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Regionally asymmetric knowledge capabilities and open innovation

Exploring ‘Globalisation 2’—A new model of industry organisation

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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. It 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 1’ 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 but not only Bioregional Innovation Systems that help move us towards a newer theory of economic geography in the knowledge economy, based on ‘regional knowledge capabilities.’ The analysis conclusively proposes ‘Globalisation 2’, a ‘ground-up’ knowledge-driven evolution of the earlier ‘top-down’ multilateral trade institution and corporately driven ‘Globalisation 1.’

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1. Introduction

As new fields settle and evolve, they diversify. Such has been the profile of innovation systems research since its 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, responding to critique and evolving a new take on globalisation. The regional field of innovation systems analysis has grown exponentially since 1992 such that recent research shows how by 2002, referred 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 to 2002, with more than 100 of these empirically based (Carlsson, 2005). New papers are published monthly and MIT, for example, now has an international comparative programme managed by its Industrial Performance Centre.²

One competing perspective on key innovation interactions focuses on the role of specific ‘entrepreneurial universities’ in relation to industry and government. This is the ‘Triple Helix’ approach. It can be said to operate intellectually at two levels. The first is at 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, at present, only 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 globalised ‘scalar envelope’ warrants at least a response, but more importantly it may serve some purpose in reminding regional scientists to make doubly clear their use of the term ‘regional’ is relational not containerised. It should also stimulate 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 scalar 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 (Nielsen and Simonsen, 2003).

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 (1959/1995) argued in the 1995 edition she

¹ This was C. Freeman’s (1987) *Technology Policy and Economic Performance: Lessons from Japan*, London, Pinter.

² MIT Industrial Performance Centre, Local Innovation Systems Project. <http://ipc-lis.mit.edu/intellectual.html>.

would have called ‘knowledge networking’ had that language been available for the first edition 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 asymmetry in the geography of innovation, since some LKS locations are more accomplished than others. Naturally this also undermines the ‘scalar envelope’ approach, as this is obviously not a linear nor, especially, uniform process. Crucially, *research* (rather than big institutions) becomes a key asset in knowledge spiralling as is increasingly recognised in firm practices. Three theoretical moves synthesise the new model of what might also be termed *ground-up globalisation*: first, a spatial interpretation of knowledge as a dynamic regional capability; second, an explanation of this in terms of ‘spatially asymmetric knowledge’; and third, a spatialisation of the concept of ‘open innovation’. The logic of the analysis here provided is that under ‘knowledge economy’ conditions, globalisation evolves from ‘Globalisation 1’ which was orchestrated by multinational corporations and multilateral trade institutions, to ‘Globalisation 2’ which is driven by the quest by multinationals for exploitable knowledge in ‘knowledgeable regions’ often quite dependent on public research funding resources. Regional innovation systems articulate these relations geographically. Intellectual debts to Akerlof (1970), and Chesbrough (2003) as well as Penrose (1959/1995) will be apparent.

2. The Triple Helix approach

The paper now embarks upon a review of alternative and critical perspectives on the role of regional innovation in contemporary economic development. This is done partly to assess the validity of claims of explanatory priority by the regional innovation systems approach, and partly to formulate more clearly the theoretical underpinnings of the concept and extrapolate its key practical implications. One of the competing views consistent with the quest to disclose the importance for economic growth of local-regional

innovation networking was Etkowitz and Leydesdorff (1997) model of the ‘Triple Helix.’ Here, in a swiftly emerging *knowledge economy* as they saw it, those places with entrepreneurial universities would increasingly see growing demand for knowledge transfer to industry and, through government, to society. Moreover, the spread of universities is less asymmetric over space than R&D. In this perspective it is proposed that industry and government will be prepared 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, which is to say the least, a successful case. In reference to this, Gunasekara (2005) examined in detail the validity of the Triple Helix model in wholly different contexts in Australia. Not surprisingly he found a model design based on MIT worked poorly for the more average universities and regions that acted as his laboratory. Comparable findings for Sweden are reported by Jensen and Tragardh (2004). This is a classic instance of the asymmetric knowledge⁴ problem that Triple Helix proponents overlook. Thus while the abstract principles of Triple Helix *rapprochement* hold in general among such distinct ‘epistemic communities’ (Haas, 1992) as the three implied, the boundary-crossing effort required can in reality 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 (see also Chataway, Tait and Wield,

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

⁴ Asymmetric knowledge derives from Nobel laureate George Akerlof’s (1970) insights into ‘asymmetric information’ as causing both market imperfections and market failure. ‘Knowledge’ is preferred to ‘information’ because of the latter’s passive and linear, ‘absorptive’ connotations, while knowledge implies active and even socially interactive meaning creation and action framing. The key interaction nodes in these relationships are: information, meaning, knowledge, and action (see Qvortrup, 2003). One *caveat* is that Akerlof contextuated his observed asymmetries within contracts between individuals in markets whereas knowledge asymmetries as understood here are mostly institutional and non-contractual.

2004). 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. Academe may in future evolve away from entrepreneurship. In this context, knowledge capabilities include receptivity to social concerns in institutional and organisational processes that integrate transdisciplinary communities of practice to form knowledge for policy learning and innovation.

Examples of this way of thinking and operating are analysed in Sotarauta and Kosonen, 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 six 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. Triple Helix thinking draws attention only to possible but weakly generalisable broad outlines of important contemporary innovation interactions. So the quoted examples of ground-up creative action absent proximity to universities per se mobilise new regional knowledge capabilities for promoting systemic innovation in the face of asymmetric knowledge in research exploitation.

3. Scalar envelopes

A broader attempt to capture the integrative and interactive nature of the knowledge economy exam-

ined from the regional perspective is contained in early work on regional innovation systems (Cooke, 1992; Cooke and 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 identified 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 exploitation⁵ *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).

Understandably, with any successful theoretical field, the regional innovation systems literature has been exposed of late to an eclectic mixture of critique, comment and conceptualisation on the issue of ‘scale’ emanating from contemporary economic geography. A certain obsession with globalisation and the contemporary state led to the perspective being attacked ‘from within’ by Dicken et al. (1997) for its conservative, linear determinism that sees ‘globalisation’ as a totalising, relentless and inevitable power, proceeding in an all-encompassing way to deny capability to other

⁵ The exploration to exploitation relationship was first mooted in March (1991). Then, but even more nowadays, trialling, testing and prototyping knowledge was rising in importance, especially after side-effects of weak or non-existent testing produced deaths affecting victims of nuclear, agro-food, automobile and pharmaceuticals innovations. Hence, it is included here as ‘examination knowledge’ and treated as of equivalent importance to the more familiar ‘exploration’ and ‘exploitation’ knowledge categories in the overall innovation process.

'scales'. Trying to escape this we see, for example, Bunnell and 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.⁶ 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 '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 and 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), 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 (Cooke and Morgan, 1998; Cooke et al., 2000). 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 et al., 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 they 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

⁶ 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'.

productive, high-level theory discussions that remain uncoupled to real-world experience.

The regional innovation systems perspective is on strong ground in its rejection of any linear, hierarchical determinism from the ‘scalar envelope’ critique. This is not least for the latter’s weak grasp upon ‘agency’; but taking a step further, it will be shown how ‘scale’ blinds these and most contemporary globalisation theorists to an inverted understanding of the real nature of the abstraction that interests them. For not only does it fly 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), it mistakes scale for power. Thus we go further in reasserting the relevance of the ‘regional’ to the study of global innovation. This arises with discoveries regarding ‘open innovation’ whereby many industries show large ‘scale’ corporations having become *supplicants* to small ‘scale’ knowledge-intensive firms and clusters due to their asymmetric knowledge weaknesses (Chesbrough, 2003).

This extension of the dynamic knowledge capabilities analysis into the regional domain underlines the centrality to globalisation of accomplished regional innovation system nodes consisting of a ‘research industry’ composed of specialist firms and research institutes, as a key asset in the formation of global knowledge networks. The contested term ‘regional innovation’ 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 and Simonsen, 2003). However, we have seen how the until now apparently settled ‘globalisation’ debate undermined that comforting presumption. It demonstrated the growing insignificance of the nation-state faced with greater extensive and intensive integration of global value chains. But it missed the key point that industry organisation has been dislocated in the asymmetric knowledge economy.⁷

⁷ The geographer’s affection for ‘scale’ is also apparent in an otherwise complementary paper to aspects of this one published by Bathelt et al. (2004). They differentiate explicit from implicit knowledge transfer geographically between ‘scale’ interactions (pipelines), and geographically proximate ones (‘buzz’). The obvious problem with this is that ‘pipeline’ interactions denote closed, confidential, even

This is because the intersection of multinational firms and local-regional clusters on a worldwide basis represents a knowledge capabilities imbalance increasingly favouring the latter (see, for example, Gereffi, 1999; Henderson et al., 2002; UNIDO, 2002). This has set in motion a process whereby increasing returns to scope and scale give the character of ‘spatial knowledge monopolies’ to knowledgeable clusters and their broader regional innovation systems. This marks a turn from ‘Globalisation 1’ towards ‘Globalisation 2.’

This relational view of spatial interaction naturally also means rejection of any ‘containerised’ notion of economic flows by the ‘scale’ proponents. For example, here disagreement is unavoidable with Bathelt (2003) who asserts 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, under conditions of asymmetric knowledge, to envisage a *country* including, even 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). The US massively imported intellectual capital since time immemorial (Saxenian, 2000).

4. Interactions between Mode 2 knowledge production and ‘Globalisation 2’

There is a clear connection between the ‘Globalisation 2’ hypothesis and literature recognising

secretive relationships not scale or distance ones. Hence a (short) ‘pipeline’ relationship can easily be envisaged in close proximity as a contractual relationship between firms in the same cluster. This is precisely the meaning given by the originators of the ‘pipeline’ metaphor (Owen-Smith and Powell, 2004). They also argue that localised knowledge spillovers arise from ‘leakage’ of pipeline knowledge in clusters due to ‘open science’ conventions among scientists (see Section 5). The deliquescence of ‘open science’ and ‘open innovation’ is clear. As for ‘buzz’ that is so weakly specified as to be best left to the bees...or the birds.

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. Mode 2 ‘transdisciplinarity’ characterised diversification of knowledge production in specialist Research Centres 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. Further ingredients included also reflexivity, and networking to tackle knowledge ‘heterogeneity’. This influential and somewhat prescient perspective was criticised later, as we have seen not least by some of its authors (in Nowotny et al., 2001). Now ‘open science’ has evolved into ‘open innovation’ in recognition of the in house knowledge asymmetries increasingly associated with corporate scale.

We may also think of the regional innovation systems capability as one that is more highly evolved than, for example a ‘learning region’ as a simple expression of asymmetric knowledge. This is revealed in the way key regional, or for that matter, national functionaries seek to capture knowledge and information from more accomplished institutional settings. They then try to apply it, not always appropriately and probably not swiftly, to problems of development, ‘lock-in’ and path dependence currently confronting them. The most notorious recent example of this is the mis-selling of a questionable ‘clusters’ policy prospectus to regional and national bodies everywhere, to little apparent policy effect. By contrast to learning ‘lemons’ of these kinds, 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 and Freeman, 1993; De la Mothe and Mallory, 2003) from collaboration and networking across institutional boundaries that exist in the transdisciplinary mix of ‘epistemic communities’. This implies the presence of institutional innovation networks integrating regional institutions to each other and beyond to other regions, national systems and glob-

ally 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 applicators (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.

5. 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 confusion, especially in geographical literature. 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 (for extended discussion, see Cooke et al., 2000).

Is the knowledge economy a mere artifice, a further 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 knowledge⁸’, at the heart of innovation and entrepreneurship (Schumpeter, 1912, p. 57).

⁸ Schumpeter’s formulation suggests that the conventional neo-Schumpeterian distinction between *incremental* and *radical* (product, process and organisational) innovation is due an overhaul. Based on the EU-TSER FP4 project *Regional Innovation Systems: Designing for the Future*, Cooke and Schall (1997, 2005) advanced the notion of ‘recombinant’ innovation to capture that intermediary category between incremental and radical when, for example, a piece of technology and expert knowledge are recombined to innovate in a new field. A case in point was ‘smart card’ technology, which firms reconfigured to solve temperature, frequency or environmental exposure problems according to user requirements. Hargadon (2003) published a book on this phenomenon but made the mistake of reducing all innovation to recombination, thus ruling out other forms of innovation, and indeed invention, in the process.

Nonaka and 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’ (Marshall, 1916, 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 (1959/1995). She founded what has now evolved into the ‘dynamic capabilities of firms’ approach to microeconomics (Teece and 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, 1959/1995, xvii–xviii)

So, in effect, as it is put by Nonaka and Takeuchi (1995) ‘...the firm is a repository of knowledge’ (p. 34). Penrose (1959/1995) 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 (1959/1995) 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, 1959/1995, 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. The logic of this paper points to the metamorphosis transforming ‘Globalisation 1’ into ‘Globalisation 2’.

The multi-level nature of governance relations is of direct relevance to the regional–global 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 et al., 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 6 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 this 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 and Drug Administration approval, would presumably rank higher than a larger DBF or bioregion with mainly ‘pipeline’⁹ 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 and Lund-Jensen (2003) showed for the

⁹ In this case, ‘pipeline’ takes on another meaning, which connotes drugs in different trialling (examination knowledge) phases, not yet given final approval for sale, a process that can take 8–10 years.

food industry, something also argued from a different perspective by Smith (2001). But as Chataway et al. (2004) demonstrate, agro-food corporates are prone to making strategic errors at least as significant as many made by, for example, pharmaceuticals firms. This is a product of ‘blind spots’ between ‘economising’ and ‘strategising’ knowledge capabilities of the agro-food sector, in which biology is a core research competence but ‘contextualisation’ is not (Nowotny et al., 2001; Teece et al., 1997). Thus large corporates like Monsanto, Aventis (Sanofi) and Bayer show certain incapacities in reading markets, 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.¹⁰ Once more this is a simple illustration of asymmetric knowledge both of the ‘contextual’ kind identified by Nowotny et al. (2001) and the technical ‘examination’ and ‘exploitation’ kinds.

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.¹¹ The role of (non-pecuniary) knowledge spillovers or what are more traditionally known as pure dynamic externalities, is important here. Why would firms cluster geographically in bioregions

¹⁰ This is discussed in Section 6, which contains profiles of specific agro-food knowledge R&D.

¹¹ 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 and 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.

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 and ‘open science’ parlayed into ‘open innovation’ 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 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.¹²

Just as there is debate, that may be approaching resolution, regarding the primacy of regional specialisation or diversification for innovation (see fn. 12) 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 and Powell (2004). The former generate data to show 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 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

¹² On knowledge network capabilities, the early work of Penrose (1959/1995) has given rise to the economics sub-field of studying ‘dynamic capabilities’ of firms to understand regional and other growth processes (Teece and Pisano, 1996; Teece et al., 1997).

- 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 their investment a mean distance of one hour’s driving time from their office base for the most part.¹³ These are localised ‘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 biotech-

nology 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 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 bioregion. Thus:

‘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

¹³ 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).

channels represent excess capacity' (Owen-Smith and Powell, 2004)

Finally, though, leaky channels rather than closed pipelines also represent 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 are otherwise subject to 'open science' conventions. This is represented in Fig. 1 below. To explain what the table shows, it suggests the following.

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 and 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.¹⁴

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-fertilisation 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 systemic. The key question is, does this model apply regarding research and innovation stimulated by large corporations in sectors other than bioscience. The answer provided by the likes of Schamp et al. (2004) for automobiles, Chesbrough (2003) for ICT and household products, and Van den Biesen (2004) for general electronics is that 'open innovation' from knowledge capable regional clusters is common to all these industries.

	<i>Specialisation</i>	<i>Diversification</i>
<i>Pipeline</i>	1. Embryonic	4. High Success
<i>Open Science</i>	2. Innovative	3. High Potential

Fig. 1. Characterisation of successful and potentially successful bioregions.

¹⁴ 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).

Table 1

Bioscientific capabilities, Public Research Organisations in Basel, Switzerland, 2001

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	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

Source: BioValley science guide [http://www.biovalley.ch/main/downloads/BioValley%20Science%20Guide%20\(c\).pdf](http://www.biovalley.ch/main/downloads/BioValley%20Science%20Guide%20(c).pdf).

6. Ground-up Globalisation counters A discourse of ‘scale’: the case of Basel and its bioscience

In this final section of the paper an illustration is provided of how the *regional knowledge capabilities* theory works for an industry and region with small scale but global reach. Of key importance is exploiting open innovation on a global basis to overcome inherent knowledge asymmetries and overturn the imbalance in an evolutionary process over time. The industries are pharmaceutical biotechnology and agro-food biotechnology and the place is the canton of Basel. Basel is a small place in a small country but it hosts four or the largest bioscientific companies in the world: Novartis,¹⁵ Roche,¹⁶ Syngenta (agro-food biotechnology), and Lonza.¹⁷ But Basel also hosts many smaller DBFs such as Actelion, Discovery Technologies and GeneData.¹⁸ Of the 200 Swiss biotechnology compa-

nies listed in the Swiss Life Sciences Database¹⁹ 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.

From this base Roche and Novartis have been the world’s most active acquirers and partners of US, especially Californian, DBFs. 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. The integration of Novartis with the San Diego bioregion warrants deeper exploration to show how small country big pharma overcame asymmetric

¹⁵ Novartis employs 36,000 worldwide.

¹⁶ Hoffmann-La Roche employs 30,000 worldwide.

¹⁷ Syngenta and Lonza employ 20,000 and 6000 worldwide, respectively.

¹⁸ 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 and cardiology, respectively.

¹⁹ www.swisslifesciences.com.

knowledge by gaining from *embeddedness*²⁰ in a local cluster with global knowledge and innovation capabilities. The strongest of these collaborations, agreed by Sandoz in 1992 and effective from 1997, was the 10 year research collaboration with The Scripps Research Institute (founded in 1955). It complemented in house 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 (Zeller, 2002, 2004).

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 investment²¹). 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 and 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.²² Venture

²⁰ 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.

²¹ This practice was emulated by and from other pharma companies. Before its acquisition by junior French firm Sanofi Synthélabo, Aventis was considering implementing a comparable strategy in Toronto. Meanwhile between 1999 and 2003, Pfizer, Wyeth (acquiring Genetics Institute), Amgen (acquiring Immunex), Aventis (acquired Ariad), Abbott (BASF divestiture) and AstraZeneca were all represented in Cambridge, Massachusetts. However, the embedding strategy of Novartis is both distinctive and, in relation to basic research, deeper.

²² In 2000 Syrrx was founded, as were Kalypsys and Phenomix in 2001.

capital comes from the Novartis BioVenture Fund.²³ Established in 2000 with \$100 million available, the fund had by 2002 invested in 11 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.

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 2). The approach taken by Roche involves partnering agreements with innovative, often relatively immature but 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 2.

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 3 the collaborative links of Novartis in the Cambridge–Boston bioregion are shown. 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

²³ Novartis also has a bioincubator at Zug in Switzerland.

Table 2

Roche collaborations with San Francisco and San Diego DBFs

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

Source: Roche and DBF Websites.

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 ther-

apy, especially bioinformatics and biochip 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. Firms seek out compatible regional knowledge capabilities, found in locations with both the

Table 3

Novartis Collaborations with Boston Biotechnology DBFs and Institutes

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 and 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

Source: Zeller (2002).

assets and the knowledge ‘leakage’ associated with ‘open innovation’. Contractual partnerships ‘cluster’ to ‘cluster’ are formed through inter-firm and inter-research institute collaborations, balancing corporate knowledge asymmetries while stimulating the globalisation of biosciences and bioregional nodes in the process. It is an almost perfect case of ‘ground-up globalisation’ (or ‘Globalisation 2’) stimulated ultimately by the imperative of moderating asymmetric knowledge. 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 The 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 (until the Vioxx catastrophe wiped billions off its market value with thousands of compensation cases in prospect) was also of the belief that in house research was the preferable form by which corporate R&D should be organised. Alternatively, Merck also engages in short term collaborations still intending to control as much of the R&D chain as possible in house. Pfizer has mainly kept its pipeline from drying by acquisition. Eight of its 13 new active substances (NAS) derived from its acquisition of Pharmacia. There is strong evidence that such megamergers as the likes of Pfizer and Glaxo have engaged in 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. HTS is supercomputers seeking inhibitor molecules for those that cause disease. 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 it was

thought only the administrative capabilities of ‘scale’ could satisfactorily master.²⁴

Regarding knowledge capabilities and their asymmetries, the following analysis re-directs our attention from the failings of ‘big pharma’ in basic *research*, that as we have seen caused their heavily increased reliance upon DBF capabilities and ‘open innovation.’ Newly emergent failures have occurred in precisely the *development* (HTS) capabilities identified as those of ‘scale’ that would be expected to 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 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 a paper by Nightingale (2000). 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 examination or testing process is fundamental to high-throughput screening (HTS). Most large pharmaceutical firms installed the new machines in sites formerly housing their laboratories, and many invested large sums in small companies specialising in HTS. For example, GlaxoSmithKline spent more than \$500 million to buy a combinatorial chemistry company.

However, the automation processes failed to work as anticipated. The head of discovery chemistry at Bristol-Myers Squibb referred to the first five or 6 years of the new technology as 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.²⁵

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 the theoretical underpinning for the widely observed rise of regional innovation systems and within them ‘knowledgeable clusters.’ It is also clear how it operates in regard to biosciences and for other industries like ICT, electronics, and automotive engineering (Chesbrough, 2003; Van den Biesen, 2004; Schamp et al., 2004) and new (and old) media (Grabher, 2002), all heavily reliant on networks of project contracts. Where these are multiple and of relatively short duration they promote clustering around key knowledge transceiving²⁶ organisations (Cooke et al., 2004). Where these also operate in a wider context

²⁵ This account is given in Landers (2004). At issue, of course is the ‘big pharma’ response to this further débâcle. Some firms began subcontracting this function to specialist screening firms, others have reduced scale. Bristol-Myers has tried to create a better mix of high technology and old-fashioned lab work with a screening machine capable of testing a million chemicals at once, taking as little as 10 µl of each chemical. Scores of mice are available nearby allowing scientists quickly to test the ‘hits’ in animals. This avoids a problem whereby scientists spend months or years refining a compound in a test tube only to find it does not work in living things. Schering-Plough’s main research laboratory has a machine that allows making several dozen variations of a chemical, all in the liquid state. The number is much smaller than older machines produce and the scientist can hand-pick the combinations and get higher quality. Hence screening is returning towards craft-skill and computational hybrids, having demonstrated total automation for scale to be unworkable.

²⁶ The analysis offered in this paper seems to find faults everywhere in regard to previous thinking about interactive innovation. Much of this derives from binary conceptualisations that have dominated the field. Thus ‘tacit’ knowledge is said to be transformed into

²⁴ This is argued forcefully to be the new core competence of big pharma by Nightingale (2000).

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 articulated setting constituting a *Regional Innovation System*. This 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 underpinned by deeper knowledge 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 key pharmaceuticals firms’ mighty impact, 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 ear-

‘codified’, not without difficulty, to be sure. But how those difficulties are overcome remains largely unexplored. The notion of ‘transceiving’ via an institution, network or individual is not entirely adequate, rooted definitionally as it is in telephony. An element of hermeneutics and transliteration is required, perhaps captured in the triplet of implicit–complicit–explicit. However, hitherto, ‘complicit’ has carried undertones of transgression, not to say illegality. Nevertheless, it captures important aspects of the revelatory process involved in this complex institutional or individual knowledge interaction.

lier as BioValley (see Table 4) 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 1) 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 providers.

BioValley supports the buoyancy of biotechnology in the cross-border region, helping with knowledge asymmetries problems by networking 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. 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, where most of Syngenta’s biotechnology research is conducted. These laboratories employ 5000 of Syngenta’s 20,000 employees. According to the company website²⁷ ‘...research within Syngenta complements hundreds of collaborative activities with leading universities, research institutes and public

²⁷ www.syngenta.com/en/about_syngenta/research_tech_where.aspx.

Table 4
Selected Agro-food Bioregions

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

Source: Ryan and Phillips (2004); Svensson-Henning (2003); Invest Skåne (2004).

* NB: Food producers; R&D institutes; raw materials and ingredients suppliers; packaging firms; industry institutes; government agencies; food organisations.

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 range of knowledge capabilities it requires, so integrates with DBF clusters²⁸ 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 eight countries. It employs 6200 people worldwide and is the leading supplier of active chemical ingre-

dients, intermediates and biotechnology solutions to the pharmaceutical and agrochemical industries. It thus plays a key processing role on the bioscience value chain as it 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 cosmeceutical and nutraceutical products. Hence Lonza occupies a key manufacturing positioning in the biotechnology value chain.

7. Conclusions

The empirical section of this paper complements the theoretical and review parts by showing how microcosms enable macrocosms to function, at least

²⁸ 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.

in biotechnology. There is strong supporting research to suggest biotechnology merely pioneered ‘open innovation’ but now many other industries are emulating it in order to overcome intra-firm knowledge asymmetries by tapping in to the regional knowledge capabilities and systemic innovation strengths of accomplished regional and local clusters. Underpinning these are *regional knowledge capabilities* that help metamorphose even macro-processes operating through globalisation. Thus it was shown how ‘Globalisation 1’ is metamorphosing into ‘Globalisation 2’ as Mode 2 knowledge production, suitably co-evolved and contextualised due to knowledge economy imperatives exerted upon multinational corporations. This demonstrates the force of a new theoretical approach to understanding economic evolution, and one argued here to be superior to competing and critiquing arguments. Moreover, it suggests current theorisation of globalisation is unconsciously linear and scale-determinist. It is evident that the analysis of globalisation benefits markedly from an interactive regionalisation perspective. The Triple Helix approach to local-regional innovation was found too macrosociological, functionalist and consensus-focused to capture the fine texture of specific knowledge capabilities. These are obscured at the microeconomic level 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. Equally, the defensive ‘scale’ critique of regional science and globalisation’s proposed annihilation of power relations among networks at the local-regional scale 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 interactive systems explored in the preceding, by means of which global knowledge exploitation is facilitated.

Taking a Regional Knowledge Capabilities approach proves 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. These both create and take sustenance from asymmetric knowledge endowments. From these capabilities

rooted initially in ‘open science’ and subsequently ‘open innovation’, a spiral of growth, operating through global network nodes is set in motion. What clearly happens is that capable knowledge actors of various kinds congregate, particularly but by no means only in biotechnology, in a few particular places we may call clusters or even ‘megacentres’. From these bases knowledge is *transceived* (or *complicitly* transformed or metamorphosed from implicit to explicit) 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 challenges now are to anatomise the ways in which such geographical clustering within regional innovation systems produces such superior knowledge performance across a variety of industries, and to better understand how asymmetric knowledge is reproduced and moderated, as various regional economic development trajectories suggest it is, albeit with difficulty. The case of Basel offers possible stylistic insights into how.

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