Systemic Innovation: Triple Helix, Scalar Envelopes, or Regional Knowledge Capabilities, an Overview.

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Abstract

This paper proposes to review and assess social scientific debate about the origins and nature of innovation in modern society. The paper focuses on three sub-sets of conceptualisation, critique and commentary that refer specifically to sub-national or *regional innovation systems*. Research in the latter field has grown enormously in recent years. Moreover, new perspectives from other disciplines than regional science have been promoted. One distinctive view of relevance in that it is focused on the role in innovation of specific 'entrepreneurial universities' in relation to industry and government is, of course, the 'Triple Helix' approach. This is reviewed and sympathetically critiqued. A second view, less sympathetically critiqued here, is one that itself attacks all so-called 'new regionalism' for stressing the importance of institutions, industry embeddedness and the micro-science of regional economic development. Dazzled by globalisation and the totalising power of 'scale' geographies, this rejection of the worth of spatial analysis at less than the global or national 'scalar envelope' is assessed for its potential insights into weaknesses of the regional innovation systems approach but found wanting in both technical accuracy and scholarly competence. Finally, the state of the art in regional innovation systems research is sketched by reference both to recent longitudinal findings and elaborations into specific technological fields, particularly Bioregional Innovation Systems that help move us towards a newer theory of economic geography in the knowledge economy, based on 'regional knowledge capabilities'.

1. Introduction

As new fields settle and evolve, they diversify. Such has been the profile of innovation systems research since it's first elaboration in 1987.[1] To manage what is becoming a substantial field of research while focusing on elements arising from debate that may not have received sufficient attention this paper takes stock, reviewing progress and responding to critique. The regional field of innovation systems analysis has grown exponentially since 1992 such that recent research shows how by 2000, refereed articles on *regional* innovation were equivalent to those on *national* systems, and way ahead of those on technological or sectoral systems. Over 200 regional innovation systems studies were published from 1987-2002, with more than one hundred of these empirically based. New papers are published monthly and MIT, for example, now has an international comparative programme managed by its Industrial Performance Centre.[2]

One distinctive view of relevance in that it is focused on the role of specific 'entrepreneurial universities' in relation to industry and government is, of course, the 'Triple Helix' approach. It can be said to operate intellectually at two 'levels', one a high level of abstraction in which macro-institutions like 'industry', 'universities' and 'government' are held to engage in more systemic interaction nowadays as the exigencies of the knowledge economy and competitiveness through innovation demand greater scientific involvement in production. The second is quite 'local', in that the exemplar 'Triple Helix' university is MIT and much of its impact through academic entrepreneurship concerns Massachusetts, particularly Greater Boston, as well as at the scale of North America and to a lesser extent, the rest of the world (e.g. the Cambridge-MIT partnership funded at $100 million by the UK Treasury to raise academic entrepreneurship by knowledge transfer). Particular studies of Triple Helix cases thus frequently focus on the impact on local-regional economies of universities like Stanford, Cambridge, Grenoble, Washington, Linköping and Oulu. However the approach can be criticised for emphasising the consensus aspects of relations among such distinctive 'epistemic communities' and a somewhat 'cybernetic' view of innovation accordingly.

A second category of what can best, at present, be considered a critique of the idea of systemic innovation, on the one hand, and regional-local analysis on the other, is that which seeks to re-assert the hierarchical power of geographical scale in understanding innovation processes. Thus far, this approach enjoys the luxury of having advanced no empirical evidence for its assertions. However its critique, and advocacy of a conception of space as a hierarchical nesting within a 'scalar envelope' warrants at least a response, but more importantly it may serve some purpose in reminding regional

[1] This was C. Freeman's (1987) *Technology Policy & Economic Performance: Lessons From Japan,* London, Pinter
[2] MIT Industrial Performance Centre – Local Innovation Systems Project. http://ipc-lis.mit.edu/intellectual.html

scientists to make doubly clear their use of the term 'regional' is relational not containerised, while stimulating us to think of clearer ways of capturing theoretically the multi-level nature of innovation inputs and outputs. At present the view of innovation in this approach is strictly linear, whereby power to effect action resides most at the highest 'global', sometimes 'glocal' and/or national levels and local-regions merely have these effects inscribed upon their undefined 'scale'. Critique of this approach is of its determinism and reification of the abstraction 'scale'. However critique from within geographical sciences that inverts directionality, arguing for ground-up causality, betrays an equivalent inability to escape the confines of linear thinking, something of which the final approach can hardly be accused.

What is here termed the 'regional knowledge capabilities' approach is the result of much recent thinking from within the regional innovation systems model about the real nature of innovation on the ground. This also partly connects to important interventions on the nature and location of 'localised knowledge spillovers' (LKS). Taking the latter first, there is also a 'debate' between those for whom the geographical setting of, for example, a cluster stimulates accomplished absorption of knowledge spillovers, while for critics of this view the argument is that these are not demonstrated to be capabilities beyond those of firms residing in a given cluster. A resolution recently proposed is to seek to understand knowledge spillover exploitation as a facet of firm resources or 'dynamic capabilities' rather as Penrose argued in 1995 she would have called 'knowledge networking' had that language been available in 1959 instead of the general term 'resources'.[3] Such dynamic capabilities, where present, stimulate knowledge transfer spiralling, that is complementary upgrading, and where it engages also innovation institutions, pulls them up the knowledge spiral. This helps understanding of spatial variation in the geography of innovation, since some LKS locations are more accomplished than others, which also tends to undermine the critique of the 'scalar envelope' approach, as this is obviously not a linear process. Crucially, *research* (rather than big institutions) becomes a key asset in knowledge spiralling as is recognised in some actual practices.

2. The Triple Helix Approach

One of the earlier forms of advocacy for a view that is consistent with local-regional innovation networking was Etkowitz & Leydesdorff's (1997) model of the 'Triple Helix' whereby in a swiftly emerging *knowledge economy* as they saw it, those places with research universities would increasingly see growing demand for knowledge transfer to industry and, through government, to society. Moreover, the spread of universities is reasonably uniform over space. For research

[3] Penrose, E. (1959/1995) *The Theory of the Growth of the Firm*, Oxford, Oxford University Press

knowledge, industry and government would be willing to pay more for privileged access to knowledge-based growth opportunities by funding more research, stimulating closer interactions among the three institutional partners, subsidising infrastructure (e.g. incubators and science parks) and stimulating academic entrepreneurship skills and funding. The exemplar *par excellence* of this phenomenon is Massachusetts Institute of Technology. In reference to this, Gunasekara (2004) examines in detail the validity of the Triple Helix model in wholly different contexts in Australia. Not surprisingly he finds a model design based on MIT works poorly for the more average universities and regions that act as his laboratory. Nevertheless, the principles hold of Triple Helix *rapprochement* among such distinct 'epistemic communities' (Haas, 1992) as the three implied, but the boundary-crossing effort required can defeat the unwary.

A further problem is that the Triple Helix model is inadequately 'contextuated', a criticism made of Gibbons et al. (1994) for a failure to recognise the role of social movements in shifting innovation targets, as with the impact of various ecological movements on mammalian testing, nuclear and genetically modified food science. Nowotny et al., (2001) have auto-critiqued their earlier work with Gibbons et al. (1994) because it remained rather lofty and science-centric whereas socio-economic context is rather seen to be causing science and society to 'co-evolve' in their development. Thus, for example, as society turned against nuclear physics because of its unsolved pollution problems, and sought greater resource attention for healthcare, so science policy shifted from physics and chemistry to biosciences. Thus in this context knowledge capabilities include receptivity to social concerns in institutional and organisational processes that integrates transdisciplinary communities of practice to form knowledge for policy learning and innovation.

Examples of this way of thinking and operating are analysed in Sotarauta's (2004) study of research rather than university-led regional development in rural Finland. Thus *Epanet* in Finland's Vaasa-Suomi region connects 20 new Chairs and Research Centres in collaborating counties, *none of which has a university*. This *Filial* model affiliates professors and centres to at least 6 universities elsewhere, thus negating the sunk costs, inertia, and vested interests of traditional 'bricks and mortar' academe. In Italy, disappointment with traditional universities as regional development engines has led to diffusion of the *Pisa* model of *Scuoli Superiore* or Advanced Study Institutes to five 'laboratory' regions (Puglia, Umbria, Marche, Lombardia, and Campania) to emulate Pisa's Institute-Corporate-Spinout system that has been judged a success (OECD, 2001). These new approaches recognise the weakness of universities *per se* as knowledge transceivers, but the centrality of research knowledge to future regional development potential. Nevertheless Triple Helix thinking draws attention to the broad outlines of important contemporary innovation interactions.

3. Scalar Envelopes

A broader attempt to capture the integrative and interactive nature of the knowledge economy examined from the regional perspective is contained in early work on regional innovation systems (Cooke, 1992; Cooke & Morgan, 1994). In the first of these, the systemic innovation dimension of the analysis evolved from a primary interest at that time in innovation arising from knowledge *networks* and processes of networking. It is noteworthy that neither article cross references any work on *national* innovation systems, suggesting the regional variant was *sui generis*. However, formally the 'innovation systems' discourse was, in Marshallian terms, 'in the air'. The list of networking partners included the base institutions like universities, research laboratories, research associations, industry associations, training agencies, technology transfer organisations, specialist consultancies, government development, technology and innovation advisory agency programme-funding, and private investors. This knowledge exploration, examination and exploitation *base* supported the innovation efforts of large and small firms *in many industries*. *A regional innovation system was not a cluster*, but capable of supporting numerous clustered and non-clustered industries. Not all interactions were perceived as only intra-regional, many were national and global, but in the most accomplished regional economies a majority of such institutional networking interactions were, and on such regular terms that the networking had become systemic (for case material, see Cooke, 2001).

To return to the sceptics from economic geography, it is necessary to say a little about the historical context of the discipline. As with many things, such as a historic failure to provide a convincing theory of location and city formation (on this, and a solution, see Krugman, 1995) there has been since the dawning of modern geography an inability by its practitioners to carve out a core area of theoretical competence of the status of, say 'class' or 'structuration' in sociology, the 'Phillips curve' explanation of the relation between unemployment and inflation in economics, or 'multi-level governance' in political science.

The last-named is of direct relevance to issues tackled in this paper, so what do it's leading propositions say? First that different levels of governance relate not in a linear, power-imposing manner, but by evolving spheres of capability among which interactions occur by negotiation between parties of consequence to specific competence areas. Study then focuses on change or evolution, including devolution, of such competences and capabilities as political systems mature. As the book reporting first findings from eleven systematically selected and hypothetic-deductively analysed European regions (Cooke, Boekholt & Tödtling, 2000) showed, it is impossible to discuss innovation processes and policies without reference to the interactions of local-regional, national and global actors and institutions. This will be especially vividly revealed

in the brief exemplar account in Section 5 of fascinating global-regional bioscientific innovation systems involving the small nation-big pharma practices of the Swiss corporate pharmaceuticals sector.

This allows contrasts of the following kind to be drawn with confidence by exponents of multi-level governance, in this case referring to the relations between national and regional electoral outcomes. Germany demonstrates a predictable relationship between regional and national outcomes since strong regional differentiation in voting is exceptional. Spain's relationship of regional to national elections is complex due to distinctive regional electoral dynamics arising from historical, cultural and linguistic expressions of difference in specific regions. Canada's regional and national electoral dynamics are mostly decoupled because of historical, cultural linguistic expressions of difference (Hough & Jeffery, 2003). The explanation is that there is geographical variation in what counts as first and second order political issues for the electorate. In other words, the larger 'scale' does not always, or indeed ever, impose its will on the lesser. For how, as an abstraction, could it?

Contrast this with an eclectic mixture of critique, comment and conceptualisation on the issue of 'scale' emanating from contemporary economic geography. Already early in being attacked by Dicken et al. (1997) for a conservative, linear determinism that sees 'globalisation' as a totalising, relentless and inevitable power, it proceeds in an all-encompassing way to deny capability to other 'scales'. Trying to escape this we see, for example, Bunnell & Coe (2001) and Mackinnon et al. (2002) saying it is both wrong to emphasise the *regional* level and wrong to overlook *regional* specificity. Scale clearly does not exclude presence of fences for sitting upon. This is an improvement upon Listian positions such as that of Bathelt (2003) writing that only *nations* have specificity and that they may also be *closed* systems, which in a world of liberal free trade and widespread immigration may serve only to unite in scepticism the 'glocalists' (e.g. Swyngedouw, 1997), with those whose interests are also in the sub-national domain. This latter commentary on *closure,* albeit moderated in ways that still privilege the national over any other scale, is especially curious, for it essays two impossible feats. The first is to advocate a nineteenth century *unitary* view of the contemporary relation of the nation (state) to its regions, namely their annihilation that is simply factually wrong[4]. This is particularly evident in the contemporary EU, in which 'region formation' has and continues to be evolved apace. Second, the sceptics attack for inattention to scale issues, authors who have empirically demonstrated precisely the presence of regional governance capabilities. These exist even where regional

[4] We discuss this further below in terms of the etymological meaning of 'region', which turns out to be perfectly compatible with its meaning in connection with 'regional innovation systems'.

'government' is absent, and display accomplishment at managing economic development and innovation support actions where national governments may have been inactive in such spheres (e.g. Asheim & Isaksen, 2002).

This resonates with a recent critique of the 'scalar envelope' scepticism of regional innovation systems thinking from Morgan (2004). In a cogently argued response he defends in the following manner. First, *regional innovation systems* analysts are said to 'take regions for granted as objects of analysis by failing to consider how they have been historically institutionalised as spaces of political-economic intervention and action' (MacKinnon et al, 2002; MacLeod, 2001). This is clearly mistaken since this approach treats the region as 'a nexus of processes' precisely in an effort to highlight the dynamic tensions inherent in the evolutionary process of socio-spatial change at the sub-national level (Cooke and Morgan, 1998) Moreover in each empirical case the evolution of the regions in question is profiled to show how they had been *historically* constituted.

The second criticism concerns 'a neglect of external networks and institutions, such as those associated with transnational corporations and nation states' (MacKinnon et al, 2002).
But in this approach to the governance dimension it is consciously shown how to circumvent these theoretical problems by locating each *regional* case study firmly within its *national* system of innovation. Regarding transnational corporations, while the approach is mainly concerned to explore the *endogenous* capacity for regional development in regional cases, this does not confuse endogenous capacity with indigenous capacity. In any case in such studies, the role of Foreign Direct Investment (FDI) and knowledge collaborations and codified knowledge uptake from global sources is normally part of the analysis. And, where systems host indigenous transnationals, the other end of the spectrum is examined, notably how large firms, possibly hitherto part of a regionally embedded system of production, engage in belated globalisation. Finally, critics of regional innovation systems analysis attack 'the tendency to provide snapshots of successful regions', so that research 'fails to address questions of adaptation and renewal in terms of how regions can sustain growth in the face of rapid changes in technologies and markets which may threaten the basis of such growth' (MacKinnon, 2002). This too misses the mark since adaptation and renewal are the most prominent themes of the evolutionary analyses that commonly denote regional innovation systems research. Moreover, such work shows how even 'successful regions' also have to negotiate the problems of adaptation and renewal, an important difference being that the former have more capacity to re-invent themselves.

Thus, outside the rigours of theoretically and empirically informed regional innovation systems analysis the field of *economic geography* (here defined as the preoccupation with regional economic

development) remains ridden with conceptual fuzziness. As a consequence, rather than producing well-defined empirical categories; a series of testable propositions; and clear policy advice, economic geography tends to be dominated by (ideographic) case studies, broad (and untestable) stylised statements on what propels regional economic development, or, even less productive, high-level theory discussions that remain uncoupled to real-world experience.

Hence we cannot support the linear, hierarchical determinism of the 'scalar envelope' approach with its weak grasp upon 'agency'. For this flies in the face of research that shows sub-national policy mobilisation regarding shaping of innovation capabilities to be common, if not yet ubiquitous (for a progenitor of spatial 'enveloping', see Brenner, 2001). But we go further in re-asserting the relevance of the 'regional' as denoted above to the study of innovation, and recent extensions of analysis of the processes involved backwards along the knowledge value change into knowledge exploration and production itself, by speaking of 'regional innovation'. This contested term is considered an artifice principally by those wedded to an increasingly questionable notion that economies are only characteristic of a national scalar envelope (e.g. Brenner, 2001; Bathelt, 2003; for a penetrative critique, see Nielsen & Simonsen, 2003). However, we have seen how the now settled 'globalisation' debate undermined that comforting presumption by demonstrating the significance of the greater extensive and intensive integration of global value chains and industry organisation occasioned by the intersection of multinational firms and local-regional clusters on a worldwide basis (see, for example, Gereffi, 1999; Henderson et al., 2002; UNIDO, 2002). This means rejection of any 'containerised' notion of economic flows. For example, we disagree with Bathelt (2003) that:

> '...only a few regions can be characterised as being economically self-sufficient hosting a full ensemble of related industries and services which could serve as a basis for the establishment of an innovation system.'(Bathelt, 2003, 796)

because it is impossible, in a *globalised* world economy, to envisage a *country* including, for example, the USA in that happy position, let alone a region as defined here as a subnational governance entity. In January 2002, the US began running, for the first time, a monthly trade deficit in advanced technology products like biotechnology and other leading edge technologies (Library of Congress, 2003). It has, of course imported a massive amount of intellectual capital since time immemorial (Saxenian, 2000).

There is a clear connection here to literature recognising interdisciplinary interaction as a key feature perceived to characterise emergent 'Mode 2' knowledge production (Gibbons et al., 1994). Traditional scholastic disciplines rooted in large-scale teaching departments of universities (Mode

1) were observed to be breaking down with the growth of funded academic research. Diversification of knowledge production in specialist Research Centres that were at arm's length from normal pedagogic activity, capable of bridging industry-academe boundaries, as occurred most fully in the Stanford University model described by Gibbons (2000), but also closely in touch with problem-focused researchers from other disciplines characterised Mode 2 'transdisciplinarity'. Further ingredients included also reflexivity, and networking to tackle knowledge 'heterogeneity'. This influential and somewhat prescient perspective was criticised later, not least by some of its authors (in Nowotny et al., 2001) because it remained rather lofty and science-centric whereas socio-economic context is rather seen to be causing science and society to 'co-evolve' in their development. Thus, for example, as society turned against nuclear physics because of its unsolved pollution problems, and sought greater resource attention for healthcare, so science policy shifted from physics and chemistry to biosciences.

So we may think of the regional innovation systems capability as one that is more highly evolved than, for example a 'learning region' the key functionaries in which seek to capture knowledge and information from more accomplished institutional settings and try to apply it, not always appropriately and probably not swiftly, to problems of development, 'lock-in' and path dependence currently confronting them. The regional innovation systems appellation denotes exploration, the quest for new knowledge, the testing of that knowledge, reflection upon it and practical application suitably shaped to enhance the capabilities of institutions and organisations, especially firms in that region. This implies making optimal use of 'Constructed Advantage' (Foray & Freeman, 1993; de la Mothe & Mallory, 2003) from collaboration and networking across institutional boundaries that exist in the transdisciplinary mix of communities of practice. This implies the presence of institutional innovation networks integrating regional institutions to each other and beyond to other regions, national systems and globally located knowledge network nodes:

> "Knowledge" refers not only to research and development in the natural sciences and engineering, but also to related scientific activities (surveys, statistics, mapping, etc.) as well as a full range of technical, managerial, and social skills and cultural contexts..... The way in which institutions can identify, appropriate, apply and disseminate knowledge is by acting as part of an innovation system. These systems include knowledge producers (such as laboratories), knowledge users and appliers (such as firms), knowledge regulators (such as food and drug inspection agencies, intellectual property agencies), knowledge diffusers (including such smart infrastructure as information highways), knowledge funders (such as granting agencies), and so on.' (de la Mothe, 2003)

Knowledge processing functions become the key elements of regional innovation systems in formation or already formed.

4. Regional Knowledge Capabilities

What is a region? The concept has its origin in the Latin *regio* from *regere* meaning 'to govern'. In the field of regional development, this is precisely the sense of 'region' intended, namely governance of policies to assist processes of economic development. So, here, the concept of 'region' as administratively defined is of primary importance. Moreover, taking the administrative dimension as prior means in definitional terms the following: *region is an administrative division of a country*, thus for example 'Tuscany is a region of Italy'. Of course, there are other definitions that explain the confusion. An abstract definition is 'any large, indefinite and continuous part of a surface or space', a slightly less abstract but still vague one is 'a unit for geographical, functional, social or cultural reasons', and intriguingly a military one is 'the part of the theatre of war not included in the theatre of operations'. Thus 'region' presented as abstract space, culture area, or military backcloth. None of these captures the precision required and supplied by our preferred definition. The final remaining qualifier is to specify 'regional' as nested territorially beneath the level of the country, but above the local or municipal level. In objective terms, this is generally how the conceptual level will align with the real. However, some countries only have national states and local administrations, no regions. Some of these, like Finland and Sweden are evolving regional administrations. But can those that are not be said to experience 'regional development'? We say unambiguously that they can, and by dint of national or even supranational policy for regional development, or local proactivity, possibly including local collaborative partnerships of municipalities pursuing aims of *constructed advantage*, they do.

Is the knowledge economy a mere artifice, a figment of the need for academics to make careers by inventing a new buzz phrase? Why do we care about the knowledge economy? What special implications does it have for regional economic development? We intend to give convincing answers to each of these questions in this section, pointing briefly to ways they contribute to and improve the current debate. In doing this we tackle the questions in the order we raised them. The first point, perhaps surprising to some readers, we make to challenge the possible argument about the 'faddishness' of the knowledge economy perspective is that it is not a new idea. Apart from Marx, who indicated that, for example, mathematics and the natural sciences were exempt from the direct influence of the social and economic infrastructure, and that superstructures were not only mere reflections of infrastructures, but could in turn react upon them (see Coser, 1977), it was Schumpeter who recognised first the importance of knowledge in the economy by his reference to

'new combinations of knowledge' at the heart of innovation and entrepreneurship (Schumpeter, 1912, p. 57). Nonaka & Takeuchi (1995) also show that Marshall (1916) recognised that:

> 'Capital consists in a great part of knowledge and organisation..... knowledge is our most powerful engine of production.....organisation aids knowledge' (p. 115)

But, typically neoclassical economics neglected what was not contained in price information and made no effort to add to economic knowledge by trying to measure its economic contribution. Thereafter, Hayek (1945; 1948) identified 'the division of knowledge as the really central problem of economics as a social science' (1948, p. 51) and its key question as addressing the puzzle of localised knowledge held by fragmentary firms and individuals nevertheless producing ordered market demand and supply:

> 'The most significant fact about this system is the economy of knowledge with which it operates, or how little the individual participants need to know in order to be able to take the right action. In abbreviated form, by a kind of symbol, only the most essential information is passed on, and passed on only to those concerned (Hayek, 1948, p. 86)

Clearly none of these writers was writing about the knowledge economy *per se* but rather its fundamental importance to the functioning of all aspects of the economy from innovation to production, organisation and markets.

Finally, a further progenitor of the view that knowledge is the most important economic resource was Penrose (1959). She founded what has now evolved into the 'dynamic capabilities of firms' approach to microeconomics (Teece & Pisano, 1996). She referenced the firm's characteristics as an administrative organisation (after Marshall, 1916 and Coase, 1937) and home to accumulated human and material resources. The latter are inputs to services rendered, and these are the product of the firm's accumulated knowledge:

> '...a firm's rate of growth is limited by the growth of knowledge within it, but a firm's size by the extent [of] administrative efficiency (Penrose, 1995, xvi-xvii)

So, in effect, as it is put by Nonaka & Takeuchi (1995) '...the firm is a repository of knowledge' (p. 34). Penrose (1995) also wrote that had the language been available at the time of the original writing in the 1950s she would have referred to the dynamic capabilities of firms residing in *knowledge networks* (for discussion, see Quéré, 2003). Thus Penrose (1995) notes the following crucial feature of the massively increased value of transferable knowledge to the wider economy for the firm:

> '...the rapid and intricate evolution of modern technology often makes it necessary for firms in related areas around the world to be closely in touch with developments in the research and innovation of firms in many centres (Penrose, 1995, p. xix)

Importantly, Penrose continues, the rise of business knowledge networks represents a *metamorphosis* in the contemporary economy. The key to the knowledge economy is at least partly revealed as this *metamorphosis* in the nature of industry organisation to facilitate interaction with rather than secrete valuable knowledge, as was common in the previous evolutionary phase of the global economy.

This is of direct relevance to issues tackled in this paper, so what do their leading propositions say? First that different levels of governance relate not in a linear, power-imposing manner, but by evolving spheres of capability among which interactions occur by negotiation between parties of consequence to specific competence areas. Study then focuses on change or evolution, including devolution, of such competences and capabilities as political systems mature. As the book reporting first findings from eleven systematically selected and hypothetic-deductively analysed European regions (Cooke, Boekholt & Tödtling, 2000) showed, it is impossible to discuss innovation processes and policies without reference to the interactions of local-regional, national and global actors and institutions. This will be especially vividly revealed in the brief exemplar account in Section 5 of global-regional bioscientific innovation systems involving the small nation-big pharma practices of the Swiss corporate pharmaceuticals sector.

What defines successful or promising 'knowledge economy' regions and where are they?
For the moment we may take bioregions as our exemplar, but later we shall underpin this with reference to other industries. The simple answers to the questions raised in the title of this sub-section are that *scale* is the normal ranking device among relevant variables like numbers of dedicated biotechnology firms (DBFs), size of research budgets, investment finance or number of life scientists. On such counts, the answer about *location* is North America, primarily the USA. *But there are obvious weaknesses in taking scale at face value*.

Thus qualitative considerations that go beyond mere numbers of firms into another scale question regarding their turnover, sales or employment enters the discussion. Similarly, a DBF (or a bioregion) with biotechnologically-derived products already on sale in healthcare markets, having passed through the three trialling phases and won US Food & Drug Administration approval, would presumably rank higher than a larger DBF or bioregion with mainly 'pipeline' products. Similarly drugs are considered more important than diagnostic kits. So a location with a handful of peak research institutes with SMEs producing cancer-defeating drugs creates more value per worker, or more value per unit of input, and value per product sold, even though its collective return is less than a multinational pharmaceuticals firm or firms that market and distribute some new therapeutic treatments, traditional (fine chemistry) drugs and a range of other products, and whose market

capitalisation is accordingly far greater. Value lies increasingly in the knowledge and organisational resources of such non-corporate actors in this field. Creativity and content are more valuable than the media, through which they flow, in this not especially controversial argument.

What may be controversial, however, is the argument that in knowledge-based industry, generating and commercialising *abstract, synthetic* and *symbolic* knowledge derived from *research* is increasingly to be found outside the corporate sector and inside knowledge-intensive research institutes, consultancies and modestly-sized but regionally agglomerated firms. There are exceptions, as always, to an emergent trend as Valentin & Lund-Jensen (2003) showed for the food industry, something also argued from a different perspective by Smith (2001). This in turn, however, is a product of the *knowledge capabilities* of the agro-food sector, in which biology is a core research competence. But even here, it can be shown, large corporates like Monsanto and Bayer show certain incapabilities, shared in *research* and, nowadays even *development* by large pharmaceuticals firms. Accordingly, the agro-food bioscience industry shows signs of spawning more specialist DBFs than hitherto[5]

It can be shown theoretically that the definition of a successful economic region is that it possesses all or most of the key value-adding functions of a specific sector as well as reasonable diversification of the economic base into other separate or connected sectors. It thus combines depth and breadth in its industrial capabilities[6]. The role of spillovers or what are more traditionally known as external economies is important here. Why would firms cluster geographically in bioregions if there were little or no functional advantage when, according to normal supply and demand rules, overhead costs would be higher than if clustering had not taken place. The obvious answer is that they gain advantage from the knowledge network capabilities that bioregions contain. These exist in the human capital 'talent' trained in local research institutes and university laboratories; the presence of 'star' scientists and their research teams; the possibilities for

[5] This is discussed in Section 5, which contains profiles of specific agro-food knowledge R&D

[6] There is a stimulating debate between two schools of innovation thought on this. One says sectoral *specialisation* produces the best results, the other says diversification. The former position is associated with Glaeser et al. (1992) and Griliches (1992) who see specialised knowledge 'spillovers' as key growth propellants. The latter view begins with Jane Jacobs (1969) and is supported by, for example Feldman & Audretsch (1999) who show sectoral diversity is most strongly associated with regional innovativeness. The specialisationists emphasise *markets* while the diversificationists give greater weight to institutional infrastructure (innovation support system) and microeconomic linkages across agents and firms (networks) thus supporting a regional innovation systems perspective. Most recently Henderson (2003) shows specialisation effects on knowledge spillovers to have strong but short-lived impact in high technology industry while diversification effects persist far longer. This suggests that as they evolve biotechnology clusters first specialise then later diversify, firms taking distinctive advantage of external economies in the process, e.g. at first, research spillovers, later investment or ICT knowledge spillovers.

collaboration with like-minded research teams or other DBFs; and the presence of understanding financial investors also attracted to the 'ideas market' that a biotechnology cluster represents[7].

Just as there is debate, that may be approaching resolution, regarding the primacy of regional specialisation or diversification for innovation (see fn. 6) favouring the former in the early phases of an industry's development, and the latter in the later phases, so there is an emerging debate about market versus social characteristics of successful or potentially successful biotechnology clusters. The 'market' perspective is propounded by Zucker et al. (1999) while a good example of the 'social' perspective is provided by Owen-Smith & Powell (2004). The former generate data to show the following. They found the following regarding the propensity to cluster by DBFs and research scientists, notably those of 'star' status:

- Especially in the early years, commercialisation of biotechnology required the mastery of a very large amount of basic scientific knowledge that was largely non-codified. Thus DBFs became inordinately dependent on research scientists to 'translate' for them. The latter were well attuned to working with industry, hence receptive to such interaction. Locations with concentrations of such knowledge to transfer thus became magnets for DBFs as 'big pharma', early users and facilitators of research discovered their own absorptive capacity problems deriving from their origins in fine chemistry not biology
- 'Untraded interdependencies' or pure knowledge spillovers (non-pecuniary) do not seem to apply in biotechnology. Discoveries do not transfer swiftly through social ties or informal seminars but rather display high 'natural excludability'. This means biotechnology *techniques* are not widely known, so 'stars' exploit this by entering contracts with DBFs to exploit surplus profits. Localisation arises as the scientist interacts with proximate DBFs because she usually retains affiliation to the academic home base.
- The innovative performance of DBFs is positively associated with the total number of articles by local university biotechnology 'stars'. However, further data disaggregation of 'stars' into those contractually tied and untied to local firms show the positive association only applies to contractual collaborators, while the coefficient loses both significance and magnitude for the others.

Finally, the commercialisation dimension is crucial, that is - the advantages of proximity to firms that 'make it happen' i.e. help turn a scientific finding into a firm that commercialises a drug, treatment or diagnostic test. These are venture capitalists, specialist lawyers and consultants, and there is econometric and case study evidence that these knowledge demands cause them to locate

[7] On knowledge network capabilities, the early work of Penrose (1959) has given rise to the economics sub-field of studying 'dynamic capabilities' of firms to understand regional and other growth processes (Teece & Pisano, 1996).

their investment a mean distance of one hour's driving time from their office base for the most part[8]. These are 'pipeline' type relationships, sealed from prying eyes and ears.

This 'market' perspective focuses specifically on those contractual relationships where exacting transactions involve potentially large returns to partners from academe and enterprise. But the alternative, 'social' position observes, albeit with social anthropological data, a different characterisation of the successful or potentially successful bioregion. That success is based on the practice of 'open science' transformed into a cluster convention of knowledge sharing rather than secreting. These authors examined the Boston biotechnology cluster and highlighted the following as key processes by which dynamic place-based capabilities are expressed in research, knowledge transfer, and commercialisation of bioscience.

- The difference between 'channels' (open) and 'pipelines' (closed). The former offer more opportunity for knowledge capability enhancement since they are more 'leaky' and 'irrigate' more, albeit proximate, incumbents. Pipelines offer more capable means of proprietary knowledge transfer over great geographical distances based on contractual agreements, which are less 'leaky' because they are closed rather than open.
- Public Research Organisations are a primary magnet for profit-seeking DBFs and large pharmaceuticals firms because they operate an 'open science' policy, which in the Knowledge Economy era promises innovation opportunities. These are widely considered to be the source of productivity improvement, greater firm competitiveness, and accordingly economic growth.

Over time the PRO 'conventions' of 'open science' influence DBFs in their network interactions with other DBFs. Although PROs may not remain the main intermediaries among DBFs as the latter grow in number and engage in commercialisation of exploration knowledge and exploitation of such knowledge through patenting, they experience greater gains through the combination of proximity and conventions, than through either proximity alone or conventions alone. This is dynamic knowledge networking capability transformed into a regional capability, which in turn attracts large pharma firms seeking membership of the 'community'.

These propositions each receive strong support from statistical analyses of research and patenting practices in the Boston regional biotechnology cluster. Thus:

[8] This is a widely accepted norm in most locations testified to in research by Zook (2002) and Powell et al. (2002) among many others. It is because of the venture capitalist's need for a 'hands-on' relationship with her investment, possibly 'at the drop of a hat'. The greater the distance away from the investment, the greater the uncertainty about management control. As a case in point, Kleiner, Perkins Caufield, Byers, the leading US venture capitalist, has 80% of its so-called 'keiretsu' investments in biotechnology and ICT within an hour's drive of its Sand Hills Road headquarters in Palo Alto (Cooke, 2001).

> 'Transparent modes of information transfer will trump more opaque or sealed mechanisms when a significant proportion of participants exhibit limited concern with policing the accessibility of network pipelines…closed conduits offer reliable and excludable information transfer at the cost of fixity, and thus are more appropriate to a stable environment. In contrast, permeable channels rich in spillovers are responsive and may be more suitable for variable environments. In a stable world, or one where change is largely incremental, such channels represent excess capacity' (Owen-Smith & Powell, 2004)

Finally, though, leaky channels rather than closed pipelines represent also an opportunity for unscrupulous convention-breakers to sow misinformation among competitors. However, the strength of the 'open science' convention means that so long as PROs remain a presence, as in science-driven contexts they must, such 'negative social capital' practices are punishable by exclusion from PRO interaction, reputational degrading or even, at the extreme, convention shift, in rare occurrences, towards more confidentiality agreements and spillover-limiting 'pipeline' legal contracts.

So we conclude the following from this analysis of two sets of competing explanations of successful bioregions. First, as with the *specialisation* versus *diversification* debate on knowledge spillovers which was concluded by observing the time difference in the prominence of one over the other in the evolution of the cluster, so we conclude that transactions are 'pipelines' when legally binding, confidential, contractual business is being transacted but is otherwise subject to 'open science' conventions. This is represented in Table 1 below. To explain what the table shows, it suggests the following.

	Specialisation	*Diversification*
Pipeline	1. Embryonic	4. High Success
Open Science	2. Innovative	3. High Potential

Fig. 1: Characterisation of Successful and Potentially Successful Bioregions

In the early stage (1) of a technology, there will be few firms or academics with the requisite combination of scientific and commercialisation expertise for technology exploitation. However when the two come together and the market potential of what has been discovered is realised, there will be a 'pipeline' type transaction to patent, arrange investment and create a firm. This was exactly the history of Genentech after Recombinant DNA Nobel Laureate Herb Boyer and partner Stanley

Cohen met Robert Swanson venture capitalist with Kleiner, Perkins, Caufield & Byers in 1976 before any cluster existed in San Francisco. Thereafter (stage 2) more DBFs formed as scientific research evolved and new DBFs sought to emulate Genentech's success. These included Biogen in Cambridge, Massachusetts and Hybritech in San Diego in the 1970s and early 1980s[9]. Once this process has begun, the sector remains specialised but more DBFs and their employees who retain, as do founders, close affiliation with their host university, open 'channels' and knowledge spillovers are accessed to create a highly innovative environment around 'open science' conventions. The third stage is reached when diversification begins and specialist suppliers, on the one hand, but more importantly, new technology research lines and DBFs form – for example after a breakthrough like decoding the Human Genome – on the other. Large research budgets are by now attracted to leading centres and this stimulates further 'open science' communication, cross-fertilization through knowledge spillovers and further DBF formation. Fourth, after this, many serious entrepreneurial transactions occurring through 'pipeline' relations with big pharma take place, trialling proves successful and licensing deals for marketing a healthcare product are regularly struck between big pharma and DBFs. Then, regarding further R&D, big pharma with public-funded leading research institutes is further engaged and a potentially successful bioregion can be said to have become highly systematic.

5. Countering A Discourse of 'Scale': the Case of Basel and Its Bioscience

Basel is a small place in a small country but it hosts four or the largest bioscientific companies in the world: Novartis[10], Roche[11], Syngenta (agro-food biotechnology), and Lonza.[12] But Basel also hosts many smaller DBFs as Actelion, Discovery Technologies and GeneData.[13] Of the 200 Swiss biotechnology companies listed in the Swiss Life Sciences Database[14] in 2003 around 40 were pure biotechnology firms (DBFs), the others being instrumentation and services firms that nevertheless link to many of the forty. Some 22% of the 200 are located in the Geneva-Lausanne 'BioAlps' region, approximately 26% are in the Basel 'BioValley' region, and about 35% are in the Greater Zurich region. Both Roche and Novartis, in particular, draw on the institutional strength of the Basel bioregional innovation system, key institutions of which are shown in Table 1.

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[9] In those days the leading DBFs were all associated with leading scientists. Alongside UCSF's Boyer with Genentech were Walter Gilbert of Harvard with Biogen, Ivor Royston of UCSD with Hybritech, Mark Ptashne of Harvard with Genetics Institute, and William Rutter of UCSF with Chiron. In the 1980s Nobel Laureate David Baltimore (MIT) founded SyStemix, Malcolm Gefter of MIT founded ImmuLogic, and Jonas Salk, Salk Institute San Diego founded Immune Response (see Prevezer, 1998)

[10] Novartis employs 36,000 worldwide.

[11] Hoffmann-La Roche employs 30,000 worldwide

[12] Syngenta & Lonza employ 20,000 and 6,000 worldwide, respectively

[13] Das (2000) holds that there were then 74 firms in Basel with a '…focus on various aspects of biotechnology.' (p.3). These included Actelion (30 employees), GeneData (12), Myocontract (4), and Nekko, specialising in endothelium, bioinformatics, high throughput screening (HTS), oncology & cardiology, respectively.

[14] www.swisslifesciences.com

Location	Institute	Speciality	Scientists
Basic Research			
Basel	Friedrich Miescher Institute	Genomics, Neurosciences, Plant Biology, Biochemistry	240
Basel	University Botanical Institute	Molecular Plant Biology	40
Basel	University Biocentre	Genomics, Neurosciences Cell Biology, Biochemistry, Structural Biology, Microbiology	330
Basel	Genome Institute	Genomics	50
Basel	University Zoological Institute	Neurosciences	60
Basel	Canton Hospital	Tissue Engineering	40
Applied Research			
Basel	Canton Hospital	Oncology, Immunology, Haematology, Pharmacology, Infectious Diseases, Neurosciences, Diagnostics, Cardiovascular,	395
Basel	University Radiological Medicine	Diagnostics	30
Basel	Tropical Institute	Infectious Diseases	35
Basel	University Biocentre	Pharmacology, Toxicology	50
Basel	Pharmaceuticals Institute	Pharmaceuticals	30
Total			*3,000*

Table 1: Bioscientific Capabilities, Public Research Organisations in Basel, Switzerland, 2001
Source: BioValley Science Guide
http://www.biovalley.ch/main/downloads/BioValley%20Science%20Guide%20(c).pdf

From this base Roche and Novartis have been the world's most active acquirers and partners of US, especially Californian, DBFs, though they are not alone in having such links. In San Diego alone Eli Lilly entered collaboration with the Scripps Institute, gaining rights of first refusal on discoveries in exchange for $50 million. Then, in 1986 Lilly acquired Hybritech, one of the earliest DBFs, only to dispose of it subsequently, thereafter investing in ownership of a leading diabetes therapeutic from Ligand Pharma. In 1996 Lilly entered a collaboration with Neurocrine Biosciences, and in 2001 did the same with Isis Pharma ($200 million). In 1996 Schering-Plough acquired Canji, a gene therapy firm with late-stage clinical trials. Johnson & Johnson also, like Lilly, began interaction early, entering a collaboration agreement with Scripps Institute, then in 1995 taking an 11% stake in Amylin, enlarging this in later years. From 1995-9 it also had collaboration with Neurocrine Biosciences and in 1996 Johnson & Johnson created an integrated Genomics Research Institute in La Jolla, extending it in 2002 after signing a partnership deal with Maxia Pharma in 2001. Warner-Lambert (now Pfizer) acquired Agouron Pharma, the most successful San Diego biotechnology firm, employing 1,000 for $2.1 billion to access its HIV treatment. Pfizer began with a research

collaboration in 1991 with Ligand Pharma, integrated Agouron into its worldwide operations in 2000 with the acquisition of Warner-Lambert, and in 2002 opened the first stage of a new research centre ($155 million) in La Jolla on the Agouron site. In 1999 Merck acquired Sibia Neurosciences, invested in its research laboratories expanding them substantially. In 1998 Ireland's Elan Corporation entered partnership with Ligand Pharma and in 2000 acquired Dura Pharma for $1.5 billion, centralising its biopharmaceuticals operations in La Jolla, before entering 8 further biotechnology collaborations. Finally, Japanese pharmas Chugai and Sankyo established research facilities in San Diego in 1995 and 1998 respectively.

However, these activities pale into insignificance in comparison with Novartis' systemic network formation in both San Francisco and San Diego from 1977 in the former case and 1990 in the latter. These are summarised for San Francisco in Table 2 below. The symbiotic

Year	Partner	Deal
1977-1988	ALZA	Controlling stake – transdermal kits; divestment & collaboration, mktg.
1986-1995	Chiron	Joint venture, vaccines; research agt.in growth factors. Acquires 48% of Chiron in1994; accesses gene sequencing.
1990	Protein Design Labs	Research, anticancer antibodies
1991	Athena Neurosciences	Anti-spasm drug in-licensing
1991-1997	SyStemix	Collaboration immunology; 60% acquisition; stem cells & immunology collaboration; completes acquisition.
1992	Affymax	Collaboration catalytic antibodies
1997-2001	Affymetrix	Acquires Gene Chip technology
1997-1998	Incyte Pharma	Bioinformatics software agreement
1997	Titan Pharma	Iloperidone global marketing rights acq.
1998	UC Berkeley	Licensing ag-bio discoveries, first refusal
1998	Stanford U.	Transplantation technology collaboration
1999	Versicor	Research collaboration, antibacterial NAS
1999	Rigel	Five drug target collaborations
2000	Axys Pharma	Combinatorial chemistry library access

Table 2: Novartis Collaborations with San Francisco Biotechnology DBFs & Institutes
(After Zeller, 2004)

integration of Novartis with the San Diego bioregion warrants deeper exploration to show how small country big pharma gains advantage from *embeddedness*[15] in the cluster. The strongest of these collaborations, agreed by Sandoz in 1992 and effective from 1997, is the ten-year research collaboration with The Scripps Research Institute (founded in 1955). It complemented in-house

[15] This concept is central to the theory of clustering. It refers to the ties between firms that may be weak or strong, but proximity in clusters offers firms both kinds. However, Novartis is rather unusual in establishing very strong ties with San Diego institutions and firms. This is true also for San Francisco, and, as we shall see Boston.

research by Novartis in immunology, neurological science, and cardiovascular diseases by giving first access to Scripps research results in these fields, and the right to commercialise 47% of Scripps discoveries. Controversial because of infringing 'open science' conventions the initially agreed financing had to be reduced from $300 to $200 million but Scripps researchers gained the right to submit research proposals to Novartis, effectively restoring the cut. A comparable agreement, continued until commercialisation by Novartis, was initiated by Ciba-Geigy with Isis Pharma. Accordingly, the AIDS-induced retinitis drug, Vitravene was introduced in 1998.

By 1997, Novartis had implemented a new functional genomics strategy. In 2002 a new $250 million genomics research institute in San Diego was announced, named the Genomics Institute of the Novartis Research Foundation (GNF). The 200 staff complemented in-house research teams at institutes in Basel and New Jersey (later also Cambridge, Massachusetts for an equivalent investment[16]). Several GNF scientists also have faculty appointments at Scripps, and 17% of post-doctoral researchers work with GNF scientists. GNF also gave rise to the Joint Centre for Structural Genomics (JCSG) and the Institute for Childhood & Neglected Diseases (ICND) funded as consortia by the US National Institutes of Health. Scripps and these other institutes are more entrepreneurial than universities. Intellectual property Novartis is disinterested in can lead to spinout firms being formed with GNF board members.[17] Venture capital comes from the Novartis BioVenture Fund.[18] Established in 2000 with $100 million available, the fund had by 2002 invested in eleven Californian firms, four of which are in San Diego by which time it had moved its headquarters from Basel to GNF in La Jolla, San Diego.

Novartis collaborations with DBFs and institutes in San Diego are listed in Table 3. It is worth noting that many academic as well as DBF partnerships are also made by GNF in San Diego, including such firms as LifeSpan Biosciences, Molsoft, Syrrxx, Sequenom, Xenogen and Immusol covering bioinformatics, genetic and proteomic mapping and oncology. In addition GNF partners the Salk Institute, UC-San Diego and, of course, the Scripps Institute. Hence, it can be seen that the extended Novartis knowledge chain is deeply embedded in the two

[16] This practice was emulated by and from other pharma companies. Currently Aventis is implementing a comparable strategy in Toronto. Meanwhile between 1999 and 2003, Pfizer, Wyeth (acquiring Genetics Institute), Amgen (acquiring Immunex), Aventis (Ariad), Abbott (BASF) and AstraZeneca were all represented in Cambridge, Massachusetts, many through acquisition. However the embedding strategy of Novartis is both distinctive and, in relation to basic research, deeper.
[17] In 2000 Syrxx was founded, as were Kalypsys and Phenomix in 2001.
[18] Novartis also has a bioincubator at Zug in Switzerland.

Year	Partner	Deal
1989	Cytel	Immunosuppression
1990-1995	Isis Pharma	Antisense technology
1992	Sibia	Amino acids receptors
1992-	Scripps Research I.	R&D
1995	IDUN Pharma	Neurological
1995-1997	Neurocrine	Multiple Sclerosis
1997	BioSite	Immunosuppression
1998	MolSim	Simulation technology
1998	Trega	Combinatorial chemistry
1998	CombiChem	Combinatorial chemistry
1999	Diversa	Seed research
1999	Invitrogen	Functional genomics

Table 3: Novartis Collaborations with San Diego Biotechnology DBFs & Institutes
Source: Zeller, 2004

Californian bioregions but more in the form of a corporate, regional-technological innovation system in San Diego (and more particularly La Jolla) whereas in San Francisco it is more market than system-focused. We shall see shortly what the relationships are in Massachusetts, where a new Novartis Institutes of Biomedical Research opened in 2004. But before that it is worth displaying equivalent information regarding the other Swiss big pharma representative, Hoffmann-La Roche, known commercially as Roche (Table 4). The approach taken by Roche involves partnering agreements with innovative, often relatively immature but

Year	Location	Partner	Deal
1990	San Francisco	Genentech	60% stake in firm
1996	San Francisco	Gilead	Hepatitis C; Influenza
1996-1998	San Francisco	PDL	Inflammation drug
2000	San Francisco	Valeant	Anti-viral treatment
2001	San Francisco	Telik	Proteomics
2001	San Francisco	Gryphon	Anaemia
2001	San Francisco	Tularik	Therapeutic antibodies
2002	San Francisco	Lipomics	Metabolomics
2002	San Francisco	Kosan Biosciences	Polyketides (organic)
2003	San Francisco	Maxygen	Interferon; HIV
1998	San Diego	Agouron	HIV treatment
2000	San Diego	Pharmingen	Immunology license
2001	San Diego	Anadys	Anaemia
2002	San Diego	Syrrxx	Proteomics

Table 4: Roche Collaborations with San Francisco & San Diego DBFs
Source: Roche and DBF Websites

specialist DBFs and these located rather more in San Francisco although some are in San Diego. Many of these agreements are relatively recent, marking a change in Roche strategy from its acquisition of 60% (nowadays 58.2%) of the highly successful biotechnology pioneer firm Genentech in 1990 to a more flexible, short-term acquisition of technology and knowledge to fit the Roche product portfolio. Results for both Californian bioregions are given in Table 4.

Finally, regarding this special in-depth examination of the 'embedding' approach of Novartis and, to a lesser extent Roche as multinational big pharma companies from small country Switzerland, extending spatial knowledge capabilities by integrating a regional-technological innovation system within leading global bioregions, what is the evidence from Boston, particularly Cambridge, Massachusetts, which is arguably the world's leading genomics research and exploitation knowledge base? Boston outstrips both San Francisco and San Diego on many but not all biotechnology benchmarking indicators. In Table 5 the collaborative links of Novartis in the Cambridge-Boston bioregion are shown. The Roche website revealed none in this

Year	Partner	Deal
1982-1984	Genetics Institute	Immunology; interleukin-2; growth factor
1984-1986	Collaborative Rsch.	Cardiac infarction enzyme
1985-1989	Corning Glass	Diagnostics
1986	Biogen	Vaccine tissue
1989	Repligen	Retroviruses
1991	Dana Farber Inst.	Oncology & signal transduction R&D agt
1993	Procept	Auto-immune substances
1993-2000	BioTransplant	Xenotransplantation
1996-1998	Focal	Surgery materials
1997	Alexion	Viral vectors gene therapy
1997	Avant Immuno	Immunotherapeutics transplantation
1999	Cubist Pharma	Anti-infection technology
2000	Vertex Pharma	Protein kinases research

Table 5: Novartis Collaborations with Boston Biotechnology DBFs and Institutes
Source: Zeller, 2002

bioregion. The Greater Boston bioregion is well-provided with a diverse set of knowledge exploration, examination and exploitation institutions and firms (Cooke, 2002). It is clear that Novartis gains distinctive basic research capabilities in Cambridge-Boston compared to San Diego, and a further commitment of $4 billion investment beyond that in the Novartis Institutes for Biomedical Research (NIBR) is testimony to this. NIBR constitutes the primary pharmaceutical-research arm in the company's strategy of post-genomic drug discovery, concentrating on the key therapeutic areas of cardiovascular disease, diabetes, infectious diseases, functional genomics, and oncology. With the aim to gain a better understanding of the molecular mechanisms of disease the

company is integrating previously segregated scientific disciplines, fostering interaction among scientists from both within and outside of Novartis and developing partnerships with academic research institutions and DBFs. This was underlined politically by the cities of Boston and Basel signing a cultural partnership in 2000. Novartis activities in San Diego are more to do with technologies like databases, combinatorial chemistry, simulation technologies and cloning technologies and even agricultural research. In San Francisco, the emphasis is more on stem cells and gene therapy, especially bioinformatics and biochip (*GeneChip*) technology. This confirms the inference that Cambridge-Boston is the world-leading post-genomics research bioregion while California's bioregions have strength in platform, diagnostic bioinformatics and gene therapy technologies linked to California's global excellence in computing and software, and that Novartis takes advantage from those distinctive knowledge categories in its global drive to redefine the process of drug discovery.

It is thus evident how Swiss big pharma conducts its research. This can be summarised for Novartis – one of the leading organisational models for the modern pharmaceuticals industry according to the following five points.

- Novartis innovation strategy is founded on three supports: internal research; linkage of internal and external research (e.g. GNF); and collaborations with external partners.
- Collaborations are varied but, first, they support in-house efforts to acquire therapeutic lead substances, drug targets and disease models, new discovery technologies, and entry into new fields. Second, partners supply active substances for integration into in-house development pipeline for clinical trials. A further activity is developing new drug discovery processes, as in the collaboration with Vertex.
- Collaborations with Scripps Research Institute and Dana Farber Cancer Institute are to get new hypotheses of diseases and drug targets.
- From such inputs Novartis gets (e.g. with Vertex) exclusive worldwide development, manufacturing and marketing rights to clinically and commercially relevant drug candidates it develops with Vertex earning royalties on collaborative products thus marketed.
- Important too, is to organise the optimal R&D mix, concentrating certain research activities in-house or externally according to corporate competences in the main global locations of Novartis Centres of Excellence. These are mapped on to globally excellent research Bioregions.

If we compare that strategy with other big pharma, it is possible to see that Novartis has thought about and developed the 'organic' model of embedding in key bioregions to a fuller extent than any other big pharma. Most of the others are more market-oriented and opportunistic. For example

Glaxo makes partnership arrangements with DBFs but still considers in-house R&D to be a priority even though its pipeline is drying as in-house R&D fails to deliver significant returns on investment. Hence, in 2002 seeing biotechnology capabilities being increasingly monopolised by DBFs and universities, Glaxo restructured its global R&D effort into six main divisions with scientists liberated from corporate bureaucracy to some extent and incentivised with stock options and equivalents to emulate DBF research performance. Merck is also of the belief that in-house research is the preferable form by which corporate R&D should be organised. Alternatively, as we have seen, Merck engages in short term collaborations and will continue to do so, but meantime intending to control as much of the R&D chain internally to the corporation. Pfizer has mainly kept its pipeline from drying by acquisition. Eight of its thirteen new active substances (NAS) derived from its acquisition of Pharmacia. There is strong evidence that such mega-mergers as the likes of Pfizer and Glaxo have engaged do not in the long term create greater R&D productivity. Hence Pfizer also has over 1,000 collaborations with DBFs and research institutes globally to attempt to cover the field for unexpected new hypotheses or discoveries.

One reason why pharma cannot reduce its collaborations with DBFs and institutes is that not only does it have declining capability in R&D but also in the kind of competence that it might be thought economies of scale would actually benefit. However, the following suggests capabilities in exploiting new technologies, notably high throughput screening (HTS), are no better than research capabilities. The change from synthetic chemistry to biology as the epistemological basis for pharmaceuticals companies brought to the fore genetics, database, screening and bioinformatics technologies allowing pharmaceuticals firms to utilise their natural economies of scale in experimentation if not basic research. The automated, mass-production analysis of patients and 'in silico' simulations using large databases to mobilise the combinatorial chemistry required to identify compounds that act as molecular disease-inhibitors gave them an optimistic future. The main reason concerned time-economies and 'throughput' capabilities that only the administrative capabilities of scale could satisfactorily master[19]

Intriguing, therefore, to read the following analysis that re-directs our attention from the failings of 'big pharma' in basic research, resulting on their heavily increased reliance upon DBF capabilities, to newly emergent failures in precisely the capabilities identified as those of 'scale' that would triumph in the face of the DBF challenge. Traditionally many pharmaceutical companies had large industrial-chemical or consumer-products businesses to smooth out the cycles of drug research. The industry shed those businesses over the years to focus on prescription medicines, which brought higher stock-market valuations. But the rise of generic copying once patents expired meant

[19] This is argued forcefully to be the new core competence of big pharma by Nightingale (2000).

companies needing consistently to bring new products to market or lose market-share and profits. Hence the attraction of 'combinatorial chemistry', the new technology of the early to mid-1990s specifically identified in Nightingale's (2000) paper. The technology involved selection of chemical molecules, and their multiple combinations. Machines created thousands of chemicals almost overnight compared to the weeks humans took to do combinatorial chemistry. Robots connected elements of each chemical into small vials containing samples of a bodily substance involved in a disease -- for example, the protein triggering production of cholesterol. If the two reacted in the desired way, a 'hit' was registered, latterly using luminescence technologies in some cases. This testing process is known as high-throughput screening (HTS). Most large pharmaceutical firms install the new machines in sites formerly housing their laboratories, and many invested large sums on contracts with small companies specialising in HTS. For example, GlaxoSmithKline spent more than $500 million to buy a combinatorial chemistry company.

However the automation processes failed work as anticipated. The head of discovery chemistry at Bristol-Myers Squibb has referred to the first five or six years of the new technology a 'nightmare' observing that many chemists became fixated on creating thousands or millions of chemicals for testing without thinking about whether any of them could turn into a usable treatment. Test tube compounds were broken down too easily in the human stomach, issues 'craft-based' capabilities embedded in traditional chemists meant were usually assessed beforehand. Some results meant scientists were forced to wrestle intellectually with chemicals that were almost impossible to deliver in humans. The struggle often led to serious delays in development schedules when, for example, a drug to prevent infection might work *in vitro* but fail to dissolve in water, the medium used in intravenous drips.[20]

We have seen how knowledge networks are the dynamic capabilities that Penrose (1959/1995) theorised as *metamorphosing* the global economic order by transforming industry organisation, and crucially we would argue, heralding a new theory of economic geography. We call that, tentatively, the *Regional Knowledge Capabilities* (RKC) theory of economic geography. It is clear how it operates in regard to Biosciences, possibly also for other S&T based industries like ICT and new (and old) media – all heavily reliant on networks of project contracts. Where these are multiple and of relatively short duration they promote clustering around key knowledge *transceiving* organisations (Cooke et al., 2004). Where these also operate in a wider context of organisational and institutional knowledge sharing rather than knowledge-secreting typical of *Industrial Economies* as compared to *Knowledge Economies* (Cooke, 2002), we may speak of the setting constituting a *Regional Innovation System.* This

[20] This account is given in Landers (2004).

is the broader geographical setting where the most important knowledge exploration and exploitation capabilities concentrate and secondary ones, attracted by increasing returns to knowledge, including localised knowledge spillovers are found as secondary nodes or even more diffused networks. There is an established theoretical basis for these processes in the work of Myrdal (1957) and Hirschman (1958) from which Krugman learned sufficient to advocate a theory of spatial monopoly based on 'increasing returns to scale'. However we do not find the 'simplistic' two-location, zero-sum model of spatial monopoly as advocated by Krugman (1995) convincing.

This is mainly because it is clearly wrong in respect to the evolution of knowledge clusters, the largest of which may act as *megacentres* defined by their geographic concentration of the full knowledge value chain (KVC) of a given industry or sectoral branch. But these exist in *symbiosis* with lesser and differentiated nodes and networks. Crucially, unlike the Industrial Age when these were spatially separated into spatial divisions of labour (Massey, 1984) knowledge-driven innovation systems concentrate practically everything in a region or regions with a sectoral knowledge epicentre in an urban or metropolitan R1 (first class research) university-laboratory complex linked to more and less proximate complementary nodes and networks.

To round off this account of Basel's mighty impact from small scale, including utilisation of and dependence upon small scale DBFs by large pharmaceuticals and agro-food/agro-chemicals corporations, we may briefly examine the positions of Syngenta and Lonza. Syngenta benefits from being part of one of the world's recognisable agro-food 'clusters' noted earlier as BioValley (see Table 6) This is a cross-border network partnership association with Freiburg in Germany and Strasbourg in France, focused on Life Sciences. The main objective of BioValley is to promote greater cooperation between companies involved in the biotechnological and biomedical sectors and the scientific institutions (Basel's in Table 6) associated with universities in the BioValley area, most of which have already established close mutual links. This addresses not only pharmaceutical issues already present in the BioValley area, but also integrates the region's numerous smaller enterprises and suppliers. It explains the creation of a network focused on knowledge and technology transfer. This prepares existing companies for global competition, creating employment in the BioValley region, and stimulating the establishment of new businesses, particularly in association with universities.

Small in scale, but centrally situated in Europe, BioValley rests on close collaboration between companies, research institutions, economic development agencies, trade associations and financial

service providers. It supports the buoyancy of biotechnology in the cross-border region, helping it to be competitive with other biotechnology clusters in Europe and further afield. The BioValley initiative, like the many others around the world specialising mainly in agro-food biotechnology, sustains systematic collaboration between all those involved in regional innovation.

Countries	Bioregion	Brand	Actors*	%Ag-Bio	Market Focus
Canada	Saskatoon (Sk.)	'Innovation Place'	115	29	Canola, Flax
	Guelph (Ont.)	'Agrifood Quality'	41	49	Corn
USA	Connecticut	'Bioscience Cluster'	110	1	Corn, fruit
	Raleigh-Durham	'Rsch.Triangle Pk.'	145	3	Corn, soybean
	St. Louis	'BioBelt'	1183	24	Corn, soybean
	San Diego	'Biotech Beach'	700	3	Forestry, fruit, vegetables
Europe	Scotland	'Innov. Triangle'	428	2	Transgenics, potato
	Sweden	'Skåne Food Cluster'	60	25	Functional foods
	Fr-Ger-Switz.	'BioValley'	459	6	Cereals, cotton, livestock
	Netherlands	'Food Valley'	48	60	Food genomics
Australia	Brisbane (QL.)	'QBio'	43	5	Forest, aqua/horticulture
	Sydney (NSW)	'BioHub'	28	18	Livestock, cereal
	Melbourne (V)	'Bio21'	24	4	Plant/animal genomics
	Adelaide (SA)	NA	25	44	Wine, plant/animal gen.
	Perth (WA)	NA	27	20	Wheat, lupins

Table 6: Selected Agro-food Bioregions
Source: Ryan & Philips (2004); Svensson-Henning (2003); Invest Skane (2004).
*NB: Food producers; R&D institutes; raw materials & ingredients suppliers; packaging firms; industry institutes; government agencies; food organisations

Syngenta has seven product lines: crop protection focused on – selective and non-selective herbicides, fungicides, insecticides and professional products; and seeds – field crops, and vegetables and flowers. The company was formed by a merger in 2000 when Novartis agribusiness was spun out and joined Zeneca agrochemicals, similarly spun out from AstraZeneca, as a viable global business. Syngenta has key research bases in the UK along the M4 Corridor in Berkshire and in Manchester, at Basel (Stein) and in North Carolina's Research Triangle Park (RTP) bioregion,[21] where most of Syngenta's biotechnology research is conducted. These laboratories employ 5,000 of Syngenta's 20,000 employees. According to the company website[22] ' …research within Syngenta complements hundreds of collaborative activities with leading universities, research institutes and public laboratories…giving Syngenta geographic balance in research and essential pools of scientific talent.' Thus, like Novartis and Roche, this global player cannot internally source the

[21] In 2001, North Carolina's Research Triangle Park hosted 910 Life Scientists, with National Institutes of Health (NIH) research funding of $470 million, 2 specialist NIH research institutes, $190 million in alliance financing with 'big pharma', and 72 dedicated biotechnology firms (DBFs) with $192 million venture capital funding. It is one of the top seven biotechnology clusters in the US (Cortright & Mayer, 2002).
[22] www.syngenta.com/en/about_syngenta/research_tech_where.aspx

range of knowledge capabilities it requires, so integrates with DBF clusters[23] like RTP and networks of academic research alliances in public research institutes and university centres.

Lonza is a Life Sciences-driven chemical company headquartered in Basel, with sales of $1.25 billion in 2002 and operating 18 production and R&D facilities in 8 countries. It employs 6 200 people worldwide and is the leading supplier of active chemical ingredients, intermediates and biotechnology solutions to the pharmaceutical and agrochemical industries. It also offers a broad range of organic intermediates for numerous applications in pharmaceuticals, agrochemicals, vitamins, food and feedstuff, dyes and pigments, adhesives and fragrances. Furthermore Lonza manufactures specialty biocides and oleochemicals and develops and produces specific polymer intermediates, unsaturated polyester-resins, compounds and composites. Lonza Biologics is the world's leading contract manufacturer of therapeutic monoclonal antibodies and recombinant proteins from mammalian cell culture. Lonza Biotec offers custom microbial fermentation and biotransformation services to supply intermediates and biologically active products to the life sciences industry, with applications in pharmaceutical, biotechnological, agrochemical products, food and feed additives as well as cosmoceutical and nutraceutical products. Hence Lonza occupies a key manufacturing positioning in the biotechnology value chain.

Conclusions

The empirical section of this paper complements the theoretical and review parts by showing how microcosms enable macrocosms to function, at least in biotechnology. Thus we examined the Triple Helix approach to local-regional innovation but found it a too macrosociological, functionalist and consensus-focused perspective in which the fine texture of specific knowledge capabilities at the microeconomic level were obscured by the macro-institutional emphasis on large *scale* institutional bodies. These seldom, in reality, forge the kinds of links between researchers and business executives that ultimately create innovation of a systemic kind. We then examined the defensive 'scale' perspective against regional science and globalisation's proposed annihilation of power relations among networks at the local-regional scale. That was found misguided, unscholarly, linear and deterministic in its denial of the microprocesses by which research functions on the ground in a knowledge economy. This perspective favours abstract power structures 'enveloping' space over the

[23] In 2001, working with Myriad Genetics of Salt Lake City, Utah, Syngenta completed the map of the rice genome, enabling the firm to access the DNA sequence of every rice genotype. Because of its genetic similarity to most other cereals this creates a huge global market for rice and maize breeders, particularly, to improve and accelerate product growth. 80% of the world's maize goes on feeding livestock. R&D spending was $697 million in 2002. One growth market is seedless melons, being grown in Egypt for the EU market, another is 'Colossus' the world's first hybrid barley, a further innovation is a new phytase enzyme, a substitute for phosphorus in pig and poultry feed. This will be produced through fermentation with Diversa Corporation (San Diego) with whom Syngenta has a research alliance in biotechnology. The enzyme will be grown in corn (maize). Finally a new insect control technology called vegetative insecticidal protein protects cotton and corn crops against insects like root and leaf worms

interactive systems explored in the preceding, by means of which global knowledge exploitation is facilitated.

Taking a Regional Knowledge Capabilities approach proved superior in explaining how research, innovation and production actually function. That is by regional knowledge capabilities in networks of the kind Penrose (1959/1995) theorised as firm 'resources' of production and administrative capabilities. From these, a spiral of growth, operating globally is set in motion. What clearly happens is that capable knowledge actors of various kinds congregate, at least in biotechnology, in a few particular places we may call clusters or even 'megacentres'. From these bases knowledge is *transceived* locally and globally. This is not the universalist, linear diffusion idealised by the 'scalar envelope' sceptics. Rather network *nodes* act as key relay points in a global-regional innovation system. This can easily be shown in pharmaceutical and agro-food biotechnology, by taking the Regional Knowledge Capabilities theoretical approach. The challenge now is to see whether it applies equally strongly in other industrial sectors.

Bibliography

Asheim, B. & Isaksen, A. (2002) Regional innovation systems: the integration of local 'sticky' and global 'ubiquitous' knowledge, *Journal of Technology Transfer*, 27, 77-86

Bathelt, H. (2003) Growth regimes in spatial perspective 1: innovation, institutions and social systems, *Progress in Human Geography*, 27, 789-804

Brenner, N. (2001) The limits to scale? Methodological reflections on scalar structuration, *Progress in Human Geography*, 25, 591-614

Coase, R. (1937) The nature of the firm, *Economica*, 4, 386-405

Coser, L. (1977) *Masters of Sociological Thought: Ideas in Historical and Social Context*, London, Harcourt Brace

Cooke, P. (1992) Regional innovation systems: competitive regulation in the new Europe, *Geoforum*, 23, 365-382

Cooke, P. (2001) Regional innovation systems, clusters and the knowledge economy, *Industrial & Corporate Change*, 10, 945-974

Cooke, P. (2002) *Knowledge Economies*, London, Routledge

Cooke, P. & Morgan, K. (1994) The regional innovation system in Baden-Württemberg, *International Journal of Technology Management*, 9, 394-429

Cooke, P. & Morgan, K. (1998) *The Associational Economy*, Oxford, Oxford University Press

Cooke, P, Boekholt, P. & Tödtling, F. (2000) *The Governance of Innovation in Europe*, London, Pinter

Cooke, P, Heidenreich, M. & Braczyk, H. (2004) *Regional Innovation Systems* (2nd Edition), London, Routledge

Cortright, J. & Mayer, H. (2002) *Signs of Life: the Growth of Biotechnology Centres in the US*, Washington DC, The Brookings Institute

Das, R. (2000) A roundup of the Swiss biotechnology industry, *American Biotechnology Laboratory*, June, 1-6

De la Mothe, J. (2003) Re-Thinking Policy in the New Republic of Knowledge, *PRIME Discussion Paper 02-01*, University of Ottawa, Program of Research in Innovation Management & Economy

De la Mothe, J. & Mallory, G. (2003) Industry-Government Relations in a Knowledge-Based Economy: the Role of Constructed Advantage, *PRIME Discussion Paper 02-03*, University of Ottawa, Program of Research in Innovation Management & Economy

Dicken, P, Peck, J. & Tickell, A. (1997) Unpacking the global, in R. Lee & J. Wills (eds.) *Geographies of Economies*, London, Arnold

Etkowitz, H. & Leydesdorff, L. (1997) *Universities & the Global Knowledge Economy*, London, Pinter

Feldman, M. & Audretsch, D. (1999) Innovation in cities: science-based diversity, specialisation and localised competition, *European Economic Review*, 43, 409-429

Foray, D. & Freeman, C. (1993) *Technology and the Wealth of Nations: The Dynamics of Constructed Advantage*, London, Pinter

Freeman, C. (1987) *Technology Policy & Economic Performance: Lessons From Japan*, London, Pinter

Gereffi, G. (1999) International trade and industrial upgrading in the apparel commodity chain, *Journal of International Economics*, 48, 37-70

Gibbons, J. (2000) The role of Stanford University: a Dean's reflection, in Lee, C., Miller, W., Hancock, M. & Rowen, H. (eds.) *The Silicon Valley Edge*, Stanford, Stanford University Press

Gibbons, M, Limoges, C, Nowotny, H, Schwartzman, S, Scott, P. & Trow, M. (1994) *The New Production of Knowledge*, London, Sage

Glaeser, E., Kallall, H., Scheinkman, J, & Shleifer, A. (1992) Growth in cities, *Journal of Political Economy*, 100, 1126-1152

Griliches, Z. (1992) The search for R&D spillovers, *Scandinavian Journal of Economics*, 94, 29-47

Haas, P. (1992) Introduction: epistemic communities and international policy coordination, *International Organisation*, 46, 1-37

Hayek, F. (1945) The use of knowledge in society, *American Economic Review*, 35, 519-530

Hayek, F. (1948) Economics and knowledge, in *Individualism and Economic Order*, Chicago, University of Chicago Press

Henderson, J., Dicken, P., Hess, M., Coe, N. & Yeung, H. (2002) Global production networks and the analysis of economic development, *Review of International Political Economy*, 9, 436-464

Henderson, V. (2003) Marshall's scale economies, *Journal of Urban Economics*, 53, 1-28

Hirschman, A. (1958) *The Strategy of Economic Development,* New Haven, Yale University Press

Hough, D. & Jeffery, C. (2003) Elections in multi-level systems: lessons for the UK from abroad, in R. Hazell (ed.) *The State of the Nations 2003*, London, The Constitution Unit & Imprint Academia

Invest Skåne (2004) *Food Skåne*, Malmö, Skåne Inward Investment

Jacobs, J. (1969) *The Economy of Cities*, New York, Random House

Krugman, P. (1995) *Development, Geography & Economic Theory*, Cambridge, MIT Press

Landers, P. (2004) Testing machines were built to streamline research – but may be stifling it, *Wall Street Journal,* February 24, wsj.com

Library of Congress (2003) *International Trade: Data & Forecasts (Issue Brief to Congress)*, Washington, The Library of Congress

MacKinnon, D Cumbers, A and Chapman, K (2002) Learning, innovation and regional development: a critical appraisal of recent debates, *Progress in Human Geography*, 26, 293-311

MacLeod, G (2001) New regionalism reconsidered: globalisation, regulation and the recasting of political economic space, *International Journal of Urban and Regional Research*, 25, 804-29

Marshall, A. (1916) *Principles of Economics*, London, Macmillan

Massey, D. (1984) *Spatial Divisions of Labour*, London, Macmillan

Morgan, K. (2004) Sustainable regions: governance, innovation and sustainability, *European Planning Studies*, 12 (forthcoming)
Myrdal, G. (1957) *Economic Theory & Underdeveloped Regions*, London, Duckworth
Nielsen, E. & Simonsen, K. (2003) Scaling from 'below': practices, strategies and urban spaces, *European Planning Studies*, 11, 911-928
Nonaka, I. & Takeuchi, H. (1995) *The Knowledge-Creating Company*, Oxford, Oxford University Press
Nowotny, H., Scott, P.. & Gibbons, M. (2001) *Re-Thinking Science,* Cambridge, Polity
Nightingale, P. (2000) Economies of scale in experimentation: knowledge and technology in pharmaceutical R&D, *Industrial & Corporate Change*, 9, 315-359
Nowotny, H, Scott, P. & Gibbons, M. (2001) *Re-Thinking Science*, Cambridge, Polity
Owen-Smith, J. & Powell, W. (2004) Knowledge networks as channels and conduits: the effects spillovers in the Boston biotechnology community, *Organization Science*, 15, 5-21
Penrose, E. (1959/1995) *The Theory of the Growth of the Firm*, Oxford, Oxford University Press
Powell, W, Koput, K, Bowie, J. & Smith-Doerr, L.(2002) The spatial clustering of science and capital: accounting for biotech firm-venture capital relationships, *Regional Studies*, 36, 291-305
Prevezer, M. (1998) Clustering in Biotechnology in the USA, in P. Swann, M. Prevezer & D. Stout (eds.) *The Dynamics of Industrial Clustering*, Oxford, Oxford University Press
Quéré, M. (2003) Knowledge dynamics: biotechnology's incursion into the pharmaceuticals industry, *Industry & Innovation*, 10, 255-273
Ryan, C. & Phillips, P. (2004) Knowledge management in advanced technology industries: an examination of international biotechnology clusters, *Environment & Planning C: Government & Policy,* 22, 217-232
Saxenian, A. (2000) Networks of immigrant entrepreneurs, in C. Lee, W. Miller, M. Hancock & H. Rowen (eds.) *The Silicon Valley Edge*, Stanford, Stanford University Press
Schumpeter, J. (1912) *The Theory of Economic Development*, Oxford, Oxford University Press
Smith, K. (2001) What is the 'knowledge economy'? Knowledge-intensive industries and distributed knowledge bases, Oslo, STEP Group
Sotarauta, M. & Kosonen, K. (2004) Strategic adaptation to the knowledge economy in less favoured regions: a South-Ostrobothnian university network as a case in point, in P. Cooke & A. Piccaluga (eds.) *Regional Economies as Knowledge Laboratories*, Cheltenham, Edward Elgar
Swyngedouw, E. (1997) Neither global nor local: 'glocalisation' and the politics of scale, in K. Cox (ed.) *Spaces of Globalisation*, New York, Guilford Press
Svensson-Henning, M. (2003) *The Scanian Food Cluster & Innovation System: an Introduction to the Case Studies on Food-Oriented Biotechnology Firms*, Lund, University of Lund
Teece, D. & Pisano, G. (1996) The dynamic capabilities of firms: an introduction, *Industrial & Corporate Change*, 3, 537-556
UNIDO (2002) *Industrial Development Report 2002/2003: Competing Through Innovation & Learning*, Vienna, United Nations Industrial Development Organisation
Valentin, F. & Lund-Jensen, R. (2003) Science-driven discontinuities and the organisation of distributed innovations: the case of biotechnology in food processing technologies, Paper to DRUID Summer Conference *'Creating, Sharing & Transferring Knowledge',* Copenhagen, June 12-14
Zeller, C. (2002) Regional and North Atlantic Knowledge Production in the Pharmaceutical Industry, in V. Lo & E. Schamp (eds.) *Knowledge – the Spatial Dimension*, Münster, Lit-Verlag
Zeller, C. (2004) North Atlantic innovative relations of Swiss pharmaceuticals and the proximities with regional biotech areas, *Economic Geography*, 80, 83-111
Zook, M. (2002) Grounded capital: venture financing and the geography of the Internet industry, 1994–2000**,** *Journal of Economic Geography*, 2, 151-177

Zucker, L, Darby, M. & Armstrong, J. (1999) Intellectual Capital and the Firm: The Technology of Geographically Localized Knowledge Spillovers, *National Bureau of Economic Research Reprint 2217*Cambridge, Massachusetts, NBER