established competencies in a particular location, while moving into new, but related fields of technology. Corporate internationalization of technological assets is indeed one way of spreading and diversifying the competence base of the firm, and acquiring new sources of competitive advantage (Cantwell and Piscitello, 2002). While various studies have illustrated the importance of studying MNEs as a portfolio of locations (Cantwell, 2005; Nachum and Song, 2011), the degree to which the complementarity of geographic profiles of firm pairs is associated with the knowledge reciprocation between them has been overlooked.

In general, firms tend to have distinct and differentiated capabilities which enable them to conduct dissimilar sets of activities. However, we expect the more closely related the geographic profile of technological competencies of any pair of firms, the greater will be the extent of technological complementarity between their activities, and hence a stronger motivation for accessing and benefiting from a combination of their respective capabilities, i.e. greater potential gains from inter-firm reciprocation. Put differently, MNEs construct coherent location portfolios, and have at least some locations in common with other firms. It is therefore reasonable to suppose that co-locating inventions may increase knowledge reciprocation, since learning processes may be influenced by a shared context within which MNE activities are undertaken, e.g. skill profiles of city-regions

(Lorenzen, 2020), or country specific advantages, i.e. economic policies, political, or national innovation systems. We therefore expect, firms at a certain geographic distance are more likely to determine an optimal process of sharing knowledge in order to access complementary areas of specialization that they lack, i.e. at a certain distance, but not too far away, as that would lead to a lack of connection between profiles. This line of reasoning leads us to the following hypothesis:

Hypothesis 1: There is a curvilinear (inverted U-shaped) relationship between co-location of inventions and the reciprocal exchange of knowledge between MNEs.

Geographic overlaps of external knowledge sourcing

An influential line of research in the innovation studies literature highlights the importance of external knowledge search (Phene and Almeida, 2008; Rosenkopf and Padula, 2008; Hagedoorn and Wang, 2012; Monteiro and Birkinshaw, 2017). MNEs in particular are likely to source specialized knowledge through international ties that provide clear prospects of returns on innovations. For example, in the context of science-based industries, where the search-facilitating knowledge is partially held in-house and partially by external sources to the firm, e.g. “public science”, one determinant of how successfully firms further exploit their competencies is their ability to access and incorporate relevant research areas from those sources outside the firm, i.e. R&D performed in universities and research institutes, or clinical applications from hospitals. The motivation to establish a knowledge tie is partly determined by the location that hosts sources of research activities (Cantwell and Piscitello, 2002), since external networks are characterized by different levels of social embeddedness.

Indeed, while the opportunities for finding important sources of complementary knowledge through inter-sectoral linkages have increased the extent of international dispersion of innovations, little is known on how geographic overlaps of sourcing patterns influence inter-MNE knowledge exchange. Moreover, prior empirical work has tended to focus primarily on how localized clusters may facilitate knowledge sharing and stimulate learning to those in a particular region (Breschi and Malerba, 2001) since the potential for knowledge exchange travels faster and more effectively over geographically proximate distances. However, with the emergence of the knowledge economy, MNEs have not only organized their inventive activities where they may benefit from localization externalities, they have also reconfigured their international connections (Mudambi, 2008; Lorenzen et al., 2020), relying especially on external sources of knowledge to complement internal research beyond geographically bounded contexts.

To be sure, a stream of literature in economic geography has focused on the kinds of technological knowledge transmitted within a city-region (Florida, 2005; Bathelt & Glückler, 2011, 2017), relating to earlier writings which have found that information is more readily transmitted via face-to-face interactions, such that any actor who participates in that region's economic sphere may benefit from its local 'buzz' (Bathelt et al. 2004; Stroper & Venables, 2004). For example, university science generated by researchers in a particular region are surrounded by a plethora of knowledge received by a mutual understanding of new research and applications within the constraints of some established institutional arrangement. Sourcing such knowledge from abroad therefore entails higher transaction costs. For this reason, MNEs which source external knowledge from abroad have a clear understanding of how this new knowledge is relevant and can be recombined.

We therefore ask – given that MNEs may rely on external sources of knowledge to complement internal research which may be located elsewhere in the world, in other cities within their home country or other countries, and given that those sources of knowledge are embedded in specific regions – to what extend does the geographic overlap of knowledge sources of firm pairs influence the reciprocal exchange of knowledge between them?

Put differently, an increased reliance on knowledge sources from geographic areas a competitor is sourcing knowledge from might increase the reciprocity between MNEs, due to a shared experience in establishing networked connections from a similar location profile, and as each firm attains a greater absorptive capacity to assimilate the new technologies sourced into their own learning processes. Merely the sourcing of, for example, the best university science-based knowledge or clinical applications from the same city-region generates various opportunities for communication, to establish network ties and increase awareness of how the more tacit and complex aspects of technical knowledge developed by external sources may be relevant to the dominant technologies of the respective firm. We therefore expect that the reciprocal exchange of knowledge between MNEs may be driven by sourcing knowledge from a similar geographic profile, i.e. when each pair of firms source external knowledge from the same city-region, which may require flexible modes of cooperation so as to combine relevant pieces of knowledge that go beyond the formal governing structures and ongoing contractual relationships during exploratory stages or the simple market exchange of codified or tangible and already-established products (see Dunning 1995 on the variety of forms of network relationships and network-related advantages of MNEs). This line of reasoning leads us to the following hypothesis:

Hypothesis 2: There is a positive relationship between the geographic overlaps of external knowledge sources and the reciprocal exchange of knowledge between MNEs.

METHODS

The empirical setting and organization of the data

The international pharmaceutical industry has a number of features that make it appropriate for our study and was selected to be the focus of our analysis. First, since around 1980, there has been a rapid growth in the number of technology-based inter-firm relationships. Second, the industry has become more networked in recent years, relying on complementary areas of external knowledge (Edris, 2019) developed by other types of organizations (e.g. universities, research institutes, and hospitals). Third, the pharmaceutical industry is the leading industry where the 'market for technology' has rapidly grown (Arora et al., 2001).

We make use of USPTO patents to examine the degree to which the location profile of inventive activity and geographic overlaps of external knowledge sources of MNEs in the pharmaceutical industry regulate knowledge reciprocity with other firms in the industry. A patent is a detailed document and a set of exclusionary rights granted by a government agency to an inventor, who then assigns the patent to an organization at the time of grant. That assignee can be identified with an ultimate owner, such as the corporate groups we consolidated or the universities and hospitals we coded. Patents also include references to previous patents. Prior work has found that these references provide a suitable proxy for knowledge building structures (Frost, 2001; Almeida 1996; Jaffe et al. 1993, 2002), i.e. the connection between an earlier cited patent and a subsequent citing patent represents a recognition of knowledge relevancy (inserted by patent applicants and patent examiners), or a step in a knowledge building process. In this way, our analytical scheme is properly grounded upon a conceptualization of technological accumulation over time (Cantwell, 1989), focusing specifically on citation ties between corporate groups as a whole, and with other organizations, across city-regions.

To construct our sample, we identified and consolidated 45 major corporate groups engaged in US patenting in the pharmaceutical field and examined the ownership structure of each of these groups using D&B Who Owns Whom directories. We then extracted from the USPTO websites all patents granted to the 45 groups identified from 1976 to 2016, which includes patents from their worldwide facilities, and all earlier patents which were cited by these. The cited organizations include universities, research institutes, and hospitals or health care providers. The patent records included the ultimate ownership (the affiliation of the assignee), the address of the inventors, as well as the year in which the patent was granted and the technological field of activity.

To test our first hypothesis, which examines the locational distribution of firm pairs, we recorded the home or headquartered country of each firm as well as the host country of their subsidiaries. Home country is defined as the country for which the cited foreign subunit’s parent company is located. Host country is defined as the country for which the cited foreign subunit is located. To test our second hypothesis, we consolidated the location of inventors of the university/research institute and hospital patents which were cited by our 45 MNEs at the level of city-regions to account for the fact that the inventor can live anywhere that is drivable distance to the central city. City-regions are defined as subdivisions of countries developed and regulated by their national governments for statistical purposes. Using google maps, we assigned cities, towns, and neighborhoods to these coded areas. For example, for each EU member country, we coded regions defined by the Nomenclature of Territorial Units for Statistics (NUTS), established by Eurostat at level 2; we marked the boundaries of city-regions in Switzerland as defined by the Swiss Federal Statistical Office; consolidated areas in Japan as defined by the Statistics of Bureau of Japan; in the US as defined by the US Census Bureau; and so on.

We also made use of the distance calculations developed by Berry et al. (2010), which have been updated in 2017 and are made freely available on the author's website, to control for cross-national differences, i.e. economic, political, administrative, demographic, and geographic distances between the headquartered countries of firm pairs.

The model and variables

The statistical analysis is conducted at the level of the pairwise combinations of 45 MNEs ($_{45}C_2$ = 45!/2!(45-2)! = 45!/2!43! = 990 possible combinations) between 1976 and 2016 (broken into 5-year intervals). To test our hypotheses, we constructed the dependent variable *Reciprocation* as an indicator of the reciprocal exchange of knowledge between two firms. To calculate this variable, we draw on the measure of intra-industry trade across sectors used in the international trade literature (Grubel and Lloyd, 1975) using the sum of cites of each firm to every other firm as follows: Reciprocation = (2 (Min | A, B |)) / (A+B), *where* A is the number of times Firm A cites Firm B, and B is the number of time Firm B cites Firm A. This measure varies between 0 and 1, rising with the extent of inter-firm knowledge reciprocity. The model to be tested is the following: $\text{Reciprocation}_{ip}$ = f(Co-location_{ipc}; Geographic overlaps of scientific sourcing_{ipr}; Geographic overlaps of clinical

$sourcing_{ipr}$; controls), *where:* i = firm pairs, p = time periods, r = city-regions, and c = countries.

To test hypothesis 1, we constructed the variable *Co-location* using the distribution of MNE inventions (USPTO patents) across countries. We calculated the degree to which the geographic profile of each combination of firms are correlated. To test hypothesis 2, we constructed two variables, *Geographic overlaps of scientific sourcing* and the *Geographic overlaps of clinical sourcing*. In the context of the pharmaceutical industry, research conducted in universities and research institutes has been particularly useful for guiding the search for innovation (Fleming & Sorenson, 2004). We also follow prior research in distinguishing between basic science and clinical applications (Hicks and Katz, 1996; Bignami et al., 2019), since hospitals use research results to identify biomedical technical opportunities in improving existing treatments, and so it's important to consider them separately. To calculate *Geographic overlaps of university sourcing,* we used the sum of cites to universities and research institutes to examine the distribution of citations to basic science across city-regions. We calculated the degree to which the geography of MNE sourcing of university/RI knowledge across city-regions are correlated. Similarly, we calculated *Geographic overlaps of clinical sourcing* by using the sum of cites to hospitals, which might refer to clinical trials and more applied research compared to the knowledge sourced from universities and research institutes, to examine the distribution of citations to clinical applications across city-regions. We calculated the degree to which the geography of MNE sourcing of hospital knowledge across city-regions are correlated.

To be sure, a high degree of technological co-specialization between the profiles of inventive activities of firms might deter them from one another, since the potential gains of reciprocating their respective technological efforts might seem too similar or redundant, such that the likelihood of reciprocation decreases. So while an increase in technological complementarity at some broad level might suggest a stronger motivation for accessing and benefiting from a combination of their respective capabilities (Cantwell and Colombo, 2000), an increase in technological co-specialization of firms at a more highly detailed level of disaggregation may be associated with a decrease in reciprocation, i.e. so the extent of organizational learning involved in attempting to combine activities falls since the activities become more obviously similar to one another, and hence there is likely to a shift away from knowledge exchange of redundant knowledge. For this reason, we controlled for the extent of *co-specialization*. We first constructed a measure of firm specialization, i.e. a Revealed Technological Advantage (RTA) index equal to, or greater than 1 in a field. An RTA index allows us to control for inter-field and inter-firm differences in the propensity to patent (Cantwell, 1989), defined as follows: RTA = $(P_{ij} / \sum_i P_{wj}) / (\sum_j P_{ij} / \sum_{ij} P_{wj})$, where P_{ij} is the number of patents in technological field j (1,…,12) by a parent firm i, and P_{wj} is the number of all patents in the same sector by all firms. Since all of our firms are in the pharmaceutical industry, we chose 12 fields or classes to be able to differentiate between our set of firms, i.e. with a roughly equal number of total patents in each of the categories chosen. We subdivided the pharmaceutical field into the 6 classes defined by the USPTO classification system, and broadly organized 6 technological fields in common groupings as defined by Cantwell et al. (2004). These are chemical, electrical, mechanical, transport, ICT, and ‘other’ technologies, which include classes or fields with low number of patents. We then calculated the degree to which the technological specialization (RTAs) of each combination of MNEs are correlated.

Finally, we included several controls related to cross national differences between the headquartered countries of MNEs, using distance calculations developed by Berry et al. (2010), which have been updated in 2017 and made available on the author's website. The variable *economic distance* controls for home country differences in economic development and macroeconomic characteristics, e.g. income, inflation, exports, imports. The variable *political distance* controls for home country differences in policy-making uncertainty, democratic character, size of the state, WTO membership, and regional trade agreements. The variable *administrative distance* controls for home country differences in ties, language, religion, and legal systems. The variable *demographic distance* controls for home country differences in demographic characteristics, e.g. age, birth rate, and life expectancy. The variable *geographic distance* controls for home county distance between the geographic center of each country. We also included a dummy variable to capture additional variation due to home country differences, i.e. we coded the variable 1 if home countries are different and 0 if home countries are the same.

Table 1 includes descriptive statistics about the MNEs in our sample. Figure 1 depicts the average degree to which countries host the same MNE inventive activities as other countries, whereas Figure 2 depict the average degree to which countries attract university and hospital knowledge sourcing activities by the same MNEs as other countries, essentially showing that countries which attract the same firms to locate there aren't necessarily attracting them for the university or hospital knowledge. Firms that collocate in a particular country aren't necessarily sourcing scientific knowledge from the same geographic profile. Table 2 summarizes the variables used in the analysis.

Insert table 7.1 here

Insert table 7.2 here

Insert figure 7.1 here

Insert figure 7.2 here

RESULTS

Table 3 provides descriptive statistics and Table 4 provides a correlation matrix of the variables. Results are reported in Table 5. Numbers in parentheses represent standard errors. Interpretation of the regression coefficient follows a normal pattern: positive, significant values indicate that an increase in that variable increases the reciprocal exchange of knowledge between MNEs, *ceteris paribus*. The results confirm that the reciprocal exchange of knowledge between leading MNEs in the pharmaceutical industry is influenced by the degree to which these firms co-locate their technological activities as well as the degree to which the geographic profile of their knowledge sources of basic science and clinical applications overlap. While the overall relationship between co-location and reciprocation is negative, closer analysis reveals an inverted U-shaped relationship, as can be seen in model 2. We essentially show that firms at a certain geographic distance are more likely to exchange knowledge in order to access complementary areas of specialization that they lack, i.e. at a certain distance, but not too far away, as that would lead to a lack of connection between profiles. This relationship is depicted in figure 3.

Insert table 7.3 here

Insert table 7.4 here

Insert table 7.5 here

Insert figure 7.3 here

As expected, we find that firms that have a similar profile of technological specialization is most similar reciprocate less, since the knowledge searched and exchanged won't contain information the firm might not already have. Though we do have reason to believe that firms that are co-specialized may be sourcing knowledge from external parties from the same place or region as their competitors. At early stages of exploratory research, these firms may be willing to exchange complementary areas of expertise which may be of relevance from the same geographic area as where their competitors are sourcing, since as is well known, external knowledge travels faster and more effectively over geographically proximate distances, and the speed and effectiveness of knowledge transfer falls as geographic distance rises. These types of exchanges might also require a steadily less formalized organizational means of cooperation, since the degree of organizational difficulty involved in coordinating activities tends to fall, particularly if the need for organizational commitment declines (Cantwell and Colombo, 2000). Indeed, our findings bear further testament to the role played by the geographic distribution of external sources of knowledge on inter-MNE knowledge sharing.

The positive and significant signs for the geographic overlap of sourcing scientific knowledge suggest that firms that draw university/RI knowledge, which involve the discovery of mechanisms and processes that underlie specific diseases, from a similar profile of city-regions increases their reciprocal exchange of knowledge. This finding is in line with prior research which has documented the degree of industry reliance on academic research contributions, the growing significance of basic science within technological knowledge, rising technological relatedness, and rising costs of internal R&D. We contribute to this work by examining the geography of university/RI sourcing on inter-

MNE knowledge exchange. Moreover, prior work has treated hospitals as part of universities, and so little is known about connections to clinical or medical practices, or indeed how these linkages impact the reciprocal exchange of knowledge of MNEs. The positive and significant signs for the geographic overlap of sourcing clinical knowledge does suggest that firms that draw hospital knowledge, which involve development processes and applied technical opportunities in improving existing treatments, from a similar profile of city-regions are more prone to exchange knowledge – however the effect size is actually quite small relative to university sourcing. This may be due to the fact that sourcing hospital knowledge isn't necessarily bound to the local context, given the codifiable nature of clinical science, since development processes which are thoroughly documented and heavily regulated (Bignami *et al.* 2019). Finally, we find that reciprocation of knowledge decreases in distance.

DISCUSSION AND CONCLUSIONS

The reciprocal exchange of knowledge is critical, not only because of the increased internal and external complexity of technology, but also because it allows MNEs to access wider networks for innovation. We investigate how a shared geography of inventive activity may increase the awareness of how new technological capabilities or knowledge ties may be relevant to subsequent developments. Moreover, while attention has been increasingly focused on the complementarity between internal and external knowledge sourcing (Phene and Almeida, 2008; Rosenkopf and Padula, 2008; Hagedoorn and Wang, 2012; Monteiro and Birkinshaw, 2017), these sources of knowledge are characterized by the regions they are a part. And so we've argued that inter-MNE reciprocity may be partially determined by the geographic profile of external networks.

In this study, we have examined the reciprocal exchange of knowledge between the leading MNEs in the international pharmaceutical industry. We looked at the impact on reciprocation of co-locating inventive activities, as revealed by their corporate patenting, and the geographic overlaps of external sourcing. Our findings show that MNEs exhibit a preference for exchanging knowledge with firms at a certain geographic distance to access complementary areas of specialization that they lack. The significant impact of the geographic overlap of external sourcing in explaining inter-MNE knowledge reciprocity highlights the role that such interdependencies play in explaining knowledge sharing between MNEs, i.e. firms that are co-specialized are likely to source scientific knowledge from the same geographic areas, and benefit from a similar profile of knowledge ties. Indeed we have found that firms sourcing knowledge from universities and research institutes from the same region reciprocate more. We also find evidence that these firms rely on a similar profile of sourcing hospital knowledge. In our judgement, our findings add important new insights to the existing literature on location choice, geography of sourcing, and inter-firm knowledge exchange, and the ways in which the direction of the firm's growth is fundamental for understanding the process by which MNEs develop ties with competitors.

Our paper makes several contributions to the literature in international business, regional science, and innovation studies. While prior research has viewed the MNE as a whole and its developments in relation to the developments of its foreign subunits, we adopt the view of the MNE as a portfolio of diverse locations (Johanson & Vahlne, 1977; Chang, 1995, 1996; Cantwell, 2005; Barkema & Drogendijk, 2007), which shapes the firms experience and technological capacity (Cohen and Levinthal, 1990; Belderbos & Zou, 2009), and the extent of inter-MNE reciprocity. Insight into the geographic distribution of knowledge sources that complement internal research is of critical importance for the understanding the potential for knowledge exchange. An important contribution of our study therefore lies in our ability to examine both, the *geographic profile of innovations* and the *geographic overlaps of external knowledge sources* of firm pairs.

A notable methodological contribution of our study is the development of measures of location portfolios and geographic overlaps of knowledge sourcing. These measures advance the ability to relate an MNE's inventive activity and search efforts to its exchanges of knowledge with competitors beyond what has been common in the literature thus far. Because of the richness of the data used to conduct the analysis, we were able to detect interfirm reciprocity. The empirical analysis here spanned firm, organizational (e.g. scientific institutes and hospitals), and geographic levels (e.g. countries and city regions), not merely the focal actor(s) within specific organizations. The first step is to examine firm innovation and the geography of their sourcing patterns. Thus, we pay attention to the evolving structures of firm, organizational, geographic, and technological field knowledge development over time to address the gap in our understanding of inter-firm knowledge exchange. We link characteristics of firm-pairs and firm-sourcing patterns in relational terms, identifying as well the universities, research institutes, hospitals and healthcare facilities from which our firms source their knowledge, as well as coding city-regions on their patent documents.

Given that knowledge sharing may be strongly supported by geographic profiles of inventive activities and external sources of science-technology spillovers, it may be useful to explore in future research the way in which MNEs cooperate to access new knowledge originated in geographically distant locations, and how this may offset intra-MNE transmission channels. Economic geographers are also very well positioned to consider the type of knowledge ties established with universities and hospitals in specific regions, and for which technological purpose, explorative or exploitative search efforts. The development of cross-border corporate integration and intraborder makes it increasingly important to examine the origin of sites of inventions and regionally concentrated sources of knowledge (Cantwell and Piscitello, 2002), as well as the degree to which different types of geographic portfolios of MNEs regulate the reciprocal exchange of knowledge between them.

CHAPTER EIGHT: CONCLUSION

In this dissertation, we sought to provide an explanation of the latest direction in the evolution of the international firm (which might be perhaps deliberately designated as encompassing the evolution of MNE international business networks, and not just confined to intra-MNE activity as such). In doing so, we make several specific contributions that distinguish our work from prior research.

In our first study (chapter 5), we contribute to the discussion on foreign subunit's desire to gain knowledge from diverse sources, which may include other subunits within the corporate group, other firms within the same or other industries, universities and hospitals. We adopt a perspective of networks within and between firms, and other organizations (Kuhn, 1962; Guler and Nerkar, 2012), that generate outcomes that result in inventions. Our motivation for adopting a networked approach is our interest in studying the wider system among actors or overall structure of the knowledge network as opposed to the more atomistic or reductionist perspective adopted in the strategy literature. We discuss the organizational affiliations and differentiated networks within which foreign-located subunits source knowledge to develop innovative activity. One key contribution of our first study is therefore to ask through which organizational link do CC and CE subunit's innovations rely in their knowledge sourcing strategies in an international business context.

Our second study (chapter 6) offers a neglected way to examine competence creating activities of contemporary, geographically dispersed MNEs, by disaggregating the activities of all its subunits, and examining the extent of intra-MNE diffusion of competence creating types of inventions to the home country and within host country settings. We complement prior literature which has suggested that novel innovations in overseas subunits benefit from greater autonomy (Andersson et al., 2007; Ambos *et al.*, 2011; Beugelsdijk and Jindra 2018). We also emphasize that embeddedness of exchange within knowledge networks across organizational and geographic space provide opportunities and constraints that may affect subsequent use of new applications.

An important contribution of our third study (chapter 7) lies in our ability to examine both, the geographic profile of innovations and the geographic overlaps of external knowledge sources of firm pairs. While prior research has viewed the MNE as a whole and its developments in relation to the developments of its foreign subunits, we adopt the view of the MNE as a portfolio of diverse locations (Johanson and Vahlne, 1977; Chang, 1995, 1996; Cantwell, 2005; Barkema and Drogendijk, 2007), which shapes the firms experience and technological capacity (Cohen and Levinthal, 1990; Belderbos and Zou, 2009), and the extent of inter-MNE reciprocity. Insight into the geographic distribution of knowledge sources that complement internal research is of critical importance for the understanding the potential for knowledge exchange. A notable methodological contribution of this study is the development of measures of location portfolios and geographic overlaps of knowledge sourcing. These measures advance the ability to relate an MNE's inventive activity and search efforts to its exchanges of knowledge with competitors beyond what has been common in the literature thus far.

Finally, because of the richness of the data used in the dissertation, our analyses spanned firm, organizational (e.g. scientific institutes and hospitals), and geographic levels (e.g. countries and city regions), not merely the focal actor(s) within specific organizations. The first step is to examine firm innovation, the geography of their sourcing patterns, and technological field knowledge development dating back to the mid-1970s. Key factors that emerged include the characteristics of the MNEs knowledge networks and innovative efforts that suggested a logic of competence-creating or competence-exploiting; the subsequent use of CC components by other subunits and/or MNEs in the industry; and the geographic dimension of the reciprocal exchange of knowledge. We also propose a revised interpretation of citation-based networks at the organizational and geographic level, in which technological knowledge is understood as being cumulatively developed (Cantwell, 1989); new technologies rely on novel combinations of prior knowledge (Arthur, 2009). This knowledge is either derived locally or globally, depending on the conditions under which technological knowledge is sourced (Frost, 2001). Thus, we pay attention to the evolving structures of geographic, organizational, and cross-technological field knowledge development over time to address the remaining gap in our understanding of the performance of MNEs.

Exploring the effects of the interaction between firms themselves from the effects due to the activities of non-firm actors (e.g. universities, hospitals, or governments) or changes in institutions on the evolution of the international organizations in a wider system holds promise in future research.

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TABLES

Table 3.1. Major developments in the history of the pharmaceutical industry

	Paradigm 1 (1850-1939)	*Paradigm 2 (1940-1989)*	*Paradigm 3 (1990-date)*
Science	▪ Chemistry	▪ Pharmacology ▪ Physiology ▪ Enzymology ▪ Microbiology	▪ Molecular biology ▪ Genetics
Technology	▪ Chemical synthesis ▪ Fermentation	▪ Transition from phenotypic to target-based discovery	▪ Combinatorial chemistry and computational tools
Business organization	▪ Hierarchical organizations/ functional specialization ▪ Scale and scope/vertical integration ▪ International expansion	▪ Managerial structure organizations ▪ In-House R&D ▪ Fully integrated ▪ Diversification via mergers	▪ Network organizations ▪ Equity/Research contracts; JVs; Licensing ▪ Divestures; Mergers/Acquisitions
Institutional environment	▪ Germany / Switzerland: Strong university training in chemistry ▪ No connections with science ▪ Food and Drug Act	▪ Diamond vs Chakrabarty Supreme Court patent decision ▪ Bay-Dohle Act, and similar national policies ▪ Orphan Drug Act ▪ Loose connections with science	▪ US: Venture capital; Entrepreneurial interest of Professors ▪ Scientific maps ▪ Worldwide: intimate connections with science
Political and economic trends	▪ International networks (including cartels) ▪ New transport/ communication technologies ▪ Energy intensity (oil based)	▪ Centralization/ metropolitan centers ▪ Nationalistic policies, world agreements and confrontation ▪ Wartime investments ▪ Crisis in the chemical industry	▪ Global and local connectivity ▪ Information intensity (ICT) ▪ External vs Internal cooperation (clusters)

Table 4.1. Listing of Major Companies

Company	Nationality	Current Product Lines	Date of Foundation
Abbvie	US	Pharmaceuticals and Biologics	2013
Abbott Labs	US	Pharmaceuticals, Diagnostics, Medical Devices	1888
Bristol Myers Squibb	US	Pharmaceuticals and Biologics	1887, merged with Squibb in 1989
Eli Lilly	US	Pharmaceuticals	1876
Johnson & Johnson	US	Pharmaceuticals, Medical Devices, Consumer Health,	1886
Merck & Co.	US	Pharmaceuticals	1891 as subsidiary of Merck; 1917 as independent
Pfizer	US	Pharmaceuticals	1849
Valeant Pharmaceuticals	CA	Pharmaceuticals	1859
AstraZeneca	UK	Pharmaceuticals and Biologics	1999 by merger of Astra & Zeneca
GlaxoSmithKline	UK	Pharmaceuticals, Vaccines, Healthcare	2000 by merger of Glaxo & SmithKline
Allergan	IE	Pharmaceuticals	2013
Sanofi Aventis	FR	Pharmaceuticals and Biologics	2004 by merger of Sanofi & Aventis
Bayer	DE	Pharmaceuticals, Diagnostics, Women Health, Plant Biotechnology	1863
Merck Group	DE	Biologics	1668
Hoffman-La Roche	CH	Pharmaceuticals, Diagnostics	1896
Novartis	CH	Pharmaceuticals, Consumer Health, Animal Health	1996 by merger of Ciba-Geigy & Sandoz
Novo Nordisk	DK	Pharmaceuticals	1923
Teva Pharmaceuticals	IL	Pharmaceuticals	1901
Astellas Pharma	JP	Pharmaceuticals	2005 by merger of Yamanouchi & Fujisawa

Daiichi Sankyo Co. Ltd	JP	Pharmaceuticals, Medical Equipment	2005 by merger of Daiichi & Sankyo
Ono Pharmaceuticals	JP	Pharmaceuticals, Diagnostics	1717
Otsuka Pharmaceuticals	JP	Pharmaceuticals	1964
Shionogi	JP	Pharmaceuticals, Diagnostics, Medical Devices	1878
Takeda Chemical Industries	JP	Pharmaceuticals	1781
Amgen	US	Biologics	1980
Biogen	US	Biologics	1978, by merger
Celgene	US	Biologics	1986, spinoff of Celanese
Gilead Sciences	US	Biologics	1987
Immunomedics	US	Biologics	1982
Incyte Pharmaceuticals	US	Biologics	1991
Ionis Pharmaceuticals	US	Biologics	1989
Regeneron Pharmaceuticals	US	Biologics	1988
Rigel Pharmaceuticals	US	Biologics	1996
Vertex Pharmaceuticals	US	Biologics	1989
Colgate Palmolive	US	Household and personal, healthcare supplies	1806
Dow Chemical	US	Chemicals, Plastics, Paints, Agrochemicals, Gas and Oil	1897
Du Pont	US	Chemicals, Plastics, Paints, Agrochemicals, Gas and Oil	1802
Monsanto	US	Agrochemicals	1901 until 2018, acquired by Bayer
Procter & Gamble	US	Personal health/consumer care	1837
Reckitt Benckiser	UK	Household and personal care, healthcare, pharmaceuticals	1999, merger of Reckitt & Colman and Benckiser
Syngenta	CH	Agrochemicals	2000

BASF	DE	Chemicals, Plastics, Paints, Agrochemicals, Gas and Oil	1865
Novozymes	DK	Biologics	2000
AkzoNobel	NL	Chemicals, paints	1994, merger of Akzo and Nobel
Mitsubishi Chemical Holdings	JP	Chemicals	2005, merger of Mitsubishi Chemical and Mitsubishi Pharma

Source: authors' own analysis.

Table 5.1. Listing of MNEs in the sample

Company	Nationality
Abbott	US
Abbvie	US
Amgen	US
Biogen	US
Bristol-Myers-Squibb	US
Celgene	US
Eli Lilly	US
Gilead	US
Immunomedics	US
Incyte	US
Ionis	US
Johnson & Johnson	US
Merck & Co.	US
Monsanto	US
Pfizer	US
Promega	US
Regeneron	US
Rigel	US
Vertex	US
Sterling Drug	US
Valeant	CA
AstraZeneca	GB
GlaxoSmithKline	GB
Reckitt	GB
Allergan	IE
Perrigo	IE
Sanofi	FR
Novartis	CH
Roche	CH
Syngenta	CH
Bayer	DE
Boehringer	DE
EMerck	DE
Gruenenthal	DE
Novo Nordisk	DK
Novozymes	DK
Akzo	NL
Astellas	JP
Eisai	JP
Ono	JP
Otsuka	JP
Sankyo	JP
Shionogi	JP
Takeda	JP
Teva	IL

Table 5.2a. Sample of foreign-located subunits

Period	*Total Patents*	*Share of CC Patents*	*Total Subunits*	*Total MNE*	*Subunit/ MNE*	*Subunits with CC Patents/ MNE*	*Patents/ Subunit*	*Host Countries*
1976 to 1980	7,510	0.10	178	26	6.85	2.85	42.19	39
1981 to 1985	5,723	0.10	153	28	5.46	1.96	37.41	31
1986 to 1990	7,676	0.14	194	30	6.47	2.63	39.57	36
1991 to 1995	9,863	0.13	272	33	8.24	3.12	36.26	36
1996 to 2000	14,117	0.09	370	44	8.41	2.57	38.15	48
2001 to 2005	9,975	0.23	355	38	9.34	3.39	28.10	48
2006 to 2010	9,678	0.29	346	39	8.87	3.15	27.97	45
2011 to 2015	15,656	0.20	453	43	10.53	2.70	34.56	46

Table 5.2b. Number of foreign-located subunits with CC activity

Period	*Distribution of CC patents over time of subunits*					*Total subunits*
	0-20%	20-40%	40-60%	60-80%	80-100%	
1976 to 1980	17	7	7	4	39	74
1981 to 1985	17	9	3	2	24	55
1986 to 1990	20	8	6	5	40	79
1991 to 1995	18	21	17	8	39	103
1996 to 2000	43	24	4	3	39	113
2001 to 2005	29	23	8	7	62	129
2006 to 2010	24	13	9	8	69	123
2011 to 2015	20	21	11	24	40	116

Table 5.3. Names and definitions of variables

Variable	Operational definition
Dependent variable	
International	Share of international cites (USPTO patent references)
Independent variables	
Intra-MNE	Share of cites to other subunits within the MNE (USPTO patent references)
Biotech	Share of cites to biotech firms (USPTO patent references)
Inter-Industry	Share of cites to firms in all other industries (USPTO patent references)
University	Share of cites to universities (USPTO patent references)
Hospital	Share of cites to hospitals (USPTO patent references)
Knowledge portfolio	Number of organizational ties (USPTO patent references)
Centrality	Eigencentrality
Economic distance	Home-Host country differences in economic development and macroeconomic characteristics, e.g. income, inflation, exports, imports (Berry website)
Political distance	Home-Host country differences in policy-making uncertainty, democratic character, size of the state, WTO membership, regional trade agreements (Berry website)
Geographic distance	Great circle distance between geographic center of home and host countries (Berry website)

Table 5.4a. Descriptive statistics

Variable	Observations	Mean	Std. Dev.	Min	Max
CE					
International	1,641	0.820	0.253	0	1
Intra-MNE	1,641	0.273	0.276	0	1
Biotech firms	1,641	0.037	0.118	0	1
Inter-industry	1,641	0.132	0.212	0	1
Universities	1,641	0.067	0.131	0	1
Hospitals	1,641	0.006	0.036	0	1
Know. port.	1,641	5.121	2.663	1	10
Centrality	1,974	.009	0.072	0	1
Econ. dist.	4,036	4.393	7.407	0.006	64.756
Pol. dist.	4,089	6.069	6.746	0.041	92.665
Geo. dist.	4,208	6,593.148	4,312.651	279.353	19,187.26
CC					
International	648	0.776	0.299	0	1
Intra-MNE	648	0.219	0.279	0	1
Biotech firms	648	0.014	0.061	0	1
Inter-industry	648	0.290	0.312	0	1
Universities	648	0.055	0.145	0	1
Hospitals	648	0.004	0.033	0	.667
Know. port.	648	4.340	2.590	1	10
Centrality	922	0.012	0.093	0	1
Econ. dist.	2,119	3.982	6.995	0	64.756
Pol. dist.	2,157	5.941	7.010	0	78.072
Geo. dist.	2,192	5,995.484	4,415.307	0	19,187.26

Table 5.4b. Descriptive statistics

Variable	1	2	3	4	5	6	7	8	9	10	11
CE											
1 International	1.000										
2 Intra-MNE	-0.133	1.000									
3 Biotech firms	0.022	0.062	1.000								
4 Inter-industry	0.022	-0.240	-0.118	1.000							
5 Universities	0.086	-0.207	0.061	-0.080	1.000						
6 Hospitals	0.023	-0.076	0.008	-0.025	0.035	1.000					
7 Know. port.	-0.307	-0.044	0.052	0.033	0.067	0.055	1.000				
8 Centrality	-0.207	0.031	-0.018	0.027	-0.021	-0.005	0.225	1.000			
9 Econ. dist.	0.164	0.001	0.033	0.029	-0.006	-0.001	-0.133	-0.241	1.000		
10 Pol. dist.	0.090	-0.072	0.014	-0.005	0.057	0.020	-0.031	-0.027	0.243	1.000	
11 Geo. dist.	-0.005	-0.015	0.086	0.038	0.087	-0.004	-0.087	-0.040	0.156	0.197	1.000
CC											
1 International	1.000										
2 Intra-MNE	-0.242	1.000									
3 Biotech firms	0.022	-0.023	1.000								
4 Inter-industry	0.011	-0.401	-0.106	1.000							
5 Universities	0.012	-0.153	0.008	-0.096	1.000						
6 Hospitals	0.005	0.007	-0.001	-0.060	0.004	1.000					
7 Know. portf.	-0.247	0.031	0.155	-0.144	0.038	0.057	1.000				
8 Centrality	-0.145	0.062	0.026	-0.032	-0.008	-0.003	0.210	1.000			
9 Econ. dist.	0.153	-0.037	0.056	-0.021	-0.011	-0.009	-0.069	-0.039	1.000		
10 Pol. dist.	0.060	-0.074	0.070	0.063	0.117	-0.016	0.011	-0.037	0.356	1.000	
11 Geo. dist.	-0.106	-0.029	0.062	0.061	0.064	0.033	-0.008	-0.031	0.144	0.179	1.000

Table 5.5 Results of regressions on international knowledge sourcing by foreign subunit's innovation, 1976-2015

	DV: International sourcing	
	Foreign subunit's CE innovations **(1)**	Foreign subunit's CC innovations **(2)**
Intra-MNE	–0.111***	–0.305***
	(0.023)	(0.045)
Biotechnology firms	0.091*	0.197
	(0.054)	(0.184)
Inter-industry	0.022	–0.121***
	(0.030)	(0.040)
Universities	0.153***	–0.060
	(0.047)	(0.081)
Hospitals	0.174	0.172
	(0.164)	(0.346)
Knowledge portfolio	–0.027***	–0.028***
	(0.002)	(0.005)
Centrality	–0.425***	–0.213**
	(0.075)	(0.101)
Economic distance	0.006***	0.007***
	(0.001)	(0.002)
Political distance	0.002**	0.001
	(0.001)	(0.002)
Geographic distance	–4.67e-06***	–9.48e–06***
	(1.51e–06)	(2.68e–06)
Constant	0.963***	1.013***
	(0.020)	(0.035)
R^2	0.164	0.173
Adj R^2	0.158	0.159
Prob > F	0.000	0.000
N	1,512	605

Standard errors in parentheses

Table 6.1. Sample of MNEs and foreign located subunits

Period	*Total MNEs*	*Total Subunits*	*Total Subunits/ MNE*	*Total Subunits with CC patents*	*Subunits with CC Patents/ MNE*	*Host Countries*
1976 to 1980	26	178	6.85	74	2.85	39
1981 to 1985	28	153	5.46	55	1.96	31
1986 to 1990	30	194	6.47	79	2.63	36
1991 to 1995	33	272	8.24	103	3.12	36
1996 to 2000	44	370	8.41	113	2.57	48
2001 to 2005	38	355	9.34	129	3.39	48
2006 to 2010	39	346	8.87	123	3.15	45

Table 6.2. Names and definitions of variables

Variable	Operational definition
Dependent variables	
Home diffusion	Number of times a CC patent gets cited in subsequent periods, where the citing patent is developed by the parent company
Host diffusion	Number of times a CC patent gets cited in subsequent periods, where the citing patent is developed by a subunit in the host country
Independent variables	
Reciprocation	Number of times focal subunit's CC inventions cite the parent firm
Relatedness	Number of times focal subunit's CC inventions were cited by the parent firm, where the citing and cited were in the same technological field.
CC share	Focal subunit's share of CC patents
Centrality	Eigenvector scores of focal subunit's CC inventions in the overall knowledge network
Diversity of ties	Focal subunit's total number of types of organizational ties (1,…,10)
Size	Focal subunit's total number patents
Patent field	Dummy variable, 1 if in the CC patent is in the pharmaceutical field, 0 otherwise
Recency	Number of cites focal subunit receives by CC patents ten years after grant
Patent age	Number of periods since grant
Economic dist	Home-Host country differences in economic development and macroeconomic characteristics, e.g. income, inflation, exports, imports (Berry, 2017)
Political dist	Home-Host country differences in policy-making uncertainty, democratic character, size of the state, WTO membership, regional trade agreements (Berry, 2017)
Geographic dist	Great circle distance between geographic center of home and host countries (Berry, 2017)

Table 6.3. Descriptive statistics

Variable	Observations	Mean	Std. Dev.	Min	Max
Home diffusion	30,619	0.033	0.507	0	48
Host diffusion	30,619	0.369	1.721	0	41
Reciprocation	30,619	0.079	0.611	0	28
Relatedness	30,619	4.225	7.901	0	39
CC share	30,619	0.552	0.367	0.003	1
Centrality	29,536	0.280	0.438	0	1
Diversity of ties	29,253	7.048	2.359	1	10
Size	30,619	435.492	490.05	1	1610
Patent field	30,619	0.236	0.425	0	1610
Recency	28,660	89.092	124.148	1	561
Patent age	30,619	2.605	1.616	1	7
Economic dist	28,841	1.674	2.134	0.006	62.604
Political dist	29,506	29,506	3.974	0.049	49.682
Geographic dist	29,945	29,945	3,748.513	279.353	18,737.04

Table 6.4. Correlation matrix

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1 Home diff.	1.000													
2 Host diff.	0.036	1.000												
3 Recip.	0.080	-0.007	1.000											
4 Related.	0.033	0.012	0.117	1.000										
5 Centrality	-0.037	-0.015	-0.055	0.187	1.000									
6 Diversity	-0.024	0.141	-0.004	0.417	0.194	1.000								
7 CC share	0.026	0.012	0.066	0.402	-0.024	0.043	1.000							
8 Size	-0.047	-0.002	-0.070	0.057	0.707	0.302	-0.491	1.000						
9 Patent field	0.019	0.036	0.026	0.403	0.028	0.149	0.589	-0.225	1.000					
10 Recency	-0.021	0.133	-0.025	0.525	0.542	0.538	0.296	0.329	0.263	1.000				
11 Patent age	-0.022	-0.102	-0.016	-0.118	-0.007	-0.399	-0.111	-0.052	-0.083	-0.242	1.000			
12 Econ dist	0.019	0.122	0.030	0.130	-0.119	0.289	0.251	-0.106	0.239	0.302	-0.290	1.000		
13 Pol dist	0.001	0.117	0.021	0.153	-0.028	0.390	0.281	-0.050	0.199	0.355	-0.383	0.521	1.000	
14 Geo dist	0.020	0.086	0.030	0.159	-0.178	0.112	0.299	-0.311	0.139	0.189	0.062	0.297	0.439	1.000

Table 6.5. Negative binomial regression results
(DV = number of subsequent citations received by each CC patent)

	Intra-firm diffusion			
Variable	*Home-country (1)*	*Home-country (2)*	*Host-country (3)*	*Host-country (4)*
Reciprocation	0.973***			
	(0.142)			
Relatedness		0.066***		
		(0.008)		
Centrality			-0.504***	-9.662***
			(0.110)	(1.396)
Centrality^2				8.978***
				(1.364)
Diversity of ties	-0.065**	-0.175***	0.121***	0.151***
	(0.034)	(0.036)	(0.016)	(0.017)
CC share	-0.490*	-0.946***	-1.716***	-1.765***
	(0.286)	(0.294)	(0.123)	(0.124)
Size	-0.003***	-0.003***	-0.001***	-0.001***
	(0.000)	(0.000)	(0.000)	(0.000)
Patent field	0.719***	0.435**	0.437***	0.457***
	(0.176)	(0.176)	(0.072)	(0.073)
Recency	0.001	-0.001	0.005***	0.005***
	(0.001)	(0.001)	(0.000)	(0.000)
Patent age	-0.330***	-0.355***	-0.355***	-0.359***
	(0.050)	(0.050)	(0.020)	(0.020)
Econ dist	0.042	0.086**	0.041***	0.029**
	(0.036)	(0.039)	(0.013)	(0.013)
Pol dist	-0.057***	-0.008	0.003	0.008
	(0.021)	(0.022)	(0.007)	(0.007)
Geo dist	0.000**	0.000	0.000***	0.000***
	(0.000)	(0.000)	(0.000)	(0.000)
Constant	-2.003***	-0.558**	-0.679***	-0.716***
	(0.361)	(0.324)	(0.152)	(0.153)
Lnalpha	3.831***	3.821***	2.281***	2.273***
	(0.086)	(0.083)	(0.025)	(0.025)
Observations	26,388	26,388	26,388	26,388
χ^2	367.94***	359.13***	1,617.14***	1,657.74***

*Note: *p<0.10; **p<0.05; ***p<.01*
Standard errors in parentheses

Table 7.1. Sample of MNEs

Period	*MNE Patents*	*MNEs*	*Countries*	*Number of firm pairs*	*Avg. corr. co-location*	*Avg. corr. Co-specialization*
1976 to 1980	21,069	30	51	339	0.33	0.11
1981 to 1985	16,579	33	35	449	0.33	0.07
1986 to 1990	19,381	38	41	605	0.38	0.06
1991 to 1995	22,708	43	42	738	0.43	0.04
1996 to 2000	28,780	45	52	988	0.51	0.08
2001 to 2005	24,529	44	53	1,162	0.57	0.12
2006 to 2010	23,426	44	47	1,297	0.59	0.13
2011 to 2016	39,331	44	49	1,324	0.61	0.20

Table 7.2. Names and definitions of variables

Variable	Operational definition
Dependent variable	
Reciprocation	The extent of the reciprocal exchange of knowledge using the sum of USPTO patent cites of firm A to firm B as follows: 2 (Min | A , B|) / (A+B).
Independent variables	
Co-location	The degree to which the geographic distribution of MNE inventions (USPTO patents) across countries are correlated
Geographic overlaps of scientific sourcing	The degree to which the geography of MNE sourcing of university/RI knowledge (sum of patent cites to universities and RI) across city-regions are correlated
Geographic overlaps of clinical sourcing	The degree to which the geography of MNE sourcing of hospital knowledge (sum of patent cites to hospitals) across city-regions are correlated
Co-specialization	The degree to which the technological specialization (RTAs) of MNEs are correlated
HQ country	Dummy, 1 if home countries are different, 0 if home countries are the same
Geographic distance	Great circle distance between geographic center of home countries
Economic distance	Home country differences in economic development and macroeconomic characteristics, e.g. income, inflation, exports, imports
Political distance	Home country differences in policy-making uncertainty, democratic character, size of the state, WTO membership, regional trade agreements
Administrative distance	Differences in ties, language, religion, and legal systems
Demographic distance	Differences in demographic characteristics, e.g. age, birth rate, and life expectancy

Table 7.3. Descriptive statistics

Variable	Observations	Mean	Std. Dev.	Min	Max
Reciprocation	6,902	0.454	0.345	0	1
Co-location	6,816	0.512	0.386	-0.066	1
Geo. Science	6,592	0.384	0.233	-0.165	0.966
Geo. Clinical	6,902	0.735	0.331	-1	1
Co-special.	6,777	0.113	0.382	-0.770	0.998
HQ	6,902	0.798	0.402	0	1
Geo. dist.	6,902	5,539.05	4,011.229	0	10,823.68
Econ. dist.	6,825	1.793	2.434	0	14.168
Pol. dist.	6,902	5.563	7.250	0	50.428
Admin. dist.	6,902	57.052	50.325	0	271.347
Demo. dist.	6,902	2.577	3.927	0	22.708

Table 7.4. Cross correlation matrix

Variable	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*
1. Reciprocation	1.000										
2. Co-location	-0.042	1.000									
3. Geo. Science	0.131	0.162	1.000								
4. Geo. Clinical	0.009	-0.165	-0.182	1.000							
5. Co-special.	-0.044	0.023	0.028	-0.031	1.000						
6. HQ	0.049	-0.591	0.036	0.021	-0.066	1.000					
7. Geo. dist	0.018	-0.538	-0.005	0.044	0.021	0.695	1.000				
8. Econ. dist	-0.037	0.081	0.083	-0.035	-0.052	0.378	0.140	1.000			
9. Pol. dist	-0.039	-0.168	0.140	-0.036	-0.012	0.394	0.235	0.388	1.000		
10. Admin. dist	-0.033	-0.478	-0.002	0.070	0.026	0.570	0.554	0.140	0.114	1.000	
11. Demo. dist	0.078	-0.269	0.058	0.003	0.086	0.330	0.410	0.097	0.203	0.438	1.000

Table 7.5. Results of cross sectional regressions on reciprocation (1976-2016)

	DV: Reciprocation	
Variable	*(1)*	*(2)*
Co-location	-0.051***	0.233***
	(0.016)	(0.049)
Co-location²		-0.312***
		(0.051)
Geographic overlaps of scientific sourcing	0.236***	0.229***
	(0.019)	(0.019)
Geographic overlaps of clinical sourcing	0.027**	0.027**
	(0.013)	(0.013)
Co-specialization	-0.028***	-0.024**
	(0.011)	(0.011)
HQ country dummy	0.107***	0.046**
	(0.019)	(0.021)
Geographic distance	5.37e-07	2.47e-06
	(1.55e-06)	(1.58e-06)
Economic distance	-0.006***	-0.003*
	(0.002)	(0.002)
Political distance	-0.004***	-0.004***
	(0.001)	(0.001)
Administrative distance	-0.001***	-0.001***
	(0.000)	(0.000)
Demographic distance	-0.008***	-0.009***
	(0.001)	(0.001)
Constant	0.377***	0.400***
	(0.021)	(0.022)
R^2	0.046	0.051
Adj R^2	0.044	0.049
Prob > F	0.000	0.000
N	6,497	6,497

*Note: *p<0.10; **p<0.05; ***p<.01*
Standard errors in parentheses

FIGURES

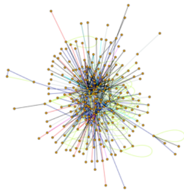
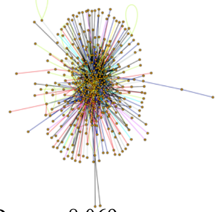
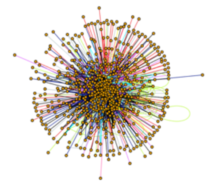
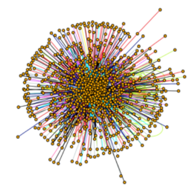
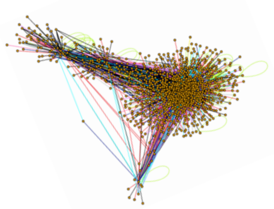
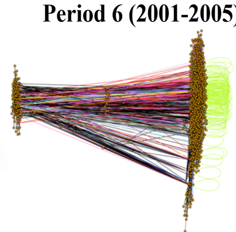
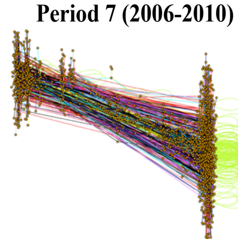
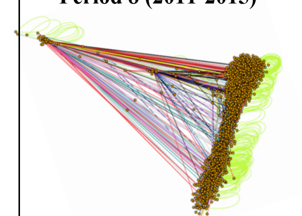
Period 1 (1976-1980)	Period 2 (1981-1985)	Period 3 (1986-1990)	Period 4 (1991-1995)
			
Degree: 6.149 Strength: 25.851 Diameter: 18 Edge density: 0.012	Degree: 8.069 Strength: 40.473 Diameter: 22 Edge density: 0.011	Degree: 9.412 Strength: 55.990 Diameter: 38 Edge density: 0.008	Degree: 10.499 Strength: 73.385 Diameter: 28 Edge density: 0.006
International:44.63% *Local:55.37%*	*International:50.53%* *Local:49.47%*	*International:47.29%* *Local:52.71%*	*International:46.75%* *Local:53.25%*
Intra-MNE:47.30% *Pharma firms:24.00%* *Biotech firms:0.12%* *Inter-industry: 11.13%* *University:0.73%* *Hospitals:0%* *Other:16.72%*	*Intra-MNE:36.22%* *Pharma firms:24.16%* *Biotech firms:0.29%* *Inter-industry:15.98%* *University:1.71%* *Hospitals:0.21%* *Other:21.43%*	*Intra-MNE:32.38%* *Pharma firms:24.18%* *Biotech firms:0.29%* *Inter-industry:18.55%* *University:2.65%* *Hospitals:0.25%* *Other:21.70%*	*Intra-MNE:33.19%* *Pharma firms:24.69%* *Biotech firms:0.48%* *Inter-industry:16.16%* *University:3.45%* *Hospitals:0.21%* *Other:21.82%*
Period 5 (1996-2000)	**Period 6 (2001-2005)**	**Period 7 (2006-2010)**	**Period 8 (2011-2015)**
			
Degree: 14.289 Strength: 101.281 Diameter: 29 Edge density: 0.006	Degree: 10.678 Strength: 63.535 Diameter: 68 Edge density: 0.004	Degree: 11.446 Strength: 90.071 Diameter: 99 Edge density: 0.004	Degree: 11.652 Strength: 164.600 Diameter: 426 Edge density: 0.003
International:59.63% *Local:40.37%*	*International:51.06%* *Local:48.94%*	*International:50.14%* *Local:49.86%*	*International:46.31%* *Local:53.69%*
Intra-MNE:33.25% *Pharma firms:25.10%* *Biotech firms:2.68%* *Inter-industry:14.42%* *University:6.17%* *Hospitals:0.59%* *Other:17.79%*	*Intra-MNE:25.13%* *Pharma firms:27.65%* *Biotech firms:3.85%* *Inter-industry: 20.69%* *University:9.15%* *Hospitals:1.01%* *Other:12.52%*	*Intra-MNE:22.77* *Pharma firms:31.32%* *Biotech firms:4.83%* *Inter-industry:17.29%* *University:8.79%* *Hospitals:1.77%* *Other:13.23%*	*Intra-MNE:15.41%* *Pharma firms:33.14%* *Biotech firms:3.95%* *Inter-industry: 29.87%* *University:6.22%* *Hospitals:0.87%* *Other:10.54%*

Figure 5.1. Evolution of the structure of foreign subunit's knowledge sourcing for CE innovations

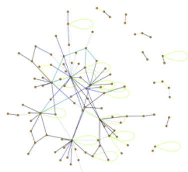
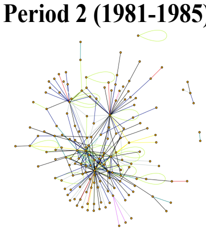
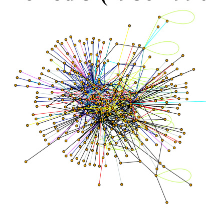
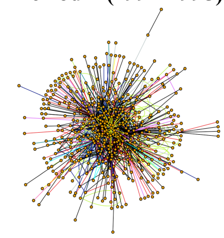
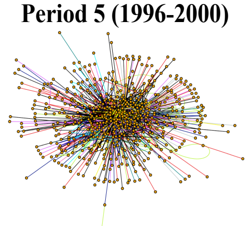
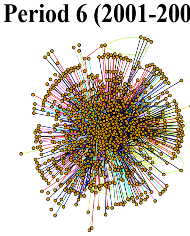
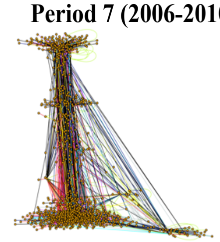
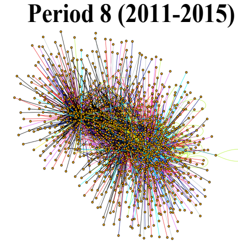
Period 1 (1976-1980)	**Period 2 (1981-1985)**	**Period 3 (1986-1990)**	**Period 4 (1991-1995)**
			
Degree: 2.569 Strength: 5.647 Diameter: 7 Edge density: 0.013	Degree: 3.251 Strength: 9.521 Diameter: 19 Edge density: 0.010	Degree: 4.695 Strength: 16.135 Diameter: 19 Edge density: 0.008	Degree: 5.172 Strength: 17.847 Diameter: 112 Edge density: 0.006
International: 48.61% *Local: 51.39%*	*International:53.74%* *Local: 46.26%*	*International:59.51%* *Local: 40.49%*	*International:55.66%* *Local: 44.34%*
Intra-MNE:40.97% *Pharma firms:19.10%* *Biotech firms: 0%* *Inter-industry: 23%* *University: 0.35%* *Hospitals: 0%* *Other:9.03%*	*Intra-MNE:39.43%* *Pharma firms:8.89%* *Biotech firms:0%* *Inter-industry:25%* *University:0.77%* *Hospitals:0.35%* *Other:25.56%*	*Intra-MNE:33.96%* *Pharma firms:22.24%* *Biotech firms:0.52%* *Inter-industry:23.40%* *University:2.27%* *Hospitals:0.12%* *Other:17.49%*	*Intra-MNE:29.92%* *Pharma firms:15.70%* *Biotech firms:0.17%* *Inter-industry:38.18%* *University:3.03%* *Hospitals:0.27%* *Other:12.73%*
Period 5 (1996-2000)	**Period 6 (2001-2005)**	**Period 7 (2006-2010)**	**Period 8 (2011-2015)**
			
Degree: 6.182 Strength: 22.297 Diameter: 71 Edge density: 0.006	Degree: 5.800 Strength: 34.123 Diameter: 101 Edge density: 0.003	Degree: 5.936 Strength: 59.440 Diameter: 181 Edge density: 0.003	Degree: 6.173 Strength: 72.867 Diameter: 100 Edge density: 0.003
International:63.27% *Local: 36.73%*	*International:40.78%* *Local: 59.22%*	*International:38.44%* *Local: 61.56%*	*International:39.06%* *Local: 60.94%*
Intra-MNE:20.77% *Pharma firms:16.51%* *Biotech firms:0.25%* *Inter-industry: 37.78%* *University:2.98%* *Hospitals:0.42%* *Other:21.29%*	*Intra-MNE:24.32%* *Pharma firms:24.69%* *Biotech firms:3.21%* *Inter-industry:27.83%* *University:6.73%* *Hospitals:0.63%* *Other:12.59%*	*Intra-MNE:20.53%* *Pharma firms:32.14%* *Biotech firms:5.90%* *Inter-industry:20.32%* *University:8.99%* *Hospitals:0.77%* *Other:11.65%*	*Intra-MNE:23.72%* *Pharma firms:25.31%* *Biotech firms:4.16%* *Inter-industry:27.44%* *University:7.97%* *Hospitals:0.84%* *Other:10.56%*

Figure 5.2. Evolution of the structure of foreign subunit's knowledge sourcing for CC innovations

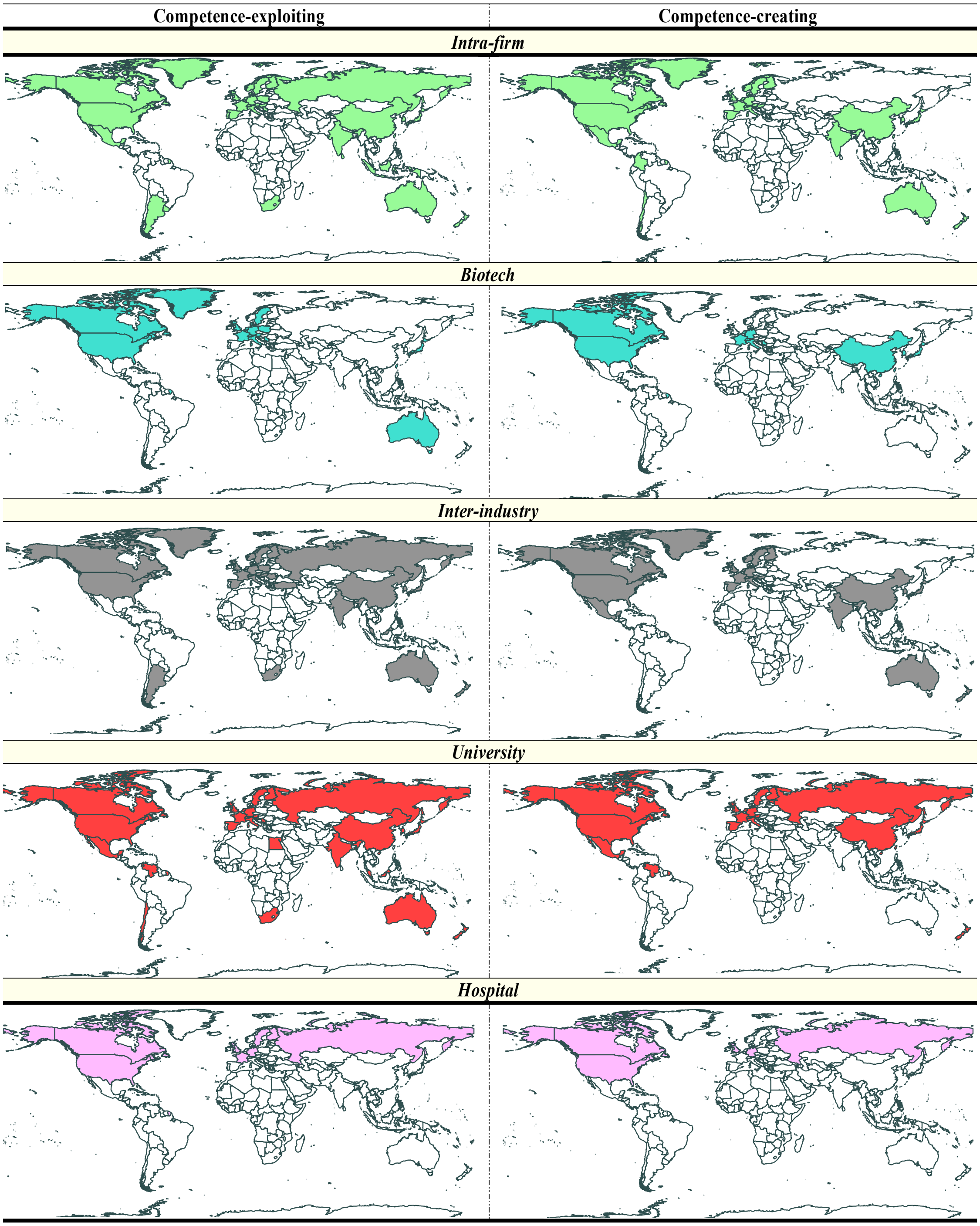


Figure 5.3. Geography of sources: competence-creating vs competence-exploiting

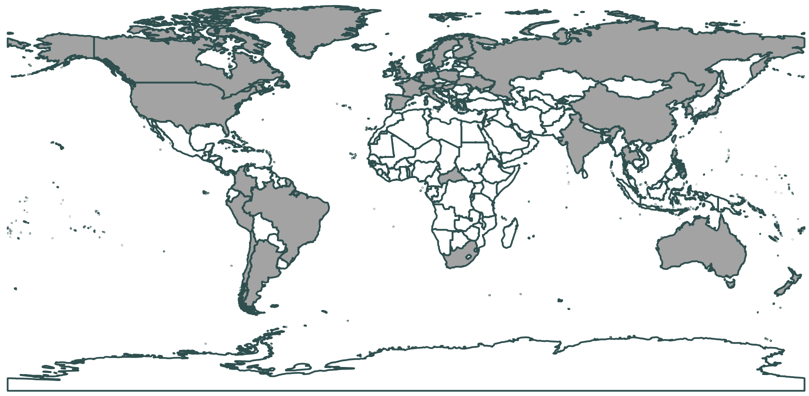


Figure 6.1. Geographic distribution of foreign-located subunits' CC innovations

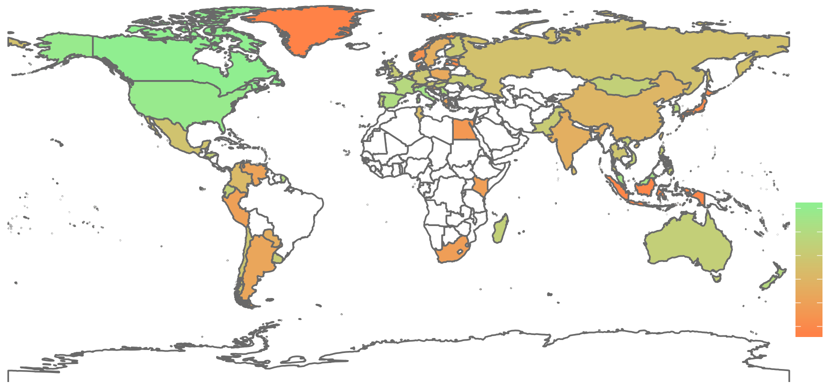


Figure 7.1. Degree to which countries host the same MNEs as other countries

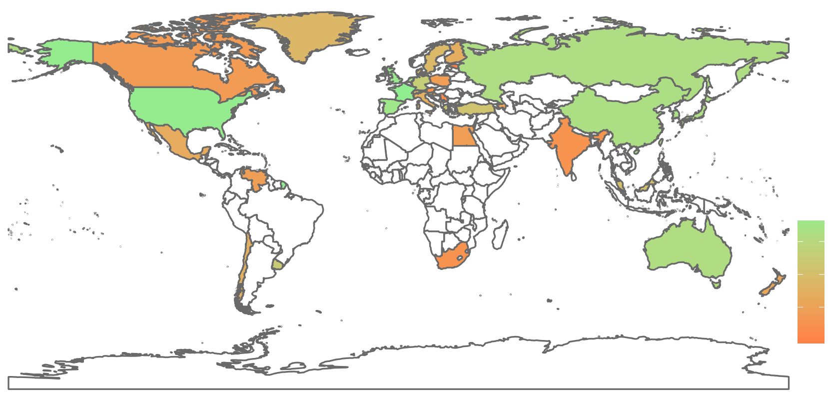


Figure 7.2. Degree to which countries attract the same MNEs to source university and hospital knowledge as other countries

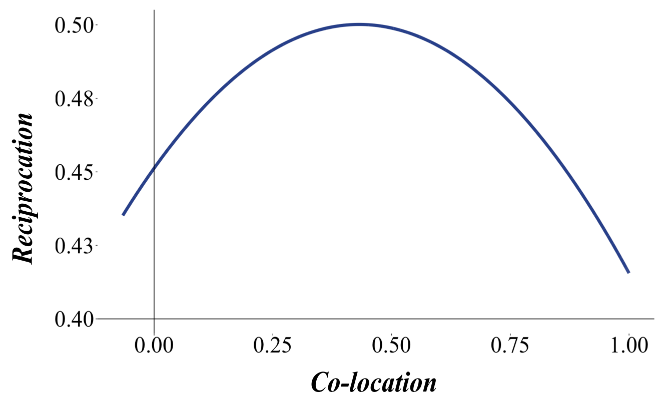


Figure 7.3. The relationship between co-location and reciprocation