MULTISCALAR CLUSTERS AND NETWORKS AS THE FOUNDATIONS OF INNOVATION DYNAMICS IN THE BIOPHARMACEUTICAL INDUSTRY

Marc-Hubert DEPRET * and Abdelillah HAMDOUCH **

Abstract – Based on the case of the biopharmaceutical industry, the aim of this paper is to challenge the core conviction now widespread within the "spatial clustering theory", which devotes a key (if not exclusive) role to geographical proximity in explaining clustering dynamics of innovation activities within specific territories. Our argument is threefold. First, mere geographical proximity is not enough; in many cases, cognitive, organizational and strategic forms of proximity are often at least as crucial as the topological closeness among innovation actors. Second, our idea is that clusters are fundamentally the territorialized outcome of combinations of inter-organizational and social networks among actors pursuing common goals, each of these actors having a specific territorial and social embedding that allows him or her (or not) to operate and interact at different spatial scales. These networks are socially and territorially embedded, but they can operate at various spatial scales. Third, sector-driven dynamics – as is in the case of biopharmaceuticals – may structurally frame the way the actors interact and collaborate in R&D projects and innovation processes. Indeed, the dynamics underlying the emergence, structuring and evolution of biopharmaceutical clusters are both multi-actor and multiscalar. In this perspective, clusters and networks appear to be intertwined phenomena, consubstantial one to each other, and co-evolving organizational modes of biopharmaceutical innovation.

Key Words: BIOCLUSTERS, FORMS OF PROXIMITY, INNOVATION NETWORKS, SPATIAL SCALES.

JEL: D85; L65; 033; R1

^{*} BETA (University Henri Poincaré, Nancy); Marc-Hubert.Depret@esstin.uhp-nancy.fr Research Network on Innovation / Réseau de Recherche sur l'Innovation.

^{**} CLERSÉ (University of Lille 1) and CEREN (ESC Business School Dijon Burgundy); Adel.Hamdouch@univ-lille1.fr (Corresponding Author), Research Network on Innovation / Réseau de Recherche sur l'Innovation.

ACKNOWLEDGEMENTS

On more or less its actual form, this article has received in May 2010 the Regional Studies Association Best International Conference Paper Award 2010. We would like to sincerely thank the RSA Award Jury chaired by Mário Vale, as well as Prof. Sir Peter Hall, Prof. David Bailey and Mrs. Sally Hardy, respectively President, Chair and Chief Executive of the Regional Studies Association for this great honor. This award has been for us a welcomed and encouraging reward for the work we have tried to push forward over the last few years toward better understanding clustering and networking dynamics in High-Tech sectors, and especially in Biopharmaceuticals. Indeed, this paper is the result of a maturation process that made successive versions of it (in French and English) evolve and improve significantly. This process went through the presentation and discussion of these versions of the paper in several workshops and conferences: International Conference on Clusters (Liège, March 2009), Workshop INSA on Clusters (Lyon, March 2009), International INOCREA Workshop on Evolutionary Economic and Geographic Approaches (Lille, December 2009), Research Network on Innovation (RNI) Forum Innovation IV (Grenoble, March 2010), Regional Studies Association Annual Conference (Pécs, May 2010) and, very recently, while the paper was under revision, ASRDLF-AIRSe International Conference (Aoste, September 2010). The paper has also already appeared in two initial versions respectively in the SSRN Working Papers Series (December 2009, in English) and as a BETA Working Paper (University of Strasbourg, WP 2010-11, April 2010, in French), and as such, it has benefited from additional suggestions and comments. Our many thanks go to all the colleagues, friends and referees who made useful suggestions for improving the paper, and specifically to Jean-Alain Héraud (BETA, University of Strasbourg) and the anonymous referees of Région et Développe-ment. Finally, we would like to express our "territorialized" thanks for the financial support provided by our two respective research labs at CNRS, BETA in Nancy, and CLERSÉ in Lille, which has greatly helped for the translation and/or English correction-adaptation-language checking of various parts of the manuscript. Of course, the usual caveats apply.

INTRODUCTION

It has become evident over the last few years that the competitive advantage of companies and the comparative advantage of states, regions and metropolises no longer exclusively depend on the simple mobilization of the resources with which "Nature", history (that is, path dependency), geography, institutions or "contingency" have provided economic actors. To survive in (and even dominate) today's global markets, it is necessary to develop pre-emptive strategies relating to a wide range of resources (financial and cognitive in particular) and skills (especially technological) that the actors do not possess a priori or are incapable of managing alone. Hence the emphasis put on greater proximity and closer coordination between the various "holders" of resources and skills. In an environment characterized by a significant redistribution of the spatial and sectoral "cards" between various stakeholders, the competitive or comparative advantage lies in the ability of rival yet complementary actors (from an organizational as much as a spatial point of view) to manage increasingly close and structural interdependencies (including extra-market interdependencies) within an extremely wide range of clusters and networks.

Noting the increasing clustering of economic activities, numerous empirical and theoretical studies in a variety of disciplines (economics, sociology, geography and management) – forming what Malmberg and Maskell (2002) call the "spatial clustering theory" – have stressed the importance of (spatial) proximity factors to explain the dynamics of competition and the structuring of organizations and markets. Following this line of argument, the idea has

emerged – now widespread among decision-makers and academics – that clusters (in the broadest sense of the term) are now key competitive tools within a context of sustained innovation dynamics and rapid globalization of industries and markets, particularly in high-tech sectors (information and communication technologies, life sciences, nanotechnologies, new materials, etc.).

However, despite the widespread exposure given to this issue, the questions raised by the richness of literature devoted to clusters (Hamdouch, 2010) remain open to discussion in three key areas. This relates, firstly, to the delimitation of the relevant geographic space (local, regional, national and even global) to enable the mapping out of cluster boundaries. A large body of literature on this subject emphasizes the decisive role played by geographical proximity and the effects of spatial clustering on the development of the innovative capacities of innovation actors (Baptista and Swann, 1998). Still, as many recent studies tend to show, it is important to put this purely "spatialised" (or territorialized or geocentric²) approach to the cluster issue into perspective, while avoiding going too far in the opposite direction by adopting an excessively network-based vision (den Hertog and Roelandt, 1999; Passiante and Secundo, 2002), in which the spatial dimension is absent or subsumed within a general undifferentiated framework (Hamdouch, 2010). In fact, although clustering factors do have a role to play in the dynamics of the emergence, structuring and development of innovation activities within clusters, they are not generally sufficient to explain the range of paths followed by many clusters. Formal and informal, inter-organizational and interpersonal complementarities – in terms of skills, strategies, organizational methods, behavior, technology and resources, particularly in a basic research context or upstream of the innovation process – between the various innovation stakeholders often have a greater impact than their geographical proximity or their inclusion within a spatially defined "territory".

¹ Geographical (or spatial) proximity refers to the short topographic distance between two or more actors interacting in a market or within the framework of an innovation process. However, the proximity is not systematically or exclusively geographic; it can be also, and is very often, organizational or cognitive (see Section 3 below).

izational or cognitive (see Section 3 below).

Geocentric (or "autarkic") approaches postulate a strong territorial anchorage of clusters (Depret and Hamdouch, 2009). In this perspective, clusters are often seen as being rooted in a specific (local, metropolitan, regional...) given territory. By contrast, polycentric or multiscalar approaches consider that a cluster can have several territorial anchorages thanks to its connections with other clusters. In certain cases, a polycentric cluster can even be multi-territorialized when its topographic boundaries transcend administrative or political borders (cf. the cases of the Medicon Valley across the borders of Denmark and Sweden, and of the Biovalley across France, Germany and Switzerland). At the same time, it must be noted here that the dichotomy geocentric vs. polycentric must not be confused with the other dichotomy structuring the literature which opposes centrifugal forces (i.e. the openness of clusters vis-à-vis other spatial scales) and centripetal forces (i.e. the lock-in within what Moulaert and Mehmood [2008] call the "localist trap") that shape clusters. Finally, one should note that the dichotomy centripetal vs. centrifugal stands beyond the traditional dichotomy local vs. global as the former doesn't exclude the possibility of polycentric or multi-spatialised territorial dynamics. Indeed, far for opposing the local and the global, the centripetal vs. centrifugal dichotomy allows for studying the continuum of the various spatial scales according to the degree of openness (centrifugal) or of closure (centripetal) of clusters (on all this discussion, see Depret and Hamdouch, 2009).

At the same time, most works devoted to clusters appear to explain their emergence and structuring dynamics in relation to just two dichotomous and relatively conflicting approaches or mechanisms (Bresnahan et al., 2004; Fromhold-Eisebith and Eisebith, 2005; Chiaroni and Chiesa, 2006). For the first approach, clusters are initiated (or "decreed") by a sort of strategic or political deus ex machina (a top-down view). According to the bottom-up view adopted by the second approach, they emerge - more or less "spontaneously" or "mysteriously" — in an autonomous or self-organizing manner when certain "space/time" conditions or circumstances (Dicken et al., 2001; Bathelt and Taylor, 2002) are in place at a given moment or in a determined place. In reality, there is nothing "fanciful" about clusters or, otherwise, "miraculous" (Hamdouch, 2010). Clusters require a pronounced institutional and/or industrial determinism and a fertile environment (scientific/technological, institutional/social, economic, financial, etc.) — just as in gardening a "healthy rose" needs a "good fertilizer", "good soil" and "plenty of sunshine" (or a "microclimate"), regular watering, but also a "good gardener" (or someone with "green fingers").

In addition, the analysis of the "morphology" and "dynamics" of clusters is often insufficient and limited (or even simplistic). This is because, on the one hand, it is based on a relatively static and standardized conception of clusters. On the other hand, the analysis of a cluster's members is generally purely focused on "agents" who are fully and directly involved (individually) in a process (territorialized, relatively static and competitive) of innovation or a process of production/dissemination/accumulation of knowledge. In reality, *it is important to consider the cluster as a complex networked entity* that is systemic, structured (around stakeholders with highly varied organizational or institutional profiles), polymorphic, dynamic (that is, it evolves over time and in space) and relatively open to the outside world (that is, "centrifugal") or even multiscalar (or polycentric).

Lastly, the inter-organizational and inter-individual relationships formed within clusters are generally seen from a purely transactional or contractual (that is, market-oriented) perspective (Cooke, 2005). Worse, they are usually presented with fairly weak formalization (Grabher, 2006), often decontextualized (Dicken and Malmberg, 2001) – that is, without any real social, informational or cognitive considerations - and sometimes even seen from a static (timeless), or a-historical (Bathelt and Taylor, 2002) viewpoint. In practice, however, this is not at all the case, as shown by numerous studies based on a more "social" perspective in contrast with the traditional "market" perspective - or "commercial" or "under-socialized", according to Granovetter's expression (1985). Recent research (in particular in the field of economic sociology) tends in fact to show the importance of social networks, power relationships (i.e. domination, subordination, control, coercion and discipline), trust, reputation, altruism, friendship, leniency, forbearance, kindliness, integrity, social capital, habitus, culture, rules, conventions, routines, rites, symbols, taboos, beliefs, myths, or, more broadly, "extra-market" relationships within clusters.

This being the case, our understanding of the mechanisms underlying the dynamics of emergence, structuring, coordination and development of the clustering of innovation processes remains incomplete, dispersed and (let's admit it) fairly flimsy (Hamdouch, 2010). To analyze clusters from a new perspective, it is then necessary to open "the 'black box' of the cluster approach" (Benneworth and Henry, 2004, p. 1012). In order to do this, we need to adopt a conception of clusters that is less "geocentric" or "autarkic" (by rejecting the idea that "there is no hope outside the cluster"), less dichotomous and determinist (by avoiding a "top-down" versus "bottom-up" conflict), less narrow (by taking into consideration all innovation stakeholders), less "centripetal" (by avoiding thinking of them as cut off from the outside world or as autarkic), less "market-based" (by taking into account the social and cognitive dimension of the relationships between the stakeholders) and less "static" (by performing a serious space/time analysis of clustering processes). From a more evolutionist perspective, we will therefore attempt, in this paper, to argue the following idea:

Although clusters are one of the permissive conditions for the innovation production and dissemination process, they neither constitute a sufficient condition in themselves (in contrast to the "naturalist" hypothesis – to use Torre's expression (2006) – argued within the framework of a traditional or geocentric/autarkic vision of clusters), nor necessarily the organizational form best suited to this end, in particular within an increasingly globalized and uncertain environment.

Our argument is that the "spatial clustering theory" can be firmly challenged for at least three reasons. First, because mere geographical proximity is not enough, or even not the most decisive dimension for producing and sustaining valuable connections among the actors; in many cases, cognitive, organizational and strategic forms of proximity (or alignment or convergence) may prove to be at least as crucial as topological closeness. Second, because clusters are fundamentally networking configurations and combinations of actors pursuing some common goals, may they be co-located or not; what is important here is not that the actors belong necessarily to the same "place", but that each of them has a specific territorial and social embedding that allows him (or not) to operate and interact at different spatial scales. Furthermore, contrary to what is suggested in most approaches composing the "spatial clustering theory", it is the inter-organizational and social networks that are the foundational building blocks of clusters. Hence, clusters are not at the root of networking phenomena - even if they can reinforce them over time. The causality relation between networking and clustering dynamics is likely to operate in an inverted way as clusters appear to be are primarily the territorialized outcome of networks (see, among others: Dicken et al., 2001; Grabher, 2006; Glückler, 2007; Phlippen and van der Knaap, 2007; Depret and Hamdouch, 2009). Third, because sectordriven dynamics – as is in the case of biopharmaceuticals, with strong complementarities among actors located in many countries and places on the surface of the globe; see below - may structurally frame the way the actors interact and collaborate in R&D projects and innovation processes. In this perspective, clusters and networks appear to be intertwined phenomena, consubstantial one to each other, and co-evolving organizational modes of biopharmaceutical innovation³. These two intertwined organizational forms are socially and territorially embedded, but they can operate at various spatial scales.

Therefore, we will adopt in this article the following definitions. A cluster is a spatial mode for the organization of innovation and related activities. A cluster "comprises an ensemble of various organizations and institutions (a) that are defined by respective geographic localizations occurring at varied spatial scales and within specific institutional environments, (b) that interact formally and/or informally through inter-organizational and/or interpersonal regular or more occasional relationships and networks, (c) and that contribute collectively to the achievement of all kind of innovations within a given industry or domain of activity, i.e. within a domain defined by specific fields of knowledge, competences and technologies. This definition is rather flexible, as it entails only that the three sets of conditions are being simultaneously verified. It could then correspond to a large variety of spatial, institutional and organizational concrete configurations of innovative dynamics. Moreover, it does not prejudge of the spatial topography of the interacting actors, nor does it impose any constraint on the way they may interact (i.e. cooperate or compete)" (Hamdouch, 2010, p. 43).

At the same time, we consider a *network* as being a specific modality for the structuring/ coordination of inter-organizational relationships among various (legally) independent actors (firms, institutions, etc.) aiming at achieving a common project in a specific domain through the control, exchange or sharing of information, know-how, knowledge, as well as products and/or capital (Hamdouch and Depret, 2001). The actors participating to a network may be colocated within the same cluster or belong to different clusters.

Hence, the articulation between cluster and network phenomena is posed as follows: a cluster can be seen as a combination of networks of socially and territorially embedded actors that can operate at one or various spatial scales (see e.g.: Castilla et al., 2000; Owen-Smith et al., 2002; Casper and Murray, 2005; Hamdouch and Depret, 2009). Thus, we consider that a cluster does not

³ The articulation of clusters – as specific Territorial Innovation Systems (TIS) – and networks vary however, depending on the authors. *A minima*, clusters can be considered as simple networks of actors, more or less co-localized in one territory (and sometimes several territories). By contrast, other research (in particular in the field of economic sociology) tends to show that clusters must be considered as *webs of social networks* comprising a potentially large variety of innovation stakeholders who interact (or co-evolve) within the framework of occasional or regular relationships, both inter-organizational and intra-organizational, and who contribute to the performance of activities in a particular area. For some, however, clusters are no longer (only) considered as geographically anchored networks, within which actors are grouped together more or less on a co-localization basis. They appear more as combinations of "multi-scaled networks", both in terms of location and the variety of actors' modes of interaction. From this viewpoint, TIS and networks are intimately connected (Amin and Thrift, 1992; Dicken et al., 2001; Nachum and Keeble, 2003; Coe et al, 2004; Gertler and Levitte, 2005; Glückler, 2007; Phlippen and van der Knaap, 2007; Ter Wal and Boschma, 2009a, 2009b). Networks of actors are therefore sometimes anchored in several clusters, which are characterized by strategies, policies and specific territorial factors, and which co-evolve (in time and in space) together and with these networks of actors.

rely only on actors that are agglomerated within a single place. It follows that if the co-localization of actors within the same geographical area may feed a local clustering dynamics (and hence build on Marshallian economies and other agglomeration spillovers induced by geographical proximity and local socialnetworking), a cluster can also benefit from the connections that some of its actors build elsewhere — either because they are multi-located actors and/or because they have built privileged relationships outside the geographical boundaries of the cluster (see: Dicken and Malmberg, 2001; Saxenian and Hsu, 2001; Oinas and Malecki, 2002; Nachum and Keeble, 2003; Coe et al., 2004; Coenen et al., 2004; Zeller, 2004; Cooke, 2005; Scott, 2006; Waxell and Malmberg, 2007; Moodysson et al., 2008). In the latter cases, the proximity among actors underlies more than mere topographic and socially localized interaction. Here, various cognitive and strategic dimensions are likely to be decisive in the "proximity" that the actors are able to build, maintain or develop (Torre, 2006). It follows also from this approach that if the multiscalar shape of many networks is now well established in the literature (see e.g.: Amin and Thrift, 1992; Bunnel and Coe, 2001; Dicken et al., 2001, among many others), the idea that clusters may also be seen as multiscalar phenomena is not so widespread. This idea builds on the fact that a cluster (and its viability) may structurally depend on actors whose activities articulate across various spatial scales, with multiple territorial locations and embeddings. Moreover, these actors may well participate to several geographical clusters which they connect through their industrial, commercial or innovation activities. Hence, as suggested by the biopharmaceutical case examined in this article (see below for the rationales of this focus), if a cluster can be considered as the result of a combination of networks, and if networking occurs locally as well as across various spatial scales, then a cluster is itself depending on multiscalar dynamics, i.e. on the connection among the different territories in which operate some of the actors who participate to the cluster, directly (by being located in it) or indirectly (by being located elsewhere, but by having more or less strong industrial, commercial or technological relationships with one or several actors of the cluster).

Mirroring this approach, our focus on the biopharmaceutical industry (which is the result of the progressive interpenetration, or even merging of the traditional pharmaceutical industry and biotechnology) case is based on two rationales. First, the analysis of bioclusters has given rise to a great deal of empirical research, some of which tends towards a renewed vision of clusters. Second, in recent years we have seen the emergence of a new form of industrial organization in which clustering strategies play a structuring role and fundamentally redefine the foundations and forms of competition that exist between a wide range of highly interdependent actors. These new forces at work within this science-based industry are, in fact, at the basis of a gradual reappraisal of market structures, a rationalization of the organizational methods used by big pharmaceutical companies, and a restructuring (both cognitive and spatial) of their scientific and technological activities. This being the case, the transformation of this industry's basic "contextual" parameters (following the sudden emergence and dissemination of scientific principles and research methods arising from the "Life Revolution") has generated new network-based forms of

proximity and interfirm coordination (Hamdouch and Depret, 2001). As we shall see, these emergence, structuring and evolution dynamics of biopharmaceutical networks and clusters are fundamentally multi-actor and multi-scalar.

Taking this as our framework, and drawing from a vast review of the empirical literature, the paper will follow a two-step approach. Firstly, we will provide a brief overview of the decisive role – as most of the empirical studies forming part of the traditional geocentric/autarkic vision of clusters reveal generally played by proximity factors and the effects of clustering in relation to the innovation dynamics at work within the biopharmaceutical industry (Section 1). In the second step, we will explain, however, why any analysis of clusters and local networks cannot be solely based on a purely "dichotomous", "geocentric", "narrow" and "centripetal" approach (Sections 2 to 5). From this perspective, we will first of all attempt to show that clusters are not all – including within the same sector and/or country – and at all times favorable to innovation (Section 2). We will stress, in particular, the key role played by History, the 'context" (economic, financial, social, political, cultural, etc.), the institutional system and the interdependencies between stakeholders in the innovation process and, as a consequence, their impact on the origins, development and evolution of clusters. We will therefore show that the emergence, structuring and development dynamics of clusters result from the combination of both "topdown" and "bottom-up" mechanisms. We will go on to demonstrate that colocation and geographical proximity (between the different members of a cluster or an innovation network) does not generally suffice to generate innovation dynamics that are both effective (or, a minima, viable) and sustainable (Section 3). We will therefore look in greater detail at the very foundations of the classic geocentric/autarkic approach to clusters as outlined in the "spatial clustering theory". We will also highlight the fact that other forms of (less "centripetal") coordination, which extend beyond traditional cluster boundaries, are often necessary to trigger virtuous ("centrifugal") innovation dynamics (Section 4). Within this context, we will show that clusters and innovation networks cover multiple forms and involve a large number of various actors. Lastly, we will endeavor to show that they often tend to be transformed over time, to co-evolve with each other, and are gradually deployed over spatial levels other than the narrow regional or local ones. This being the case, we will show that clusters and innovation networks are often more open to the "outside world" than what the "geocentric" literature generally suggests, and that they are thereby subject to complex "space/time" dynamics (Section 5). The last section concludes the paper by outlining the underlying theoretical and methodological challenges facing future research in this field, in particular in order to more effectively take into account the spatial, organizational and interpersonal (or cognitive) dimensions of the coordination modes among the various innovation stakeholders.

1. THE "GEOCENTRIC" CONCEPTION OF (BIO)CLUSTERS AND ITS LIMITS

Historically, innovation in the pharmaceutical field has always tended to be located close to major public and private research centres (Achilladelis and Antonakis, 2001). The major pharmaceutical R&D labs are, in fact, almost all

located within large "centres of excellence" (for example, the Research Triangle Park in North Carolina, the Boston region, California, etc., in the US; in the regions around Paris, Lyon and Toulouse in France; Leverkusen, Heidelberg and Bavaria in Germany; Basel in Switzerland; etc.) where most of the sector's innovation actors are clustered around universities and university hospitals: university research centres, pharmaceutical and biotechnology companies, service providers, specialist suppliers, institutional structures, business incubators, foundations, investors, venture capitalists, law firms, consulting firms, head hunters, training institutes, public relations companies, etc.

Organized into clusters, these local highly specialized innovation systems represent, in fact, networked contact points where various innovation stakeholders can access (or have priority access) to a large range of knowledge, skills, resources and technologies. These "inputs" have a significant tacit, idiosyncratic, interactive and cumulative dimension, which makes their production, acquisition and/or their pre-emption random, difficult and relatively expensive⁴, particularly outside one-on-one relationships and neighboring situations. Hence, there is a push for better coordination and, therefore, for greater (spatial) *proximity* between the various "holders" of knowledge, skills, resources and/or technologies.

Within this framework, the geographic concentration of activities, the physical linking of actors and the organization of local innovation networks generally enable stakeholders to benefit from the *technological externalities of agglomeration* (access to strategic information via a "trickle-down effect" or through dissemination, a drop in transaction and/or interaction costs, lower marginal costs, etc.) and (geographical) *proximity effects* (pre-emptive access to knowledge, skills [technical, legal, organizational], resources [human and financial] and strategic technologies; localized collective learning effects; access to new outlets, etc.) that such a spatial organization of activities generally provides – consequently and on condition that, however, they have what Cohen and Levinthal (1990) call a good "absorptive capacity".

The increasing geographic integration of innovation actors within these clusters fosters interaction opportunities (both formal and informal), creates new investment, entrepreneurial and recruitment opportunities, helps develop supporting infrastructures (material and immaterial) and, in fine, creates a "climate"

⁴ In recent years, there has been a massive increase in spending on R&D and marketing in the pharmaceutical industry: you now need around \$1200/1300 million to launch a new innovative therapeutic product onto the market (DiMasi and Grabowski, 2007); the same amount or so is also necessary for the marketing and commercial launch of the product. The reasons for this are, on the one hand, the growing demands made by health authorities responsible for authorizing the commercialization of drugs and the decreasing yields of the traditional (pharmacochemical) paradigm and, on the other hand, the increasing interdependence between the various "skill holders" throughout the pharmaceutical value chain. It is within this framework that *funding constraints* tend to become increasingly significant and impose a certain *constrained proximity* between, on the one hand, biopharmaceutical companies and on the other hand, their "funders" (venture capitalists, industrial partners, public and local authorities, institutional investors, individual shareholders, business incubators, "biotech-centres", etc.). On this, see Hamdouch and Depret (2001).

that is a priori relatively favorable to innovation. Cumulatively, spatial clustering also heightens the attractiveness (Bathelt, 2005) of the cluster and its members through "increasing agglomeration and proximity returns" (Depret and Hamdouch, 2004) and the mimetic effects of a self-fulfilling and self-strengthening reputation (Appold, 2005; Gertler and Levitte, 2005).

In reality, this "idyllic" vision – which makes clusters a "winning formula" for innovation -, despite being shared by numerous academics and political decision-makers (as revealed by a recent trend towards innovation policies based on the stereotyped development⁵ of clusters), needs to be put into perspective once one widens the focus beyond success stories (Silicon Valley, Route 128, San Francisco Bay Area, Research Triangle Park, "Italian districts", Baden-Württemberg, etc.) and/or high-tech (or science-based) industries which is often the case in geocentric/autarkic studies devoted to clusters or regional innovation systems (Malmberg and Maskell, 2002; Oinas, 2002; Coenen et al., 2004; Doloreux and Parto, 2005). This widening of the perspective is needed, firstly because the formation of clusters does not guarantee innovation (see Section 2 below). Secondly, the technological externalities of agglomeration and (spatial) proximity effects are not always present within clusters (see Section 3 below). Finally, because innovation can also be fostered by forms of organization - less "centripetal" (see Section 4 below) and less "geocentric" (see Section 5 below) – other than "traditional" clusters. This is what we intend to demonstrate in the following sections by putting forward a series of arguments that question the three main presumptions on which this "idyllic" vision of clusters is based.

2. INNOVATION CANNOT BE MANDATED, EVEN WHEN SUPPORTED BY A (BIO)CLUSTER

The first of these three presumptions states that organizing stakeholders into a cluster is enough to create (even artificially) virtuous innovation dynamics. The facts, unfortunately, appear to cast doubt on this hypothesis to the extent that some (bio)clusters clearly "function" much better (or are more "viable") than others – including within a single country or region –, while numerous others fail, despite the determination of those who decided to set up the cluster.

This finding can be explained by the fact that the emergence, development and dissemination of biopharmaceutical innovations require a fairly long maturing period and a relatively complex "alchemy" (scientific and technological, institutional and social, economic and financial). As it has been already

⁵ To such an extent that the term "cluster" has become a type of "brand" (Martin and Sunley, 2003; Benneworth and Henry, 2004) with its models (Silicon Valley, Route 128, etc.), best practices, "gurus" (M. Porter, etc.) and its followers (particularly major international institutions). As a result, as noted by Martin and Sunley (2003, p. 6), "from the OECD and the World Bank, to national governments (...), to regional development agencies (...), to local and city governments (...), policy-makers at all levels have become eager to promote local business clusters. (...) Clusters, it seems, have become a world-wide fad, a sort of academic and policy item".

stated elsewhere (Depret and Hamdouch, 2007), "the environment" in which innovation stakeholders operate is, in fact, the result of systemic, multifactor and co-evolutionary dynamics (see in particular: von Tunzelmann, 2003) specific to the sector and/or the territory in question.

Numerous works (see, among others: Swann and Prevezer, 1996; Audretsch, 2001; Orsenigo, 2001; Powell et al., 2002; Waluszewski, 2004; Glaeser, 2005) have already established that the creation of a high-performance biocluster cannot be mandated (or else you take a fairly significant risk of failure in the mid- to long-term). It also follows that the pre-existence (more or less "spontaneous" or "fortunate") of specific and particularly favorable conditions is not sufficient to guarantee the success of a biocluster. For example, Orsenigo (2001) has shown precisely why the development of a biotechnology cluster in Lombardy failed, not because of a lack of political determination on the part of the public authorities (quite the opposite in fact!), but rather because of the absence of a solid base of pre-existing technological skills (in addition to other factors, such as the absence of links between academics and manufacturers, a lack of capital, and the inappropriateness of intellectual property laws)⁷.

In fact, in addition to the favorable "climate" or fairly dynamic "atmosphere" – dear to A. Marshall (1919) – in which the members of a cluster are "immersed", multiple factors explain why clusters do not systematically foster innovation. Numerous studies (see, among others: Niosi and Bas, 2001; Orsenigo, 2001; Folta et al., 2006) stress the (apparently necessary) "critical size" of bioclusters. Some studies (see, in particular, Folta et al., 2006) reveal the existence of an upside inverted U curve between the size of a cluster and the performance of its members and, as a result, the existence of an "optimal size" (that is, an optimal number of members)⁸. That is also why most studies stress the importance of the intensity of competition within clusters – that is, their horizontal dimension (Bathelt and Taylor, 2002; Malmberg and Maskell, 2002).

The composition of the cluster and the quality of its member organizations (and institutions) are also significant, according to several authors. Llobrera et al. (2000) show how the networking structures and actors' diversity of clusters largely condition their success, as illustrated by the example of the Philadelphia biocluster (highly diversified in its composition). The presence of "star scientists" (Zucker and Darby, 2007), "critical interfaces" (Carrincazeaux et al., 2001), "gatekeepers" (Casper and Murray, 2005), specialist (public and/or private) "entrepreneurial" investors (Audretsch, 2001; Cooke, 2001; Powell et al., 2002), business leaders (or "anchors") or "pioneer" entrepreneurs (Feldman,

⁶ On this, see, among others: Feldman and Francis (2002); Hamdouch and Moulaert (2006); OECD (2007).

⁷ Dodgson et al. (2008) made exactly the same findings in relation to Taiwanese bioclusters.
⁸ This has led Niosi and Bas (2001) to the conclusion that, in Canada, only major regional metropolises that are dynamic in the biotechnology field should implement sustained clustering policies supported at national level. The studies made into the BioRegio competition (Dohse, 2000; Zeller, 2001; Kaiser and Prange, 2004) seem to confirm this recommendation, even if BioRegio does not entirely explain the competitiveness of the German biotechnology sector. For a more theoretical argument on "coalition optimal size", see Hamdouch (2002).

2003; Stuart and Sorenson, 2003; Waluszewski, 2004; Wolfe and Gertler, 2004; Jong, 2006) and dense social networks (Liebeskind et al., 1996; Owen-Smith et al., 2002; Waxell and Malmberg, 2007; Ter Wal and Boschma, 2009b) within the cluster also has a significant impact.

It is in fact generally around these components that clusters are formed, develop and take root. Casper and Murray (2005) explain the superiority of the Cambridge biocluster over the Munich biocluster by the presence (Cambridge) or not (Munich) of large pharmaceutical companies in the cluster. For Owen-Smith et al. (2002), the development differential of the biotechnology sector between the US and Europe can be explained by the degree of the internal therapeutic specialization of the clusters. It also stems from the different nature of the existing links between university research, public research and the private sector. Indeed, in the US, there is a wider therapeutic and organizational diversity (with in particular a greater proportion of biotechnology companies, venture capital companies, business angels and research foundations) than in Europe. That is why, according to the authors, American clusters, which cover a diverse range of therapeutic fields and include a large number of heterogeneous stakeholders 10 seem more viable and effective than European clusters, which are more specialized (from a disciplinary or therapeutic point of view) and less diversified (from an organizational point of view). In fact, the complementarities (particularly in terms of knowledge, resources and/or skills) between the members of a biocluster appear to be crucial in numerous studies¹¹

This forms the basis for Jong's (2006) explanation as to why most "pioneering" biotechnology companies in California are from the San Francisco region rather than the neighboring regions of Berkeley and Stanford. Otherwise, as demonstrated by Paytas et al. (2004), the impact of universities on the local development of innovative companies within a cluster depends in large part on the "alignment" between the fields of expertise of university research departments and the fields of specialization of the companies (for a similar point of view, see: Audretsch, 2001; Romanelli and Khessina, 2005).

Other studies focus on the central role played by the cognitive quality and the mobility of researchers, engineers, technicians and managers within the cluster (Dicken and Malmberg, 2001; Zeller, 2001; Wolfe and Gertler, 2004;

¹⁰ The heterogeneity (organizational and/or cognitive) of stakeholders characterizes what some authors (see: Malmberg and Maskell, 2002; Bathelt and Taylor, 2002) call the "vertical dimension" of clusters.

⁹ In the US, the philanthropic foundations have always played (and still play) a vital role in terms of biomedical research (see Morange, 2000).

¹¹ This idea, according to which the industrial diversification of the cluster (and therefore of available professions and skills) promotes the individual innovation capacity of innovation stakeholders, is not generally agreed upon. Baptista and Swann (1998), for example, while agreeing that a company has a greater chance of being innovative if employment linked to its specific sector is available in the region in which it is located, do not find a convincing relationship between the degree of the cluster's industrial diversification and the strong innovative tendencies of businesses. In the same way, Phlippen and van der Knaap (2007) show that technological and therapeutic diversity only have a positive effect within "relatively small clusters".

Casper and Murray, 2005; Waxell and Malmberg, 2007). The existence of a wide and diverse local employment market, which gives rise to a turnover of researchers and the formation of social networks, often ensures the dynamism and sustainability of a cluster because it fosters the dissemination of knowledge and facilitates interaction.

Some clusters, lastly, perform better than others because of their internal organizational (or governance) practices. Very often, in fact, the effectiveness of the mechanisms governing coordination and cooperation between innovation stakeholders (at each spatial level in question), the balance established between centralized and decentralized decision-making within the cluster and the cluster's capacity to adapt over the long-term, seem to play a decisive role in its future performance (or otherwise) (see e.g.: Zeller, 2001; Paytas et al., 2004; Glaeser, 2005). Hence the importance of public, part-government owned and private support stakeholders (local authorities and institutions, business service organizations, technology transfer institutions, business incubators, think tanks, etc.), infrastructures (property, transport, etc.), venture capital, consulting and law firms, which act as coordinators, "go-betweens" (or "intermediaries"), advisors, scrutinizers and "proselytes" within the cluster (Wolfe and Gertler, 2004; Hamdouch and Moulaert, 2006; Waxell and Malmberg, 2007; Champenois, 2008).

In total, as these various studies tend to show, (bio)clusters are basically the result of different approaches (scientific and technological, economic and financial, historical and institutional) and mechanisms (both top-down and bottom-up), which are largely contingent, often interdependent on and co-evolve with each other, and most of which already existed or were established concomitantly with the clusters. Clusters are consequently intrinsically complex and idiosyncratic phenomena resulting from a process that is often self-organizing (Feldman and Francis, 2002). This also explains their chronic (Longhi, 1999) or even chaotic (Stuart and Sorenson, 2003) instability ¹². For all of these reasons, clusters do not represent a sinecure, and even less a panacea (Martin and Sunley, 2003), particularly for public authorities wishing to place them at the centre of their innovation policies (Bathelt and Taylor, 2002).

3. GEOGRAPHICAL PROXIMITY IS NEITHER SUFFICIENT NOR ALWAYS NECESSARY FOR INNOVATION

The prevailing wisdom about clusters is based on a second presumption, which also needs to be put into perspective. According to this idea, the colocation of actors (that is, their geographical proximity) within a cluster is a decisive factor in the knowledge production/ dissemination/ accumulation process because it would automatically generate the positive externalities of localization and (spatial) proximity effects (see Section 1 above).

¹² It also sometimes accounts for their temporary and transient nature (Asheim, 2002; Bathelt and Taylor, 2002; Maskell et al., 2004). This hypothesis is, however, the subject of debate, in as much as clusters, even "end-of-cycle" clusters, do not generally "die": they are transformed, except in rare cases of a territory's socio-economic desertification.

240

Once again, some recent works refute (or qualify) this hypothesis by putting forward a series of six complementary arguments — in addition to those already outlined (see Section 2 above), according to which the innovation process is only viable under certain conditions.

- 1) Firstly, the geographical proximity of innovation stakeholders alone in no way indicates the existence of a cluster. This is particularly the case when these stakeholders do not share the same skills and fields of specialization (Paytas et al., 2004) or if the "chemistry is not right" to work together effectively (Longhi, 1999)¹³. In fact, within the same cluster, the nature of the relationships between the actors counts for more than their geographical proximity (Zucker et al., 1994).
- 2) Conversely, actors based relatively far away geographically can perfectly well maintain "strong links" (in terms of resources, knowledge, technology, skills and expertise), including within the framework of a production or innovation process involving collaborations or exchanges (physical or virtual¹⁴) on a regular and/or long-term basis (Asheim, 2002; Bathelt et al., 2004; Bresnahan et al., 2004; Coenen et al., 2004; Maskell et al., 2004; Niosi and Zhegu, 2005; Ernst, 2006; Glückler, 2007; Hamdouch, 2010).

In fact, the various actors in clusters are, very often, not all co-located (even if they usually are), which does not prevent them from closely interacting (physically and/or virtually) in a formal and/or informal manner, and codifying and exchanging knowledge and/or skills, sometimes tacitly (Breschi and Lissoni, 2001; Torre, 2006; Hamdouch, 2010). A study by Audretsch and Stephan (1996) shows that 70% of formal links between academics and American biotechnology companies are formed outside the local framework. More generally, most studies (see for example: Tether, 2002; Freel, 2003; Gay and Dousset, 2005; Roijakkers and Hagedoorn, 2006) show that stakeholders in cooperation networks mostly collaborate with partners who are not located in the same agglomeration or region (see Section 4 below), particularly when the latter are relatively specialized (Phlippen and Knaap, 2007) – and that, as a consequence, it is necessary to look "elsewhere" for the knowledge, skills and resources required in order to innovate (Hussler and Rondé, 2005) -, or when the actors are more inclined towards operation or imitation rather than exploring new opportunities (Lévêque et al., 1996).

¹⁴ Learning plays an increasingly central role within virtual networks of actors electronically connected to each other via fibre optics, information networks, satellites, and virtual reality and videoconferencing systems (Passiante and Secundo, 2002; Amin and Cohendet, 2005).

¹³ In other words, just as a cluster cannot be mandated (see Section 2 above), it is impossible to force two actors to work together simply because they are neighbors.

videoconferencing systems (Passiante and Secundo, 2002; Amin and Cohendet, 2005).

This is particularly the case with "temporary clusters" (Maskell et al., 2004), "global lifeworlds" [or "market conventions 'at a distance"] (Lagendijk, 2002), "restricted technological, organizational or professional 'space'" (Storper, 1997), epistemic community or community of practice (see Wenger and Snyder, 2000).

- 3) In addition, as highlighted by Markusen (1996) and Torre (2006), co-location can sometimes be the result of highly diverse factors far removed from the desire to transfer knowledge (for example, attractive property prices, tax cuts, the quality of the local employment market, the "critical size" of the outlets offered by the local market, the reputation of the cluster). It can even, in certain cases, be the result either of a "historical accident" or a "non-choice" (Champenois, 2008), of purely subjective individual factors (Autant-Bernard et al., 2008), or even of a "copycat effect" (Appold, 2005; Gertler and Levitte, 2005) of "chain location" (Caplin and Leahy, 1998).
- 4) Next, there is certainly a non-linear relationship between geographic distance and knowledge flows to the extent that, beyond a certain threshold (not to say intrinsically), spatial proximity no longer has an impact (or a sufficient impact) on the dissemination of knowledge and the capacity to innovate (Madiès and Prager, 2008). As stated by Oinas (1999, p. 364), many studies (see for example: Grotz and Braun, 1997; Suarez-Villa and Walrod, 1997) have shown that "local relationships are actually 'missing' where hypotheses suggest that they might exist or such local relationships do not as clearly correlate with the innovativeness/performance expected".

Other studies have also shown that, in some cases, spatial proximity may even give rise to negative agglomeration externalities (or agglomeration diseconomies) (see: Swann and Prevezer, 1996; Uzzi, 1997; Nooteboom, 2000; Bathelt and Taylor, 2002; Boschma 2005; Hassink, 2005; Martin and Sunley, 2006; Torre, 2006): industrial espionage; cognitive "hold-up"; congestion effects; cut-throat competition; saturated local markets; laying-off of qualified staff; geographic and/or industrial lock-in; inertia, organizational entropy and isomorphism; over-embeddedness, under-socialization, over-emphasis, blind confidence and gullibility of stakeholders; "distanced neighbor" paradox; etc.

This "weakness of strong ties" – to borrow from Grabher (1993), echoing the "strength of weak ties" advanced by Granovetter (1973) – to which excessive spatial proximity often gives rise, occurs particularly when innovation stakeholders are engaged in a routine process of utilizing knowledge and innovations (Bathelt and Taylor, 2002).

5) In addition, although spatial proximity appears to be a permissive condition for interaction between innovation stakeholders and although, as a result, it appears to facilitate the establishment and operation of interactions (intraorganizational and inter-organizational) between the actors, at the same time, it generally cannot transform them into "actual" interactions unless it is combined with other forms of proximity.

In fact, as highlighted by followers of the "French school of proximity" (see e.g.: Filippi and Torre, 2003; Torre, 2006), proximity should not be understood according to its sole spatial and geographic dimension (on this, see also: Breschi and Lissoni, 2001; Coenen et al., 2004; Zeller, 2004; Boschma, 2005; Hussler and Rondé, 2005; Moodysson and Jonsson, 2007).

This is because, on the one hand, geographic space is an economic and sociocultural reality that reflects the economic and geographic separation of the stakeholders (individuals, organizations, institutions) and the relationships that bring them closer together (and/or places them further apart) when solving a given economic problem (Gilly and Torre, 2000) at a given moment (Dicken et al., 2001). This "spatial reality" is therefore to a large extent conditioned by the role of institutions (Torre, 2006). On the other hand, the idea of proximity also covers other forms at least as important as the geographical proximity. It is the case of organizational proximity, that refers to the concept of belonging to the same organization, to the same network or, more generally, to sharing the same "community of destiny". Equally crucial is cognitive (or technological) proximity, referring here to the adherence of various actors to the same idea of innovation, to the same paradigm (technological and/or organizational), routines, heuristics, algorithms of thought, conventions, traditions, beliefs, internal codes, languages and/or learning, deliberation, decision-making and governance processes (Depret and Hamdouch, 2004). Cognitive proximity therefore exists within organizations, networks and communities, that is, between various social actors of an innovation process.

Moreover, without organizational and cognitive proximity, spatial proximity has a tendency to remain inactive (Filippi and Torre, 2003) – like two neighboring actors that do not belong to the same organization (or the same network) and do not understand each other cognitively or, more often, like people in the same neighborhood who are unaware of each others' existence (Hamdouch, 2010). In the same way, without geographical or cognitive proximity, organizational proximity alone seems highly unlikely – like two employees in the same company (or the same network) or two companies in the same cluster or the same network that do not have any form of interpersonal contact (formal or informal) because of the distance between them and a lack of common values, rules or languages. Lastly, cognitive proximity without geographical and organizational proximity (such as two stakeholders who, despite being cognitively close, are remote geographically and organizationally) is not generally sufficient and may sometimes be dangerous (risk of sclerosis or organizational inertia; see Boschma, 2005).

Other studies show also that the role played by geographical proximity in the biopharmaceutical industry tends in fact to decrease over time (Lemarié et al., 2001; Sørenson, 2003; Ter Wal and Boschma, 2009a; Aharonson et al., 2008) – that is, after the first stages of the lifecycle of the company, sector or cluster during which the innovation social networks are essentially local and relatively closed to the outside – in favor of, initially, organizational proximity and, subsequently, cognitive proximity.

In this regard, the effectiveness of a cluster cannot be assessed solely on the basis of the degree of spatial proximity between its members. In fact, the most efficient clusters – and/or the most "creative" ones (Fleming et al., 2004) – are generally those that offer to their members spatial, organizational (through networks, even informal ones) and cognitive (by adhering to the same "weltan-schauung" [i.e. a "vision (or perception) of the world"]) proximity to innovation

or the same objectives in the mid- to long-term – on condition that the "environment" (scientific and technological, social and institutional, economic and financial) is favorable (see Section 2 above).

6) Lastly, it should be pointed out that there are other less "geocentric" types of coordination for innovation stakeholders which, on the one hand, go beyond the traditional boundaries of clusters and local innovation networks and, on the other hand, are often necessary to set in motion virtuous innovation dynamics (see Sections 4 and 5 below).

On the whole, the various innovation stakeholders need to reach various compromises between their local commitments and their integration into an increasingly global economy, between spatial proximity and other forms of proximity, and between their embeddedness (or even over-embeddedness) within clusters and their openness to the outside world. This is precisely what we will attempt to show now by underlining the actual diversity, both organizational and cognitive, dynamic nature and openness of clusters.

4. THE CLUSTER: A POLYMORPHIC AND NETWORKED ENTITY

In parallel with the criticisms outlined above, the traditional "naturalist" vision (see Torre, 2006) of clusters can also be criticized for its too clearly "centripetal" conception. As such, clusters and networks are too often perceived as overly static in terms of their development (1) or too narrow in their composition (2) and diversity (3).

1) In reality, clusters in general (and bioclusters, analyzed specifically here) have particularly pronounced evolutionary properties. Just like networks (Glückler, 2007), clusters are developed and transformed over time ¹⁶, but also in space (Dicken et al., 2001; Bathelt and Taylor, 2002; Ter Wal and Boschma, 2009a, 2009b).

They are characterized, however, by a certain "dynamic stability" (Hamdouch and Depret, 2002) in the sense that their components can change without losing their identity and without systematically harming the uniqueness, flexibility and pliability of their architecture, or without compromising their capacity for action and to adapt themselves to external stimuli.

2) At the same time, (bio)clusters are often considered to be simple organizational groupings (fairly closed or autarkic) of agents (fairly passive, homogenous, undifferentiated or depersonalized). Whereas in reality they often group together all stakeholders (organizations, institutions, individuals) involved or participating in (nearby or remotely) the innovation process – including institutions (financial, legal and regulatory) and service provider partners (supplying expertise, assessment, advice, training services, etc.), who influence (even indirectly) the initiation, support and operation of these clusters.

¹⁶ For some authors, the dynamic development of clusters forms part of a lifecycle (see for example: Pouder and St John, 1996; Porter, 1998; Ter Wal and Boschma, 2009a, 2009b).

As such, and building on the definition of clusters given in the introduction, *bioclusters* can be considered as combinations of networks comprising a potentially large variety of innovation stakeholders:

- who interact (formally and/or informally) within the framework of occasional or regular relationships, both inter-organizational and intra-organizational;
- who are defined by their specific organizational nature, their history, their domains of specialization an their specific resources and capabilities, their geographic location, and their scientific, institutional and socioeconomic environment;
- and who contribute to the performance of activities (R&D, production, commercialization, funding, etc.) in a particular area (therapeutic, technological or economic) defined by specific fields of resources, knowledge, competences and technologies.
- 3) Bioclusters are, lastly, much more polymorphic than they are generally portrayed in research literature. They can, in fact, take multiple forms, which themselves can be broken down into more specific forms according to the nature (formal/informal, strong/weak) of the relationships established between their members, the reasons why the members take part in the cluster, the nature of their proximity (geographic, organizational and/or cognitive) and the spatial scale (local, regional, multinational and global) of which these forms are part (see Hamdouch, 2010).

It is this multiscalar and evolutionary dimension (which is particularly operating within the biopharmaceutical industry) that is examined with some detail in the next section.

5. CLUSTERS AS SPATIAL AND INTERACTIONAL MULTISCALAR NETWORKS

Last but not least, the majority of research work devoted to clusters (in all their forms) generally presents them as being firmly rooted in a territory (geographic and/or sectoral) fairly spread out locally, but always relatively well defined in most approaches¹⁷. The emphasis is placed, on the one hand, on the decisive role played by co-location, geographical proximity and spatial clustering effects (see Section 3 above), and on the other hand, on the formative importance of territorialized dynamics (scientific and technological, social and institutional, economic and financial).

Most of this research work does not, however, exclude (far from it) other territorial innovation dynamics. However, the links between the different spatial scales are often neglected in those papers, although they appear to us to be of fundamental importance. Indeed, several authors openly consider that clusters (or other forms of territorial innovation systems) interlink with each other or, at the very least, must be envisaged on several spatial scales. From this perspec-

¹⁷ This criticism can also be addressed to most of the works devoted to other "territorial innovation systems" (Depret et al., 2009).

tive, "non-local relationships may be as important as local ones for the success of firms and their (...) environments" (Oinas, 2002, p. 66). Consequently, it is no longer so much the co-location of innovation stakeholders that counts as the nature and intensity of their "connectivity" and the fact of belonging to the same social innovation network, "interlinked community" (Amin and Cohendet, 2005) or "innovation system" and/or adhering to the same technological paradigm. Clusters appear in the form of combinations of spatial (that is, locally and regionally established, but also open to other regions and internationally) and interactional (that is, grouping various heterogeneous stakeholders) multiscalar social and inter-organizational networks (Hamdouch, 2010).

5.1. The necessary openness of networks and clusters ...

Several series of recent studies point towards the hypothesis of the multiscale openness – or "permeability" (Bathelt and Taylor, 2002) – of clusters and innovation networks. We are referring, first of all, to research performed by various authors that shows that what they respectively call "multiplex relationships" (Uzzi, 1997), "spatial innovation systems" (Oinas and Malecki, 2002), "systems of governance" (Dicken and Malmberg, 2001), "networks of linkages "(Nachum and Keeble, 2003), "selection environments "(McKelvey, 2004), "creative fields" (Scott, 2006) or "fields of interaction" (Waxell and Malmberg, 2007) generally operate at several spatial levels (see also Pohoryles, 2001; Zeller, 2004)¹⁸, even extending along a "continuum of scales" (Dicken and Malmberg, 2001).

In this context, clusters may be seen as "a complex intermingling of different geographical scales (global, regional, national and local)" (Dicken et al., 2001, p. 95). They represent a sort of "broader institutional matrix" (Wolfe and Gertler, 2004) combining a local, regional, national and, often, supranational dimension¹⁹ – to the extent that only some clusters are actually self-sufficient (in terms of competences in particular). The different spatial scales therefore fit together, one inside the other – see the notion of "nested (geographical) scales"

¹⁸ Scott (2006) states however that the urban and regional space is no doubt the most significant. Yet we would point out that there is no consensus on this hypothesis since, for some, national and/or international relationships are sometimes stronger than local or regional relationships (Keeble et al., 1998; Hendry et al., 2000). This is especially the case when innovation stakeholders are located in "international cities" (Simmie et al., 2002). On the other hand, when stakeholders are located in regional cities, the relevant geographic scale is more local or regional. For Malerba (2005) or Waxell and Malmberg (2007), the relevant geographic scale depends on the nature of the "fields of interaction" considered: more local for interactions within the employment market and social interaction; mainly regional (or national) for financial and institutional interaction; and more global for industrial and "cognitive" relationships. Lastly, for other authors, the relevant geographic scale depends on the "maturity" of the innovation stakeholders and therefore the stage reached in the "lifecycle" of the sector, technology or system under consideration (Owen-Smith et al., 2002; Gertler and Levitte, 2005; Coenen et al., 2006; DeMartino et al., 2006; Waxell and Malmberg, 2007).

¹⁹ Pohoryles (2001, p. 31) argues a similar point, defining the "knowledge production system" as "complex interactions and interdependencies between actors positioned at three levels of social aggregation – institutional, national and international – and the interactions between these levels" (see Hamdouch and Moulaert, 2006).

identified by Bunnell and Coe (2001) and by Dicken et al. (2001) building on the work of Swyngedouw (1997) -, while impacting on each other (Wolfe and Gertler, 2004), taking into consideration their intermingling, overlapping and interpenetration (Dicken et al., 2001), their interdependence (Moodysson and Jonsson, 2007) or their interconnection (Coenen et al., 2006). In other words, "these scales, and the relations between them, are not fixed, but instead are fluid, contested and perpetually being transgressed" (Coe, 2000, p. 394). As stated by Asheim and Gertler (2005, p. 315), "regional innovation systems are not sufficient on their own to remain competitive in a globalizing economy. Production systems seem to be more important than innovation systems at the regional level. Thus local firms must also have access to national and supranational innovation systems, as well as to corporate innovation systems from the local firms that have been brought. This line of reasoning is followed to a point where the regional innovation system expands beyond its own boundaries through a process of economic integration and globalization." From this clearly "scalar perspective" (Swyngedouw, 1997; Lagendijk, 2002), innovation networks and clusters "transcend" the different spatial scales (Dicken et al., 2001).

This view is also held by a number of authors (see: Gertler et al., 2000; Hendry et al., 2000; Bathelt et al., 2004; Coe et al., 2004; Coenen et al., 2004, 2006; Maskell et al., 2004; Wolfe and Gertler, 2004; Zeller, 2004; Amin and Cohendet, 2005; Asheim and Gertler, 2005; Bathelt, 2005; Cooke, 2005; Benneworth and Hospers, 2007; Phlippen and van der Knaap, 2007; Waxell and Malmberg, 2007) who show that, in some clusters, external exchanges (formal or informal) – through "trans-local pipelines", "global pipelines", "global bridgings" and "mobile brokerings" – are often more favorable to transfers of (certain forms of) knowledge than the cluster's internal exchanges – based on the "local buzz" (Storper and Venables, 2004), also called "noise" (Grabher, 2002), "local broadcasting" (Owen-Smith and Powell, 2002), "local brokering" and "local bridging" (Glückler, 2007). In fact, local exchanges are often based on weak or routine links that only rarely (Bathelt et al., 2004) or insufficiently (Asheim, 2002) foster learning, knowledge transfer, and synergetic effects and, therefore, major innovations²⁰.

For other authors, the opening of networks and clusters is a "natural" phenomenon that forms part of their "lifecycle". Owen-Smith et al. (2002) show that local intra-cluster links generally tend to decline in significance at the end of the cluster's initial local construction phase in favor of more diversified (from an organizational and cognitive point of view) and more geographically distant links, which often take the form of a network. They also point out that a

²⁰ Some authors stress the risk, for local stakeholders, of a progressive and often irreversible cognitive lock-in within the cluster and/or network (see the phenomena of "over-embeddedness" [Uzzi, 1997], "over-socialization" [Granovetter, 1985], "over-emphasis of the local market" and "distanced neighbor' paradox" highlighted by Bathelt [2005]), which is sometimes fatal (see the notion of "entropic death" mentioned by Camagni [1991]). Worse, "[certain] clusters contain the seeds of their own destruction and may potentially disappear or die (...) if they [don't] develop ways to access external markets, adjust power relations in a fluid way and reproduce [their] structures through 'powerful' institutions" (Bathelt and Taylor, 2002, p. 106, our square brackets).

cluster can, from the time it is formed or very quickly after, be structured (then developed) around an interregional (see also below the case of Medicon Valley - located in both Denmark and Sweden), or even an international multi-spatial dynamics (see also: Zeller, 2004; Fontes, 2005; Scott, 2006; Glückler, 2007). For their part, Gertler and Levitte (2005) show that inter-organizational relationships within clusters and networks (within the Canadian biotechnology industry) tend to become, over time, increasingly "non-local". Coenen et al. (2006) draw the same conclusion in their comparative study of bioclusters in the province of Skåneland and the city of Saskatoon in Canada. These authors show, in particular, that this extra-regional openness generally takes place gradually as part of a "concentric circles" dynamics. The Medicon Valley cluster is a good example of such evolution (Moodysson and Jonsson, 2007): it opened up by developing relationships (measured by co-publications by members of the cluster together with organizations located outside the cluster) initially with clusters in Stockholm/Uppsala and Frankfurt and subsequently with clusters in London, Munich, Goteborg and Oslo. The same is true for Waxell and Malmberg (2007) in their study of the Uppsala cluster in Sweden, which reveals that, for this cluster's young biotechnology businesses, the "local environment" is the benchmark space. In contrast, as soon as they enter into a dynamic of growth and internationalization, they develop mainly outside the local environment – see also DeMartino et al. (2006) for a similar conclusion in relation to the photonics industry in the State of New York.

For others, the openness of networks and clusters in biopharmaceuticals results from the degree of specialization (technological and/or therapeutic) of clusters and networks – and, as a consequence, is therefore inherent in the nature of the "sectoral innovation system" (Malerba, 2005). Phlippen and van der Knaap (2007) thus show that, in Europe, the most specialized bioclusters are generally more open – that is, the number of non-local links is proportionally greater – than more diversified clusters.

Apart from these differences, all of these authors share the same idea, according to which the openness (to the "outside" world) of social networks and clusters does not necessarily translate into a reduction of the intensity and density of local links between members of the cluster. In contrast, as illustrated by the example of the biocluster in Boston, this openness may represent a factor in making inter-organizational relationships more viable and stronger (see: Owen-Smith et al., 2002; Owen-Smith and Powell, 2002, 2004; Powell et al. 2002). Moodysson and Jonsson (2007) even estimate that public authorities would gain by encouraging local innovation stakeholders to play a greater role in the "global arena" rather than to vainly attempt to "foster" the formation of "'second-best' local networks'".

²¹ This reconnects with the idea (outlined above) according to which geographical proximity decreases over time in favor of other forms of proximity (organizational and cognitive, in particular).

lar).

²² A commitment to ensuring innovation clusters (created as a result of proactive policies, as is the case in Europe – at European Union level and within certain member countries –, in China and Japan) adhere to the principles of openness and international competitiveness also reveals a great-

5.2. ... Is striking in the biopharmaceutical industry ...

In the biopharmaceutical industry, the "openness" of innovation networks and clusters has been the subject of numerous recent empirical studies²³ that highlight the networked, dynamic, polymorphic and multiscalar nature of certain bioclusters (for a review of these studies, see Hamdouch, 2008)²⁴.

All of these particularly well-documented studies share the distinction of showing that biopharmaceutical clusters tend to broaden their scope to include other spatial scales through a broader range of interregional, national, international or global formal and/or informal relationships. This is particularly the case for integrated or polycentric networks that exist within the biopharmaceutical industry. This form of network is generally more (organizationally) complex and more dynamic (that is, co-evolving with other factors) than other forms of clusters and networks (see Hamdouch, 2010). This is because, on the one hand, their organizational "perimeter" changes over time and in space. This concurs with the hypothesis of the (space/time) co-evolution of networks and clusters put forward by Ter Wal and Boschma (2009a, 2009b). It is also due, on the other hand, to the fact that, within the network, several dynamic "circles" of relationships cohabitate, link up and co-evolve (Hamdouch, 2010): some are dense, close and regular – called "small world" networks (see: Watts and Strogatz, 1998; Watts, 1999) or "cliques" (see Burt, 1992) –; others are looser, more distant and occasional networks - corresponding to the "weak ties" highlighted by Granovetter (1973) –; others, lastly, are relatively fortuitous, random or virtual – as in "scale free networks" (see Albert and Barabasi, 2002). Thus, as stressed by Glückler (2007, p. 627, our square brackets), "the major source of contingency and variation in a network structure is the bridging [and brokering] of unconnected network clusters [or parts of networks]". From this renewed evolutionist perspective – which breaks with the traditional view of interfirm networks presented as "small worlds which are essentially characterized by high local clustering and short global separation (Watts, 1999) and display a high

er willingness on the part of local and regional stakeholders to take part in international or global research and innovation networks.

23 This includes for example works the content of the content of

²⁴ It should be noted that these different studies relate to bioclusters located both in countries (or regions) that are leaders or pioneers of the biotechnology economy (Massachusetts, California, Switzerland, Canada, Germany, France) as well as countries (or regions) less or more recently involved in the "genome race" (Australia, Israel, Sweden, Singapore, Scotland, Portugal). This would tend to show the relatively universal (or natural) character of the (interregional or international) opening process for bioclusters.

²³ This includes, for example, works dedicated to bioclusters in Boston (Owen-Smith and Powell, 2002, 2004; Powell et al., 2002), Saskatoon (Ryan and Phillips, 2003; Coenen et al., 2006); Medicon Valley (Coenen et al., 2004, 2006; Moodysson et al., 2008; Moodysson and Jonsson, 2007), Uppsala (Waluszewski, 2004; Eliasson and Eliasson, 2006; Waxell and Malmberg, 2007), San Diego (Zeller, 2004), Singapore (Finegold et al., 2004), Basel (Cooke, 2005), Vancouver (Rees, 2005), Melbourne (Gilding, 2008), Sophia-Antipolis (Ter Wal, 2010), etc. It also includes studies devoted to bioclusters in Germany (Zeller, 2001), Israel (Kaufmann et al., 2003), Sweden (McKelvey et al., 2003; McKelvey, 2004), Scotland (Leibovitz, 2004), Australia (McKelvey, 2004), Portugal (Fontes, 2005), Austria (Trippl and Tödtling, 2007) and European bioclusters (Phlippen and van der Knaap, 2007).

degree of robustness (Kogut and Walker, 2001)" (Glückler, 2007, p. 626) –, "while networks are embedded within territories, territories are, at the same time, embedded into networks" (Dicken et al., 2001, p. 97)²⁵, so that "the global economy is constituted by [a variety of] 'spaces of networks relations'" (ibid., our square brackets).

These works also highlight a relatively greater degree of openness of clusters and innovation networks in the biopharmaceutical industry, compared with other sectors. There are at least three possible complementary explanations for this phenomenon, which can also be seen in other innovative sectors (Depret and Hamdouch, 2009).

Firstly, in this sector in particular, geographic borders have tended for several years to become more permeable to the influence of external factors (Hamdouch and Depret, 2001). As a result, they increasingly subject national and regional spaces to these developments (scientific, technological, institutional, social, economic, financial, strategic and organizational) in part influenced by dynamics outside the territories: strategies of multinational firms, monetary and economic developments at a global level, regional integration policies and their effects, free trade agreements, etc. (Hamdouch and Moulaert, 2006).

At the same time, the growing spatial interdependencies of various innovation stakeholders – intensified, on the one hand, by the processes of interregional integration, economic globalization and corporate internationalization and networking, and, on the other hand, by decentralization policies (political, administrative, economic and social) – tend to redefine the space and the means of expression of their respective rationalities and the ways in which they interact and, as a result, to interlink different spatial levels in determining and developing these institutional frameworks within which the innovation processes take place in territories (ibid.).

The openness of bioclusters can, lastly, be interpreted as the result of an extremely uncertain and competitive environment in the biopharmaceutical sector (Hamdouch and Depret, 2001). On the one hand, this is due to the difficulties encountered in this sector by a certain number of innovation stakeholders in gaining access to resources (financial²⁶ and human resources in particular), knowledge, skills and technology, as well as to outlets within their cluster. On the other hand, it stems from their pressing need to keep up with the latest practices in the sector (benchmarking), to spot promising future "(bio)technological solutions" and to form closer ties with future markets.

Within this context, the potential for innovation and the competitive positioning of biopharmaceutical innovation actors lie increasingly in their differen-

ler, 2007, p. 22).

²⁶ Powell et al. (2002) have shown that biotechnology companies financed by venture capital companies outside of their cluster of origin were generally more mature, bigger and positioned more downstream of the R&D process than biotechnology companies financed by local investors.

²⁵ As Storper and Walker (1989) demonstrated more than twenty years ago, "places do not only constrain network formation but social interaction in networks also shape its geography" (Glückler, 2007, p. 22).

tiated capacity to work with a wide variety of partners - those with key complementary skills and significant specific resources, and/or benefiting from competitive advantages in terms of location (Hamdouch, 2002). This reveals the importance of coalitions and networks (of a highly varied nature) that go beyond geographic borders and therefore the territorialized dynamic of clusters.

5.3. ... But is not enough to trigger virtuous and sustainable innovation dynamics

This necessary openness of networks and clusters is not, however, sufficient to trigger and ensure the long-term viability of virtuous innovation dynamics.

Building on the work already produced by Alger (1988) and Amin and Thrift (1992), Gertler and Levitte (2005) show that the probability of innovating is greater for Canadian biotechnology companies benefiting from a favorable "local *milieu*"²⁷, but also from close links with "global networks of knowledge, capital and people". Nachum and Keeble (2003) develop more or less the same idea in their study devoted to the London media industry. They show that, in this sector, there are several local "neo-Marshallian" clusters linked to "global networks" structured by multinational companies in the sector²⁸. The importance of the combination/ complementarity of skills and local and non-local knowledge within clusters and networks has also been highlighted in other recent studies devoted to oil complexes (Cumbers et al., 2003) and various industries considered in multiple regions or countries: mechanical engineering in Germany (Grotz and Braun, 1997), electronics in California (Suarlez-Villa and Walrod, 1997; Sturgeon, 2003), optoelectronics in three European countries (Hendry et al., 2000), machine tools in the US (Kalafsky and MacPherson, 2002), metalworking in Sheffield (Wood et al., 2004), winegrowing in Chile (Giuliani and Bell, 2005), car industry in the Styria region (Tödtling and Trippl, 2005), chip design in Asia (Ernst, 2006), "knowledge intensive industries" in Ottawa (Doloreux and Mattson, 2008), etc.

In the same way, for Bell and Albu (1999), Bathelt and Taylor (2002) and Giuliani (2005), the dynamism of a cluster depends on the capacity of its members to absorb knowledge (or innovations) outside the cluster²⁹ and to disseminate them subsequently within their own cluster in order to "hybridize" them with the knowledge or innovations developed within the cluster. Consequently, the creation of new knowledge (or the innovation process) can be seen as "a result of a 'combinaison' of close and distant interactions' (Oinas, 1999, p. 365).

See also Coe (2000), Bathelt (2005), Brail and Gertler (1999), Britton (2007), and Vang and Chaminade (2007) for similar analyses devoted to the film and media industries.

²⁷ Some authors also talk about "small local islands of cooperation" (see Bathelt, 2005) or "local webs" (see Keeble et al., 1998).

²⁹ Similarly, Fleming et al. (2004) show that the "creativity" of a territory is all the greater when it is "connected" to a high proportion of "talents" outside the territory (see also Bathelt, 2005).

The linkage/coordination of the different spatial scales therefore represents a key to the virtuous and sustainable innovation dynamics. This has led Bresnahan et al. (2004) to say that the (extra-local) openness of clusters is undoubtedly the key to a successful (local) clustering process (see also: Keeble et al., 1998; Saxenian and Hsu, 2001; Asheim, 2002; Bathelt and Taylor, 2002; Cumbers et al., 2003; Coenen et al., 2004; Giuliani, 2005; Ernst, 2006; Glückler, 2007; Waxell and Malmberg, 2007). In other words, the interregional and international openness of clusters and networks enable "nodal points" (Amin and Thrift, 1992; Lagendijk, 2002; Coenen et al., 2004; Maskell et al., 2004; Gertler and Levitte, 2005) to enter into resonance, such that the global level intensifies the local or regional level... and vice versa (see Coe, 2000). From this point of view, as emphasized by Bathelt (2005), the "local buzz" and "trans-local pipelines" form "double- or triple-loop learning processes".

This "dynamic tension" (Wolfe and Gertler, 2004) between the "local" and the "global" seems to be particularly strong within a context of accelerated globalization, where "global value chains are integrating with regional clusters" (Cooke, 2001, p. 7; see also: Humphrey and Schmitz, 2002; Hamdouch and He, 2009) and where large firms form significant "global oligopolies" (Keeble et al., 1998). This is especially the case when these global connections or networks themselves constitute a "network of networks" (or a "network within networks"), a system ("system within systems") or a global "hub" (Dicken and Malmberg, 2001; McKelvey et al., 2003; Nachum and Keeble, 2003; Coenen et al., 2004; Zeller, 2004; Amin and Cohendet, 2005) – as is the case for numerous biopharmaceutical innovation actors whose resources (cognitive and financial), partners (financial and industrial) and outlets are (sometimes from the moment they are created) international (Lemarié et al., 2001).

This "duality" (Phlippen and van der Knaap, 2007) or this "polycentric spatiality" (Mattsson, 2007) of clusters and biopharmaceutical networks (that is, both locally and regionally embedded and at the same time open internationally or globally) appears to be an essential condition for their effective performance and sustainability. In so doing, far from neutralizing each other, or being mutually exclusive, the local development and the openness of the cluster to the "outside world" seem, on the contrary, to mutually strengthen (Keeble et al., 1998; Bathelt et al., 2004). As Lagendijk quite rightly states (2002, p. 84, our square brackets): "yes, the extra-local [relationships] should be accounted for, but it comes as a supplement to relationships and properties pertaining to the local level". That is why very often there needs to be a balance between the openness and the over-embeddedness of innovation stakeholders within clusters (Bathelt and Taylor, 2002).

³⁰ This opposition takes different forms in the research literature. Lagendijk (2002) contrasts indiscriminately "in here" with "out here", the "regional 'lifeworld" with the "global 'systemworld", the "local world" with the "global world" and "local relationships" with "extra-local relationships". This echoes the traditional contrast between (see above), on the one hand, the "local buzz", the "face-to-face", the "day-to-day", "local broadcasting", "local bridging" and "local brokering", and on the other hand, the "global (or trans-local) pipeline", the "global network", "global bridging" and "mobile brokering".

This balance is generally possible thanks to the structuring role of certain key innovation players. Within the drugs industry, such a role is generally played by major pharmaceutical companies³¹. The latter (highly internationalized, including at the R&D level) play an interface role – as a "node" (see: Coenen et al., 2004, 2006; Maskell et al., 2004; Gertler and Levitte, 2005) or "tertius" (according to the meaning Burt [1992] gives to this term) - between the various clusters and networks in which they participate (via their different R&D and/or production centres). This is the case, for example, with the major Swiss pharmaceutical laboratories (Novartis, the result of a merger between Ciba-Geigy and Sandoz, and Roche) which, for a long time, have built "bridges" – or "open channels" to use the expression of Owen-Smith and Powell (2004) – between clusters on the West coast of the US (San Diego and San Francisco essentially), clusters on the East coast of the US (particularly Boston, New Jersey and Maryland) and European clusters (Basel, Heidelberg, Munich, Fribourg, Oxford, Cambridge, Paris and Strasbourg in particular) (see: Zeller, 2004; Cooke, 2005). These major pharmaceutical companies have as a result managed to reconcile what Asheim and Isaksen (2002) call the "local 'sticky" and "global 'ubiquitous'" approaches. In other words, they have succeeded in creating "sticky places in slippery spaces" – to use the expression fashioned by Markusen (1996) – by combining operating or "routine" approaches (fostered by strong links forged at the local level) and exploration or "breakaway" approaches (made possible by weak links built up at the extra-local level). These major pharmaceutical companies have therefore managed to "remotely control" the global networks that they have themselves helped shape and that they have progressively "opened" (from a spatial as well as an organizational point of view) (Dicken et al., 2001) in order to achieve visibility and viability at the international level.

CONCLUDING REMARKS

The key point established in this paper is that, although clusters and networks represent the essential foundations for innovation dynamics of high-tech sectors in general (Depret and Hamdouch, 2009) – and in the biopharmaceutical industry in particular –, their morphology, their dynamics (or lifecycle) and the way in which they structure innovation processes at the spatial and organizational level are extremely complex and varied. In particular, the multiplicity and nesting of spatial and organizational scales appear to represent a solid dimension for the analysis of the networking and clustering processes of innovation actors in these now globalized sectors. The hypothesis of clusters corresponding, in terms of their emergence, structuring and development, to combinatory

³¹ This role may also be played by venture capital companies (see Section 2 above) and/or (but more rarely) by universities (see Benneworth and Hospers, 2007) or by established biotechnology companies.

³² By using a fairly similar metaphor, Waxell and Malmberg (2007) also highlight how local interaction within a cluster acts "as [a] 'glue' between actors". Other researchers underline the crucial role played by certain organizations or institutions acting as an "anchor" for other innovation stakeholders (see, for example: Feldman, 2003; Wolfe and Gertler, 2004).

dynamics of "multi-scaled networks" (Hamdouch, 2010) at a spatial and "interactional" level finds its theoretical and empirical justification, at least partially, in the arguments discussed in the paper, and as a result opens up a stimulating avenue for future research.

As exemplified by the biopharmaceutical industry case, the "spatial geometry" characterizing the geographical and organizational shapes of innovation dynamics is not only varied, but also fairly flexible within complex-evolutionary space-time configurations linking (through superposing-combining various networks) actors as well as territories. This "evolutionary geogeometry" of innovation dynamics also underlies a wide spectrum of relationships (formal and informal, "strong" and "weak", regular and occasional, social and inter-organizational, etc.) among actors and across territories. Finally, it is quite obvious from the research material examined that such dynamics are building on as much historical, geographical, economic and social "ingredients" as scientific, technological, organizational and strategic sector-based factors.

In this perspective, the hypothesis raised above is both grounded – in its conception as in the way it could be mobilized on a theoretical level and explored in terms of empirical research – on the conviction that the understanding of networking and clustering processes requires both an authentically multidisciplinary approach based on complementary inputs from a wide range of social science fields, and on the possibility to undertake methodologically comparable sectoral investigations.

The basic driving forces behind contemporary innovation dynamics are in fact intertwined mechanisms that assert the need, at a basic level, for interdisciplinary dialogue and collaboration between researchers working on these issues or, more probably, for a more structural integration within research teams and networks that are diversified in terms of skills and open on a cognitive level and geographically. From this point of view, and beyond the social sciences per se, several mathematical and statistical tools proposed by some "hard sciences" (neural networks, genealogies among biological species, relationships within natural ecosystems, chain-reaction modeling of chemical components, electric networks, convergence of laser-rays fields, etc.) may be combined with social sciences approaches and methodologies, and therefore truly help in the analysis of clustering processes – as has been demonstrated in general and one several empirical cases by the "new' science of networks"; see Watts (2004). In short, it is our conviction that the future of research on clusters and innovation networks requires researchers to build (or to participate to) research networks that are themselves multiscalar in nature.

At the same time, the analysis of emergence, structuring and evolution of clusters should be pushed forward by exploring other High-Tech "frontier" sectors, notably cleantech and nanotech, but also some prominent more "established" High-Tech sectors (e.g. ICT and aerospace) or more mature industries (car industry, chemicals, textiles, etc.). Here, it could be useful to compare the morphogenesis of clusters in various sectors at different development stages and

in/across different territories, and assess how multiscalar networking may be crucial or not.

Besides these two challenges, further theoretical and empirical investigation efforts could be engaged in at least two directions.

Firstly, a more systematic and precise (spatiotemporal) mapping of innovation clusters and networks in different sectors should be undertaken. This could also help progress toward a better grounding and illustrating of the varied ways clusters and networks can articulate and shape innovation dynamics within and across more or less nested territorial settings.

Secondly and lastly, one should question the normative consequences on industrial policy design of the various approaches to clustering dynamics. Following Moodysson and Jonsson (2007), one can therefore wonder if public authorities shouldn't better push the members of their local (and also, very often, of modest size) clusters to be integrated in global networks rather than (often vainly) try to constitute "second-best' local networks". The European Commission (2008) is not far from thinking in this way if one refers to its recent strategic claim of privileging the "development of a greater number of World-class clusters". The will of certain countries (Japan, Germany, France, China, etc.) to design their clusters in a more international open and competitive perspective is equally a sign of this orientation toward stronger participation within global innovation clusters and networks.

REFERENCES

- Achilladelis, B., Antonakis, N., 2001, "The Dynamics of Technological Innovation: The Case of the Pharmaceutical Industry", *Research Policy*, 30(4), pp. 535-588.
- Aharonson, B.S., Baum, J.A.C., Plunket, A., 2008, "Inventive and Uninventive Clusters: The Case of Canadian Biotechnology", *Research Policy*, 37(6-7), pp. 1108-1131.
- Albert, R., Barabasi, A.-L., 2002, "Statistical Mechanics of Complex Networks", *Review of Modern Physics*, 74(1), pp. 7-97.
- Alger, C.F., 1988, "Perceiving, Analyzing and Coping with the Local-Global Nexus", *International Social Science Journal*, 40(117), pp. 321-340.
- Amin, A., Cohendet, P., 2005, "Geographies of Knowledge Formation in Firms", *Industry and Innovation*, 12(4), pp. 465-486.
- Amin, A., Thrift, N., 1992, "Neo-Marshallian Nodes in Global Networks", *International Journal of Urban and Regional Research*, 16(4), pp. 571-587.
- Appold, S., 2005, "Location Patterns of US Industrial Research: Mimetic Isomorphism and the Emergence of Geographic Charisma", *Regional Studies*, 39(1), pp. 17-39.

- Asheim, B.T., 2002, "Temporary Organisations and Spatial Embeddedness of Learning and Knowledge Creation", *Geografiska Annaler*, B84(2), pp. 111-124.
- Asheim, B.T., Coenen, L., 2005, "Knowledge Bases and Regional Innovation Systems: Comparing Nordic Clusters", *Research Policy*, 34(8), pp. 1173-1190.
- Asheim, B.T., Gertler, M.S., 2005, "Regional Innovation Systems and the Geographical Foundations of Innovation", in: Fagerberg, J., Mowery, D., Nelson, R.R. (Eds.), *Oxford Handbook of Innovation*, Oxford University Press, Oxford, pp. 291-317.
- Asheim, B.T., Isaksen, A., 2002, "Regional Innovation Systems: The Integration of Local 'Sticky' and Global 'Ubiquitous' Knowledge", *The Journal of Technology Transfer*, 27(1), pp. 77-86.
- Audretsch, D.B., 2001, "The Role of Small Firms in U.S. Biotechnology Clusters", *Small Business Economics*, 17(1-2), pp. 3–15.
- Audretsch, D.B., Stephan, P., 1996, "Company-Scientist Locational Linkages: The Case of Biotechnology", *American Economic Review*, 86(3), pp. 641-652.
- Autant-Bernard, C., Massard, N., Charlot, S., 2008, «Les déterminants géographiques de l'innovation : diffusion spatiale des connaissances et choix de localisation », in : Madiès, T., Prager, J.-C. (Eds.), *Innovation et compétitivité des régions*, La Documentation Française, Paris, pp. 227-265.
- Baptista, R., Swann, P., 1998, "Do Firms in Clusters Innovate More?", *Research Policy*, 27(5), pp. 525–540.
- Bathelt, H., 2005, "Cluster Relations in the Media Industry: Exploring the 'Distanced Neighbour' Paradox in Leipzig", *Regional Studies*, 39(1), pp. 105-127.
- Bathelt, H., Malmberg, A., Maskell, P., 2004, "Clusters and Knowledge: Local Buzz, Global Pipelines and the Process of Knowledge Creation", *Progress in Human Geography*, 28(1), pp. 31-56.
- Bathelt, H., Taylor, M., 2002, "Clusters, Power and Place: Inequality and Local Growth in Time-Space", *Geografiska Annaler*, B84(2), pp. 93-109.
- Bell, M., Albu, M., 1999, "Knowledge Systems and Technological Dynamism in Industrial Clusters in Developping Countries", *World Development*, 27(9), pp. 1715-1734.
- Benneworth, P., Henry, N., 2004, "Where Is the Value Added in the Cluster Approach? Hermeneutic Theorising, Economic Geography and Clusters as a Multiperspectival Approach", *Urban Studies*, 41(5-6), pp. 1011-1023.
- Benneworth, P, Hospers, G.-J., 2007, "The New Economic Geography of Old Industrial Regions: Universities as Global–Local Pipelines", *Environment and Planning*, C 25(6), pp. 779–802.

- Boschma, R.A., 2005, "Proximity and Innovation: A critical assessment", *Regional Studies*, 39(1), pp. 61-74.
- Brail, S.G., Gertler, M.S., 1999, "The Digital Regional Economy: Emergence and Evolution of Toronto's Multimedia Cluster", in: Braczyk, H.-J., Fuchs, G., Wolf, H.-G. (Eds.), *Multimedia and Regional Economic Restructuring*, Routledge, London, pp. 97-130.
- Breschi, S., Lissoni, F., 2001, "Knowledge Spillovers and Innovation Systems: A Critical Survey", *Industrial and Corporate Change*, 10(4), pp. 975-1005.
- Bresnahan, T., Gambardella, A., Saxenian, A., 2004, "Old Economy' Inputs for 'New Economy' Outcomes: Cluster Formation in the New Silicon Valleys", *Industrial and Corporate Change*, 10(4), pp. 835-860.
- Britton, J.N.H., 2007, "Path Dependence and Cluster Adaptation: A Case Study of Toronto's New Media Industry", *International Journal of Entrepreneurship and Innovation Management*, 7(2-5), pp. 272-297.
- Bunnell, T.G., Coe, N.M., 2001, "Spaces and Scales of Innovation", *Progress in Human Geography*, 24(4), 569-589.
- Burt, R.S., 1992, "The Social Structure of Competition", in: Nohria, N., Eccles, R.G. (Eds.), *Networks and Organizations: Structure, Form and Action*, Harvard Business School Press, Boston, pp. 57-91.
- Camagni, R., 1991, "Local Milieu, Uncertainty and Innovation Networks: Toward a New Dynamic Theory of Economic Space", in: Camagni, R. (Ed.), *Innovation Networks: Spatial Perspectives*, Belhaven Press, London, pp. 121-144.
- Caplin, A., Leahy, J., 1998, "Miracle on Sixth Avenue: Information Externalities and Search", *The Economic Journal*, 108(446), pp. 60-74.
- Carrincazeaux, C., Lung, Y., Rallet, A., 2001, "Proximity and Localisation of Corporate R&D Activities", *Research Policy*, 30(5), pp. 777-789.
- Casper, S., Murray, F., 2005, "Careers and Clusters: Analyzing the Career Network Dynamic of Biotechnology Clusters", *Journal of Engineering and Technology Management*, 22(1-2), pp. 51–74.
- Castilla, E., Hwang, H., Granovetter, E., Granovetter, M., 2000, "Social Networks in Silicon Valley", In: Moon-Lee, C., Miller, W. F., Cong Hancock, M., Rowen, H.S. (Eds), *The Silicon Valley Edge*, Stanford University Press, Stanford, pp. 218-247.
- Champenois, C., 2008, «La co-localisation d'entreprises innovantes comme non-choix : L'exemple de l'industrie allemande des biotechnologies », *Géographie Economie Société*, 10(1), pp. 61-86.
- Chiaroni, D., Chiesa, V., 2006, "Forms of Creation of Industrial Clusters in Biotechnology", *Technovation*, 26(9), pp. 1064–1076.

- Coe, N.M., 2000, "The View from out West: Embeddedness, Inter-personal Relations and the Development of an Indigenous Film Industry in Vancouver", *Geoforum*, 31(4), pp. 391-407.
- Coe, N.M., Hess, M., Yeung, H.W.C., Dicken, P., Henderson, J., 2004, "'Globalizing' Regional Development: A Global Production Networks Perspective", *Transactions of the Institute of British Geographers*, 29(4), pp. 468-484.
- Coenen, L., Moodyson, J., Asheim, B.T., 2004, "Nodes, Networks and Proximities: On the Knowledge Dynamics of the Medicon Valley Biotech Cluster", *European Planning Studies*, 12(7), pp. 1003-1018.
- Coenen, L., Moodyson, J., Ryan, C.D., Asheim, B.T., Phillips, P., 2006, "Comparing a Pharmaceutical and an Agro-food Bioregion: On the Importance of Knowledge Bases for Socio-spatial Patterns of Innovation", *Industry and Innovation*, 13(4), pp. 393–414.
- Cohen, W.M., Levinthal, D.A., 1990, "Absorptive Capacity: A New Perspective on Learning and Innovation", *Administrative Science Quarterly*, 35(1), pp. 128-152.
- Cooke, P., 2001, "Regional Innovation Systems, Clusters and Knowledge Economy", *Industrial and Corporate Change*, 10(4), pp. 945–974.
- Cooke, P., 2005, "Regionally Asymmetric Knowledge Capabilities and Open Innovation Exploring 'Globalisation 2': A New Model of Industry Organisation", *Research Policy*, 34, pp. 1128–1149.
- Cumbers, A., Mackinnon, D., Chapman, K., 2003, "Innovation, Collaboration, and Learning in Regional Clusters: A Study of SMEs in the Aberdeen Oil Complex", *Environment and Planning*, A 35(9), pp. 1689–1706.
- DeMartino, R., McHardy Reid, D., Zygliodopoulos, S.C., 2006, "Balancing Localization and Globalization: Exploring the Impact of Firm Internationalization on a Regional Cluster", *Entrepreneurship & Regional Development*, 18(1), 1-24.
- Den Hertog, P., Roelandt ,T.J.A., 1999, "Cluster Analysis and Cluster-based Policy Making: The State of the Art", in: Roelandt T.J.A., den Hertog P. (Eds.), Cluster Analysis and Cluster-based Policy: New Perspectives and Rationale in Innovation Policy, OECD, Paris, pp. 413-427.
- Depret, M.-H., Hamdouch, A., 2004, "Proximités spatiale, organisationnelle et cognitive, réseaux d'innovation et dynamique concurrentielle dans l'industrie biopharmaceutique", *Quatrièmes Journées de la Proximité*: "*Proximité*, réseaux et coordination", Marseille, 17-18 juin, 23 p. (http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1207206)
- Depret, M.-H., Hamdouch, A., 2007, "Changements technologiques, logiques institutionnelles et dynamiques industrielles: esquisse d'une approche co-évolutionnaire appliquée à l'industrie pharmaceutique et aux biotechnologies", *Innovations Cahiers d'Economie de l'Innovation*, 25 (2007-1), pp. 85-109.

- Depret, M.-H., Hamdouch, A., 2009, "Clusters, réseaux d'innovation et dynamiques de proximité dans les secteurs High-Tech: Une revue critique de la littérature récente", *Revue d'Economie Industrielle*, 128, pp. 21-52.
- Depret, M.-H., Hamdouch, A., Monino, J.-L., Poncet, C., 2009, "Regional Policies, Key Levers of Regional Innovation Dynamics", *Regional Studies Association Annual Conference: "Understanding and Shaping Regions: Spatial, Social and Economic Features"*, Leuven, 6-8 April, 33 p. (http://www.regional-studies-assoc.ac.uk/events/leuven09/papers/Hamdouch.pdf.)
- Dicken, P., Kelly, P.F., Olds, K., Yeung, H.W.-C., 2001, "Chains and Networks, Territories and Scales: Towards a Relational Framework for Analyzing the Global Economy", *Global Networks*, 1(2), pp. 89-112.
- Dicken, P., Malmberg, A., 2001, "Firms in Territories: A Relational Perspective", *Economic Geography*, 77(4), pp. 345-363.
- DiMasi, J. A., Grabowski, H.G., 2007, "The Cost of Biopharmaceutical R&D: Is Biotech Different?", *Managerial and Decision Economics*, 28(4-5), pp. 469-479.
- DiMasi, J. A., Hansen, R. W., Grabowski, H. G., 2003, "The Price of Innovation: New Estimates of Drug Development Costs", *Journal of Health Economics*, 22(2), pp. 151-185.
- Dohse, D., 2000, "Technology Policy and the Regions: The case of the BioRegio Contest", *Research Policy*, 29(9), pp. 1111-1133.
- Doloreux, D., Mattson, H., 2008, "To What Extent do Sectors 'Socialize' Innovation Differently? Mapping Cooperative Linkages in Knowledge-Intensive Industries in the Ottawa Region", *Industry and Innovation*, 15(4), pp. 351-370.
- Doloreux, D., Parto, S., 2005, "Regional Innovation Systems: Current Discourse and Unresolved Issues", *Technology in Society*, 27(2), pp. 133–153.
- Eliasson, G., Eliasson, A., 2006, "The Pharmacia Story of Entrepreneurship and as a Creative Technical University: An Experiment in Innovation, Organizational Break Up and Industrial Renaissance, *Entrepreneurship & Regional Development*, 18(5), pp. 393-420.
- Ernst, D., 2006, "Innovation Offshoring: Asia's Emerging Role in Global Innovation Networks", *East-West Center Special Reports*, 10, July, 48 p.
- European Commission, 2008, "Towards World-class Clusters in the European Union: Implementing the Broad-based Innovation Strategy", *Communication from the Commission of 17 October 2008 on How to Implement the Innovation Strategy throughout the European Union*, COM(2008) 652 final/2, November 11th, 10 p.

- Feldman, M.P., 2003, "The Locational Dynamics of the US Biotech Industry: Knowledge Externalities and the Anchor Hypothesis", *Industry and Innovation*, 10(3), pp. 311-328.
- Feldman, M.P., Francis, J.L., 2002, "The entrepreneurial Spark: Individual Agents and the Formation of Innovative Clusters in Complexity and Industrial Clusters", in: Quadro Curzio, A., Fortis, M. (Eds.), *Complexity and Industrial Clusters*, Springer Verlag, Heidelberg, pp. 195-212.
- Filippi, M., Torre, A., 2003, "Local Organisations and Institutions: How Can Geographical Proximity be Activated by Collective Projects?", *International Journal of Technology Management*, 26(2-4), pp. 386-400.
- Finegold, D., Wong, P.-K., Cheah, T.-S., 2004, "Adapting a Foreign Direct Investment Strategy to the Knowledge Economy: The Case of Singapore's Emerging Biotechnology Cluster", *European Planning Studies*, 12(7), pp. 921-941.
- Fleming, L., Colfer, L., Marin, A., McPhie, J., 2004, "Why the Valley Went First: Agglomeration and Emergence in Regional Inventor Networks", *Wharton Technology Mini-Conference*, University of Pennsylvania, Philadelphia, 51 p.
- Folta, T.B., Cooper, A.C., Baik, Y.-S., 2006, "Geographic Cluster Size and Firm Performance", *Journal of Business Venturing*, 21(2), pp. 217–242.
- Fontes, M., 2005, "Distant Networking: The Knowledge Acquisition Strategies of 'Out-Cluster' Biotechnology Firms", *European Planning Studies*, 13(6), 899-920.
- Freel, M.S., 2003, "Sectoral Pattern of Small Firms Innovation, Networking and Proximity", *Research Policy*, 32(5), pp. 751-770.
- Fromhold-Eisebith, M., Eisebith, G., 2005, "How to Institutionalize Innovative Clusters? Comparing Explicit Top-Down and Implicit Bottom-up Approaches", *Research Policy*, 34(8), pp. 1250-1268.
- Gay, B., Dousset, B., 2005, "Innovation and Network Structural Dynamics: Study of the Alliance Network of a Major Sector of the Biotechnology Industry", *Research Policy*, 34(10), 1457-1475.
- Gertler, M.S., Levitte, Y.M., 2005, "Local Nodes in Global Networks: The Geography of Knowledge Flows in Biotechnology Innovation", *Industry and Innovation*, 12(4), 487-507.
- Gertler, M.S., Wolfe, D.A., Garkut, D., 2000, "No Place Like Home? The Embeddedness of Innovation in a Regional Economy", *Review of International Political Economy*, 7(4), 688-718.
- Gilding, M., 2008, "The Tyranny of distance': Biotechnology Networks and Clusters in the Antipodes", *Research Policy*, 37(6-7), pp. 1132-1144.
- Gilly, J.-P., Torre, A., 2000, "Introduction générale", in: Gilly, J.P., Torre, A. (Eds.), *Dynamiques de proximité*, L'Harmattan, Paris, pp. 9-33.

- Giuliani, E., 2005, "Cluster Absorptive Capacity: Why Do Some Clusters Forge Ahead and Others Lag Behind?", *European Urban and Regional Studies*, 12(3), pp. 269-288.
- Giuliani, E., Bell, M., 2005, "The Micro-determinants of Meso-level Learning and Innovation: Evidence from a Chilean Wine Cluster", *Research Policy*, 34(1), pp. 47-68.
- Glaeser, E.L., 2005, "Reinventing Boston: 1630-2003", *Journal of Economic Geography*, 5(2), pp. 119-153.
- Glückler, J., 2007, "Economic Geography and the Evolution of Networks", *Journal of Economic Geography*, 7(5), pp. 619-634.
- Grabher, G., 1993, "The Weakness of Strong Ties: The Lock-in of Regional Development in the Ruhr Area", in: Grabher, G. (Ed.), *The Embedded Firm: On the Socioeconomics of Industrial Networks*, Routledge, London, pp. 255-277.
- Grabher, G., 2002, "The Project Ecology of Advertising: Tasks, Talents and Teams", *Regional Studies*, 36(3), pp. 245-262.
- Grabher, G., 2006, "Trading Routes, Bypasses and Risky Intersections: Mapping the Travels of 'Networks' Between Economic Sociology and Economic Geography", *Progress in Human Geography*, 30(2), pp. 163-189.
- Granovetter, M., 1973, "The Strength of Weak Ties", American Journal of Sociology, 78(5), pp. 1360-1380.
- Granovetter, M., 1985, Economic Action and Social Structure: The problem of Embeddedness, *American Journal of Sociology*, 91(3), pp. 481-510.
- Grotz, R., Braun, B., 1997, "Territorial or Trans-national Networking: Spatial Aspects of Technology-oriented Co-operation Within the German Mechanical Engineering Industry", *Regional Studies*, 31(6), pp. 545-557.
- Hamdouch, A., 1998, "Concurrence et coopération inter-firmes", *Economie Appliquée*, LI(1), pp. 7-51.
- Hamdouch, A., 2002, "Complémentarités inter-firmes, préemption de partenaires et rendements croissants de coalition: Une formalisation des processus de rapprochement entre firmes face aux nouvelles technologies et à la globalisation", *Région et Développement*, 16, pp. 161-189.
- Hamdouch, A., 2008, "Start-up biotechnologiques et dynamique des clusters et réseaux d'innovation dans la biopharmacie: Une revue de la littérature empirique", *Journal des Entreprises Familiales*, 1(3), pp. 7-43.
- Hamdouch, A., 2010, "Conceptualizing Innovation Clusters and Networks", In: Laperche, B., Uzunidis, D., Sommers, P. (Eds), *Innovation Clusters and Networks: The Knowledge Backbone*, Peter Lang, Brussels, pp. 21-63.
- Hamdouch, A., Depret, M.-H., 2001, *La nouvelle économie industrielle de la pharmacie*, Elsevier, Paris.

- Hamdouch, A., Depret, M.-H., 2002, "Coalitions et réseaux de firmes : Les nouvelles stratégies concurrentielles dans la globalisation", *Gestion 2000 : Management & Prospective*, 19(1), pp. 35-53.
- Hamdouch, A., Depret, M.-H., 2009, "Surveying the Literature on Territorial Innovation Systems: A Suggested Interpretation Framework", SSRN Working Papers Series, December.
 (http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1207206)
- Hamdouch, A., He, F., 2009, "R&D Offshoring and Clustering Dynamics in Pharmaceuticals and Biotechnology: Key Features and Insights from the Chinese Case", *Journal of Innovation Economics*, 4, pp. 95-117.
- Hamdouch, A., Moulaert, F., 2006, "Knowledge Infrastructure, Innovation Dynamics and Knowledge Creation/Diffusion/Accumulation Processes: A Comparative Institutional Perspective", *Innovation: The European Journal of Social Science Research*, 19(1), pp. 25-50.
- Hassink, R., 2005, "How to Unlock Regional Economies from Path Dependency? From Learning Region to Learning Cluster", *European Planning Studies*, 13(4), pp. 521-535.
- Hendry, C., Brown, J., Defillippi, R., 2000, "Regional Clustering of High Technology-based Firms: Opto-electronics in Three Countries", *Regional Studies*, 34(2), pp. 129–145.
- Humphrey, J., Schmitz, H., 2002, "How Does Insertion in Global Value Chains Affect Upgrading in Industrial Clusters?", *Regional Studies*, 36(9), pp. 1017-1027.
- Hussler, C., Rondé, P., 2005, "Les réseaux d'innovation des chercheurs universitaires sont-ils géographiquement circonscrits?", *Revue d'Economie Industrielle*, 109, pp. 69-90.
- Jong, S., 2006, "How Organizational Structures in Science Shape Spin-Off Firms: The Biochemistry Departments of Berkeley, Stanford, and UCSF and the Birth of the Biotech Industry", *Industrial and Corporate Change*, 15(2), pp. 251-283.
- Kaiser, R., Prange, H., 2004, "The Reconfiguration of National Innovation Systems: The Example of German Biotechnology", *Research Policy*, 33(3), pp. 95-408.
- Kalafsky, R.V., MacPherson, A.D., 2002, "The Competitive Characteristics of US Manufacturers in the Machine Tool Industry", *Small Business Economics*, 19(4), pp. 355-369.
- Kaufmann, D., Schwartz, D., Frenkel, A., Shefer, D., 2003, "The Role of Location and Regional Networks for Biotechnology Firms in Israel", European Planning Studies, 11(7), pp. 822-840.

- Keeble, D., Lawson, C., Lawton-Smith, H., Moore, B., Wilkinson, F., 1998, "Internationalisation Processes, Networking and Local Embeddedness in Technology-intensive Small Firms", *Small Business Economics*, 11(4), pp. 327-342.
- Kogut, B., Walker, G., 2001, "The Small World of Germany and the Durability of National Networks", *American Sociological Review*, 3(3), pp. 317-355.
- Lagendijk, A., 2002, "Beyond the Regional Lifeworld against the Global Systemworld: Towards a Relational-Scalar Perspective on Spatial-Economic Development", *Geografiska Annaler*, B84(2), pp. 77-92.
- Leibovitz, J., 2004, "Embryonic' Knowledge-based Clusters and Cities: The Case of Biotechnology in Scotland", *Urban Studies*, 41(5-6), pp. 1133-1155.
- Lemarié, S., Mangematin, V., Torre, A., 2001, "Is the Creation and Development of Biotech SMEs Localised? Conclusions Drawn from the French Case", *Small Business Economics*, 17(1-2), pp. 61-76.
- Lévêque, F., Bonazzi, C., Quental, C., 1996, "Dynamics of Cooperation and Industrial R&D: First Insights into the Black Box II", in: Coombs, R., Richards, A., Saviotti, P.P., Walsh, V. (Eds.), *Technological Collaboration: The Dynamics of Cooperation in Industrial Innovation*, Edward Elgar, Cheltenham.
- Liebeskind, J.P., Oliver, A.L., Zucker, L., Brewer, M., 1996, "Social Networks, Learning and Flexibility: Sourcing Scientific Knowledge in New Biotechnology Firms", *Organization Science*, 7(4), pp. 428-443.
- Llobrera, J.T., Meyer, D.R., Nammacher G., 2000, "Trajectories of Industrial Districts: Impact of Strategic Intervention in Medical Districts", *Economic Geography*, 76 (1), pp. 68-98.
- Longhi, C., 1999, "Networks, Collective Learning and Technology Development in Innovative High Technology Regions: The Case of Sophia-Antipolis", *Regional Studies*, 33(4), pp. 333-342.
- Madiès, T., Prager, J.-C., 2008, *Innovation et compétitivité des régions*, La Documentation Française, Paris.
- Malerba, F., 2005, "Sectoral System of Innovation: A framework for linking Innovation to Knowledge Base, Structure and Dynamics of Sectors", *Economics of Innovation and New Technology*, 14(1-2), pp. 63-82.
- Malmberg, A., Maskell, P., 2002, "The Elusive Concept of Localization Economies: Towards A Knowledge-based Theory of Spatial Clustering", *Environment and Planning*, A34(3), pp. 429-449.
- Markusen, A., 1996, "Sticky Places in Slippery Space: A Typology of Industrial Districts", *Economic Geography*, 72(3), pp. 293-313.
- Marshall ,A., 1919, *Industry and Trade*, Macmillan, London.

- Martin, R., Sunley, P., 2003, "Deconstructing Clusters: Chaotic Concept or Policy Panacea?", *Journal of Economic Geography*, 3(1), pp. 5-35.
- Martin, R., Sunley, P., 2006, "Path Dependence and Regional Economic Evolution", *Journal of Economic Geography*, 6(4), pp. 395-437.
- Maskell, P., Bathelt, H., Malmberg, A., 2004, "Temporary Clusters and Knowledge Creation: The Effects of International Trade Fairs, Conventions and Other Professional Gatherings", *Working Paper SPACES*, n° 2004-04, Philipps-University of Marburg, 34 p.
- Mattsson, H., 2007, "Locating Biotech Innovation: Places, Flows and Unruly Processes", *Geografiska Regionstudier*, n° 73, Uppsala University, Department of Social and Economic Geography, 49 p.
- McKelvey, M., 2004, "Evolutionary Economics Perspectives on the Regional–National–International Dimensions of Biotechnology Innovations", *Environment and Planning*, C22(2), pp. 179-197.
- McKelvey, M., Alm, A., Riccaboni, M., 2003, "Does Co-location Matter for Formal Knowledge Collaboration in the Swedish Biotechnology—Pharmaceutical Sector?", *Research Policy*, 32(3), pp. 485-501.
- Moodysson, J., Coenen, L., Asheim, B.T., 2008, "Explaining Spatial Patterns of Innovation: Analytical and Synthetic Modes of Knowledge Creation in the Medicon Valley Life Science Cluster", *Environment and Planning*, A40(5), pp. 1040-1056.
- Moodysson, J., Jonsson, O., 2007, "Knowledge Collaboration and Proximity: The Spatial Organization of Biotech Innovation Project", *European Urban and Regional Studies*, 14(2), pp. 115-131.
- Morange, M., 2000, *A History of Molecular Biology*, Harvard University Press, Cambridge (MA).
- Moulaert, F., Mehmood, A., 2008, "Analyser le développement régional : De l'innovation territoriale à la géographie de "dépendance de sentier"", *Géographie, Economie, Société*, 10(2), pp. 199-222.
- Nachum, L., Keeble, D., 2003, Neo-marshallian Clusters and Global Networks: The Linkages of Media Firms in Central London, Long Range Planning, 36(5), pp. 459-480.
- Niosi, J., Bas, T.G., 2001, "The Competencies of Regions: Canada's Clusters in Biotechnology", *Small Business Economics*, 17(1-2), pp. 31–42.
- Niosi, J., Zhegu, M., 2005, "Aerospace Clusters: Local or Global Knowledge Spillovers?", *Industry and Innovation*, 12(1), pp. 5-29.
- Nooteboom, B., 2000, "Learning by Interaction: Absorptive Capacity, Cognitive Distance and Governance", *Journal of Management and Governance*, 4(1-2), pp. 69-92.

- OECD, 2007, Competitive Regional Clusters: National Policy Approaches, OECD Publishing, Paris.
- Oinas, P., 1999, "Activity-Specificity in Organizational Learning: Implications for Analyzing the Role of Proximity", *GeoJournal*, 49(4), pp. 363-372.
- Oinas, P., 2002, "Competition and Collaboration in Interconnected Places: Towards a Research Agenda", *Geografiska Annaler*, B84(2), pp. 65-76.
- Oinas, P., Malecki, E.J., 2002, "The Evolution of Technologies in Time and Space: From National and Regional to Spatial Innovation Systems", *International Regional Science Review*, 25(1), pp. 102-131.
- Orsenigo, L., 2001, "The (Failed) Development of a Biotechnology Cluster: The Case of Lombardy", *Small Business Economics*, 17(1-2), pp. 77–92.
- Owen-Smith, J., Powell, W.W., 2002, "Knowledge Networks in the Boston Biotechnology Community", *Conference on 'Science as an Institution and the Institutions of Science'*, Siena.
- Owen-Smith, J., Powell, W.W., 2004, "Knowledge Networks as Channels and Conduits: The Effects of Spillovers in the Boston Biotechnology Community", *Organization Science*, 15(1), pp. 5–21.
- Owen-Smith, J., Riccaboni, M., Pammolli, F., Powell, W.W., 2002, "A Comparison of U.S. and European University-Industry Relations in the Life Sciences", *Management Science*, 48(1), pp. 24-43.
- Passiante, G., Secundo, G., 2002, "From Geographical Innovation Clusters to Virtual Innovation Clusters: The Innovation Virtual System", *ERSA Conference* 2002, Dortmund, 27-31 August.
- Paytas, J., Gradeck, R., Andrews, L., 2004, "Universities and the Development of Industry Clusters" *Report prepared for the Economic Development Administration of the U.S. Department of Commerce*, Carnegie Mellon Center for Economic Development, Pittsburgh, 102 p.
- Phlippen, S., van der Knaap, B., 2007, "When Clusters become Networks", *Tinbergen Institute Discussion Papers*, n° TI 2007-100/3, 32 p.
- Pohoryles, R.J., 2001, "Internationalisation of Research: Institutional Innovation, Culture and Agency in the Framework of Competition and Cooperation", *INNOCULT Final Report*, European Commission, DG Research, Brussels, June, 125 p.
- Porter, M.E., 1998, "Clusters and the New Economics of Competition", *Harvard Business Review*, 76(6), pp. 77-90.
- Pouder, R., St John, C.H., 1996, "Hot Spots and Blind Spots: Geographical Clusters of Firms and Innovation", *The Academy of Management Review*, 21(4), pp. 1192-1225.

- Powell, W.W., Koput, K.W., Bowie, J.I., Smith-Doerr, L., 2002, "The Spatial Clustering of Science Capital: Accounting for Biotech Firm-venture Capital Relationships", *Regional Studies*, 36(3), pp. 291-305.
- Rees, K., 2005, "Interregional Collaboration and Innovation in Vancouver's Emerging High-Tech Clusters", *Tijdschrifl voor Economische en Sodale Geografie*, 96(3), pp. 298-312.
- Roijakkers, N., Hagedoorn, J., 2006, "Inter-firm R&D Partnering in Pharmaceutical Biotechnology since 1975: Trends, Patterns and Networks", *Research Policy*, 35(3), pp. 431-446.
- Romanelli, E., Khessina, O.M., 2005, "Regional Industrial Identity: Cluster Configuration and Economic Development", *Organization Science*, 16(4), pp. 344-358.
- Ryan, C.D., Phillips, P.W.B., 2003, "Intellectual Property Management", in: Wolfe D.A. (Ed.), *Clusters Old and New: The Transition to a Knowledge Economy in Canada's Regions*, McGill-Queen's University Press, Kingston, pp. 95-120.
- Saxenian, A., Hsu, J.-Y., 2001, "The Silicon Valley-Hsinchu Connection: Technical Communities and Industrial Upgrading", *Industrial and Corporate Change*, 10(4), pp. 893-920.
- Scott, A.J., 2006, "Entrepreneurship, Innovation and Industrial Development: Geography and the Creative Field Revisited", *Small Business Economics*, 26(1), pp. 1-24.
- Simmie, J., Sennett, J., Wood, P., Hart, D., 2002, "Innovation in Europe: A Tale of Knowledge and Trade in Five Cities", *Urban Studies*, 36(1), pp. 1095-1112.
- Sørenson, O., 2003, "Social Networks and Industrial Geography", *Journal of Evolutionary Economics*, 13(5), pp. 513-527.
- Storper, M., 1997, *The Regional World: Territorial Development in a Global Economy*, The Guilford Press, New York.
- Storper, M., Venables, A., 2004, "Buzz: Face-to-Face Contact and the Urban Economy", *Journal of Economic Geography*, 4(4), pp. 351-370.
- Storper, M., Walker, R., 1989, *The Capitalist Imperative: Territory, Technology and Industrial Growth*, Blackwell Publishers, New York.
- Stuart, T., Sorenson, O., 2003, "The Geography of Opportunity: Spatial Heterogeneity in Founding Rates and the Performance of Biotechnology Firms", *Research Policy*, 32(2), pp. 229-253.
- Sturgeon, T.J., 2003, "What Really Goes on in Silicon Valley? Spatial Clustering and Dispersal in Molecular Production Networks", *Journal of Economic Geography*, 3(2), pp. 199-225.

- Suarlez-Villa, S., Walrod, W., 1997, "Operational Strategy, R&D and Intrametropolitan Clustering in a Polycentric Structure: The Advanced Electronics Industries of Los Angeles", *Urban Studies*, 34(9), pp. 1343-1380.
- Swann, P., Prevezer, M., 1996, "A Comparison of the Dynamics of Industrial Clustering in Computing and Biotechnology", *Research Policy*, 25(7), pp. 1139-1157.
- Swyngedouw, E., 1997, "Neither Global nor Local: 'Glocalization' and the Politics of Scale", in: Cox, K. (Ed.), *Spaces of Globalization: Reasserting the Power of the Local*, Guilford Press, New York, pp. 137-166.
- Ter Wal, A.L.J., 2010, "Cluster Emergence and Network Evolution: A Longitudinal Analysis of the Inventor Network in Sophia-Antipolis", *Regional Studies* (1360-0591, First published on 01 June 2010).
- Ter Wal, A.L.J., Boschma, R.A., 2009a, "Co-evolution of Firms, Industries and Networks in Space", *Regional Studies* (1360-0591, First published on 06 May 2009).
- Ter Wal A.L.J., Boschma R.A., 2009b, "Applying Social Network Analysis in Economic Geography: Framing Some Key Analytic Issues", *Annals of Regional Science*, 43(3), pp. 739-756.
- Tether, B.S., 2002, "Who Co-operates for Innovation and Why? An Empirical Analysis", *Research Policy*, 31(6), pp. 947-967.
- Tödtling, F., Trippl, M., 2005, "Networking and Project Organization in the Styrian Automobile Industry", in: Lagendijk, A., Oinas, P. (Eds.), *Proximity, Distance and Diversity: Issues on Economic Interaction and Local Development*, Ashgate Publishing, Aldershot, pp. 89-109.
- Torre, A., 2006, "Clusters et systèmes locaux d'innovation: Retour critique sur les hypothèses naturalistes de transmission des connaissances à l'aide des catégories de l'économie de la proximité", *Région et Développement*, 24, pp. 5-44.
- Trippl, M., Tödtling, F., 2007, "Developing Biotechnology Clusters in Non-high Technology Regions: The Case of Austria", *Industry and Innovation*, 14(1), pp. 47-67.
- Uzzi, B., 1997, "Social Structure and Competition in Interfirm Network: The Paradox of Embeddedness", *Administrative Science Quarterly*, 42(1), pp. 35-67.
- Vang, J., Chaminade, C., 2007, "Global-local linkages, Spillovers and Cultural Clusters: Theoretical and Empirical insights from an exploratory study of Toronto's Film Cluster", *Industry and Innovation*, 14(4), pp. 401-420.
- Von Tunzelmann, N., 2003, "Historical Coevolution of Governance and Technology in the Industrial Revolutions", *Structural Change and Economic Dynamics*, 14(4), pp. 365-384.

- Waluszewski, A., 2004, "A Competing or Co-operating Cluster or Seven Decades of Combinatory Resources? What's Behind a Prospering Biotech Valley?", *Scandinavian Journal of Management*, 20(1), pp. 125-150.
- Watts, D.J., 1999, "Networks, Dynamics and the Small-World Phenomenon", *American Journal of Sociology*, 105(2), pp. 493-527.
- Watts, D.J. 2004, "The 'New' Science of Networks", *Annual Review of Sociology*, 30, pp. 243-270.
- Watts, D.J., Strogatz, S.S., 1998, "Collective Dynamics of 'Small World' Networks", *Nature*, 393, pp. 440-442.
- Waxell, A., Malmberg, A., 2007, "What is Global and what is Local in Knowledge-generating Interaction? The Case of the Biotech Cluster in Uppsala, Sweden", *Entrepreneurship & Regional Development*, 19(2), pp. 137-159
- Wenger, E., Snyder, W., 2000, "Communities of Practice: The Organizational Frontier", *Harvard Business Review*, 78(1), pp. 139-145.
- Wolfe, D., Gertler, M.S., 2004, "Clusters from the Inside and Out: Local Dynamics and Global Linkages", *Urban Studies*, 41(5-6), pp. 1071-1093.
- Wood, A., Watts, H.D., Wardle, P., 2004, "Growth-Oriented Small Firms and the Nature and Extent of Local Embeddedness: The Case of a Traditional Metal Working Cluster", *Growth and Change*, 35(4), pp. 419-433.
- Zeller, C., 2001, "Clustering Biotech: A Recipe for Success? Spatial Patterns of Growth of Biotechnology in Munich, Rhineland and Hamburg", *Small Business Economics*, 17(1-2), pp. 123–141.
- Zeller, C., 2004, "North Atlantic Innovative Relations of Swiss Pharmaceuticals and the Proximities with Regional Biotech Arenas", *Economic Geography*, 80(1), pp. 83–111.
- Zucker, L.G., Darby, M.R., 2007, "Virtuous Circles in Science and Commerce", *Papers in Regional Science*, 86(3), pp. 445-470.
- Zucker, L.G., Darby, M.R., Amstrong, J., 1994, "Intellectual Capital and the Firm: The Technology of Geographically Localized Knowledge Spillovers", *NBER Working Paper*, 4946.

LES CLUSTERS ET RÉSEAUX MULTI-ÉCHELLES COMME FONDEMENTS DE LA DYNAMIQUE D'INNOVATION DANS L'INDUSTRIE BIOPHARMACEUTIQUE

Résumé – S'appuyant sur le cas de l'industrie biopharmaceutique, l'objectif de cet article est de remettre en cause la conviction centrale, aujourd'hui très diffusée, de la « spatial clustering theory » selon laquelle la proximité géographique aurait un rôle clé (voire exclusif) dans l'explication des dynamiques de clustering des activités d'innovation au sein de territoires spécifiques. Notre argumentation s'appuie sur trois points. Premièrement, la simple proximité géographique n'est pas suffisante ; dans de nombreux cas, les formes de proximité cognitive, organisationnelle et stratégique sont souvent au moins aussi décisives que la proximité topologique des acteurs de l'innovation. Deuxièmement, l'article défend l'idée que les clusters sont fondamentalement le résultat territorialisé de combinaisons de réseaux inter-organisationnels et sociaux d'acteurs poursuivant des buts communs, chacun de ces acteurs ayant un ancrage territorial et social spécifique qui lui permet (ou non) d'opérer et d'interagir à différentes échelles spatiales. Ces réseaux sont socialement et territorialement enchâssés, mais ils peuvent se déployer au sein de dynamiques multi-échelles. Troisièmement, enfin, des dynamiques sectorielles spécifiques, comme dans le cas de l'industrie biopharmaceutique, peuvent structurellement conditionner la manière dont les acteurs sont en mesure d'interagir et de collaborer au sein de projets de R&D et de processus d'innovation spécifiques. De fait, les dynamiques soutenant l'émergence, la structuration et l'évolution des clusters biopharmaceutiques combinent des logiques à la fois multi-échelles et multi-acteurs. Dans ce cadre, les réseaux et clusters constituent des phénomènes imbriqués, consubstantiels l'un de l'autre, et des modes organisationnels co-évolutifs de l'innovation biopharmaceutique.