Industry and Innovation
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/ciai20

NEW ECONOMY INNOVATION SYSTEMS: BIOTECHNOLOGY IN EUROPE AND THE USA

Philip Cooke

Available online: 14 Jul 2010

To cite this article: Philip Cooke (2001): NEW ECONOMY INNOVATION SYSTEMS: BIOTECHNOLOGY IN EUROPE AND THE USA, Industry and Innovation, 8:3, 267-289

To link to this article: http://dx.doi.org/10.1080/13662710120104583

Industry and Innovation, Volume 8, Number 3, 267–289, December 2001

New Economy Innovation Systems: Biotechnology in Europe and the USA

Philip Cooke

The learning processes by which European biotechnology firms are seeking to emulate, catch-up and even overtake US biotechnology, constitute a matter of wide public interest.[1] There are three key mechanisms to be explored, in all of which the US and the European cases (which focus on the UK and Germany) have adopted different routes to a similar destination. The three elements that will structure the account are: exploitation of basic science; venture capital; and cluster-formation. In the UK, as in the USA, functioning biotechnology clusters can be found in a number of locations, albeit there are major scale advantages in the US case, not least because commercialization activity began seriously at least 10 years ahead of the UK. It could be said that Germany's progress is about 10 years behind the UK, at least in respect of our three key variables of exploitation, financing and clustering. Of course, these are not the only mechanisms at work in explaining the evolution of biotechnology. Basic research funding, invention, regulatory variations between national business and innovation systems need to be taken into account, as do the nature of markets, the structure of industry and qualitative aspects like 'entrepreneurship'.

However, it will be argued that the three variables selected for analysis are the most important in explaining how the industry has developed at different speeds in the three leading countries under investigation. This is because each is highly proximate to the technology in question whereas the other variables are more contextual and influence every industry to some extent and in distinctive ways. Nevertheless, on some occasions matters of specific relevance to learning and, importantly, impediments to it, which are particularly strongly influenced by these contextual factors, will be brought into play as appropriate. Early in the paper an effort is made to capture key "new economy" conventions and explore their implications for systemic innovation. What follows is structured into a threefold exploration of

1 This paper was helped to fruition by a number of advisers and commentators. Its origins lie in the author's stint as a member of UK Minister of Science's Biotechnology Clusters task force in 1999. Commercialization and clustering were examined in interviews conducted in the UK and USA. This was followed by a commission from the UK Department of Trade & Industry to review the progress of the German biotechnology sector, thus enabling a three-way country and cluster comparison. None of the views contained in the paper can be attributed to anyone other than the author. In tracing the history of biotechnology discoveries from the 1950s, I was assisted by Samuel Ogunsalu of the UK BioIndustry Association, to whom I express gratitude. The "new economy" innovation system elements were stimulated by invitations to speak at a Regional Science Association conference in Miami, April 2000, and the DRUID Summer 2000 Conference at Aalborg, in May 2000. Thanks to John Rees and Bengt-Åke Lundvall for their kindness. Finally, I wish to thank Jens Frøslev Christensen for editorial comments, and two anonymous referees for commenting critically but constructively on the original draft.

1366-2716 print/1469-8390 online/01/030267-23 © 2001 Taylor & Francis Ltd
DOI: 10.1080/13662710120104583

exploitation, financing and clustering with stylized accounts of advantage-taking and missing, early and late moving behaviour, and sources of impetus for catch-up. Reference is made to the extent of success or failure in such efforts for each country. Where useful accounts of key phases already exist, these are cited and outlines only provided. Towards the end, some reflections on the current phase of "new economy" innovation-induction, developed particularly strongly in California, will be offered.

IS ANYTHING NEW ABOUT THE 'NEW ECONOMY'?

When it first started being written about by Kelly (1998), Micklethwait and Wooldridge (2000) and Norton (2000) the "new economy" looked strange, not least because of the conceptual exaggeration and binary opposition explicitly used to contrast its key conventions (North 1990) with those purporting to represent the "old economy". Of particular inappropriateness has proved to be the view that the new economy had conquered the business cycle. Moreover, the practice of investing massively in "new economy" businesses well before they even demonstrated they had the slightest chance of entering profitability has been significantly revised as venture capital and share-option losses piled up. Nevertheless, practices of reasonably sober investment firms, over decades rather than months, became clearer during the dot.com frenzy, and demonstrated an effortless superiority in, for example, cluster-building activity over public-sector efforts. The *keiretsu* model of building inter-trading 'EcoNets'[2] of complementary assets by the likes of Kleiner, Perkins, Caufield & Byers, Silicon Valley's leading venture capitalist (VC), is the most obvious case, since emulated by others, notably Intel's corporate venturing arm, as a means of building up internal, knowledge-economy clusters.

This is probably the most interesting "new economy" organizational innovation intellectually and from a policy viewpoint. It is so, not because of the investment aspect, but because of the early recognition of the central importance in the new, knowledge-driven economy, of management support for technologically expert but organizationally weak start-up businesses. Thus VC managers are placed in many firms in the portfolio, and they become the network managers that advise on best or better practice. Firms and VCs have a shared incentive to give and take best advice, in the process becoming closely networked and forming inter-trading, knowledge-assets linked by managers whose job it is to maximize equity-value in the investee and investor businesses. Incentives and capabilities to commercialize innovation in this way are generally not available to public servants, though the emergence of public venture capital may cause moderation of that judgement (Doran and Bannock 2000).

To return to the context for this kind of development, a flavour of the "new economy" convention-set or paradigm can be given briefly at the outset. This is important because even though much VC in Europe is conservative, preferring safe management buy-outs or buy-ins to risky early stage investment in new technology businesses, VC-led commercialization of new knowledge is present in varying degrees.

---

2 As will become clear below, EcoNets refer to an ecology of complementary firms networked by virtue of equity held by a single venture capitalist, corporate venturer or other kind of investor. The placing of a few managers on numerous boards of equity holdings means interactive learning is speeded up massively compared to normal market processes and even more so compared to public modes of knowledge transfer.

This occurs especially in and around cities like Amsterdam, London and Stockholm, whose national economies form the first three entrants in the European Venture Capital Association's index of VC as a percentage of GDP. Importantly, if it is commercialization rather than management-buyout VC it will incline to a similar EcoNet logic, speeding-up evolutionary, cluster-building tendencies as displayed in the USA, for the same reasons of efficiency and effectiveness in incentivized knowledge-transfer. That is, both investor and investee share an interest in successful, rapid firm growth. The new model, which we call New Economy Innovation Systems is localized in or near innovative cities or urban agglomerations which host knowledge-driven clusters, and regionalized in States or sub-national administrative areas with benign or proactive policies towards the promotion of systemic innovation. This is represented by substantial historic investment in universities and research institutes, active policies to support university–industry interaction, encouragement for widespread skills-development, and efforts to provide innovation and commercialization infrastructures where there is market-failure, as well as low entry-barriers for private suppliers of innovation support once demand has grown. Such systems are strongly conditioned by geographical proximity, but a main function is also to be receptive and attuned to absorbing all-important basic research funding that comes from external foundations or higher levels of governance such as the federal or supranational (Cooke *et al.*, 2000).

Key elements of new economy conventions are captured in Table 1, a reduced composite of the contributions of Kelly (1998), Micklethwait and Wooldridge (2000) and Norton (2000). Key cognitive innovations are conventions like tolerance of treachery (the expectation that your partner today will be your competitor tomorrow, but probably again your partner the day after), low litigation (why bother when you can innovate to escape your imitator?), intelligence (distributed rather than hierarchical), and the widespread use of stock options as compensation (still stressed as a reason "brain-drain" entrepreneurs will not return from the USA where taxation on realized income from selling options is significantly less). Thus innovation is the fundamental source of value, seeking it out is an investment imperative, and systemic search and selection (i.e. active "scouring" of research labs) procedures by VCs is the

TABLE 1: OLD AND NEW ECONOMY CONVENTIONS

Old economy	New economy
Skill	Lifelong learning
Industrial conflicts	Teams
Constant returns	Increasing returns
Value scarcity	Value abundance
Rising prices	Falling prices
Monopolies	Competition
Plants	Intelligence
Standardization	Customer choice
Litigation	Investment
Incremental innovation	Disruptive innovation
Confidentiality	Tolerance
Hierarchical	Distributed
Wages	Stock options

TABLE 2: ASPECTS OF REGIONAL AND NEW ECONOMY INNOVATION SYSTEMS

Regional innovation system (RIS)	New economy innovation system (NEIS)
Research & development driven	Venture capital driven
User–producer relations	Serial start-ups
Technology-focused	Market-focused
Incremental innovation	Incremental & disruptive
Bank borrowing	Initial public offerings
External supply-chain networks	Internal EcoNets
Science park	Incubators

main means of exploiting gains from public investment in basic research. In traditional innovation systems analysis (e.g. Lundvall 1992; Edquist 1997), there is an emphasis on the role of public agencies and even strategies, some promoted at regional level, particularly in the EU. Whether by accident or not, EU innovation rates are low compared to the USA, and VC is more pronounced in the USA. The logic of the last two statements suggests the vigorous investment strategies of private investors and innovators, revealed most clearly in new economy sectors like biotechnology and IT, help explain the difference in innovation performance to a considerable extent.

If we want to translate these "new economy" ways of thinking into an approach to innovation systems then Table 2 is an attempt to capture key dimensions of difference between the kind of Regional Innovation System (RIS) discovered in some EU regions in the 1990s. These were often, but not exclusively, those where industrial change had caused regional administrations to seek new trajectories for their economies away from "old economy" sectors threatened with decline, or specific, inherited industrial monocultures (Braczyk *et al.* 1998; Cooke *et al.* 2000; Cooke 2001b). These economies had R&D in large firms with supply-chains that were technology-centred to suppliers engaged in incremental innovation that was assisted by public technology transfer from public or industry research laboratories and skills-provision designed to fit supply to demand from that occupational structure (see, for instance, Cooke *et al.* 2000). Modernization entailed encouraging spin-off businesses to set up on science and technology parks where inward investors might be attracted to reproduce the model in the new sectors, e.g. automotives replacing textiles or electronics replacing steel (Tödtling and Sedlacek 1997). There was some attempt, not always successful, to shift from a linear, R&D-driven culture to a more interactive, network-driven approach, but firms used to hierarchies and power-games found it hard to adjust, so networks eroded and innovation declined.

The systemic nature of innovation in "new economy" settings derives from VC searching knowledge-centres for start-up opportunities. Businesses may be established by serial entrepreneurs, but VCs are also seeking a constant flow of start-up deals. These they aim, frequently unsuccessfully, to take to market as initial public offerings (IPOs) from where they will realize their equity share for future investment. Losses are compensated by the rule of thumb that from ten investments, eight will fail, one will break-even and one will be highly profitable. Thus innovation, the more disruptive (in Schumpeterian terms) the better, is the value-source of the whole process. To secure intense value-sources, VCs will retain shares in portfolios of successful, complementary businesses and build internal (intra-portfolio) value-based network relationships among investees that take on cluster-like characteristics as they engage in increasing inter-trading, joint innovation and other forms of interaction. Eventually, VCs seek, as do others, like management consultants, upstream integration into the start-up management process itself by supporting, sharing or owning incubation facilities. This has developed to the point where some VCs present themselves as "incubators", identifiers of upstream, close to scientific knowledge start-ups whom they nurture, while others are "accelerators", or those who seek to take incubated firms quickly to market to realize superprofits. This, in a nutshell, is the New Economy Innovation System.

EXPLOITATION OF BIOSCIENCE FOR BIOTECHNOLOGY

One of the sectors in which this approach was pioneered was biotechnology in the USA. It quickly becomes clear, in hindsight, why this aggressive "scouring" mentality came to dominate. It was because VC provided the financial means for knowledge exploitation of the kind described, but American science did not produce enough disruptive technologies (unlike in IT where there were some) so discoveries were imported, almost exclusively from Europe where, from the 1950s, a number of startling inventions and discoveries were made but not exploited commercially. Hence, the history of current American hegemony in biotechnology looks strange if Table 3 is scrutinized. This shows how important European, and particularly UK-based and funded research has been for *invention* of new knowledge in the life sciences. Since the beginning, with Watson and Crick's discovery of DNA structure (the double helix), and the Argentine/German partnership of Milstein and Köhler, who discovered monoclonal antibodies, the UK in general, particularly Cambridge, has been the leading discovery location, a characteristic which as Table 3 indicates, shows no sign of diminishing. Hence it is clear that the raw ideas for biotechnology have always been first available not in the USA but in Europe, particularly the UK. However, exploitation mechanisms were always stronger and swifter in the USA,

TABLE 3: SELECTED KEY BIOTECHNOLOGY INNOVATIONS

Date	Innovation	Scientists	Country
1953	DNA structure	Watson/Crick	UK
1974	*In vitro* recombinant DNA	Cohen/Boyer	USA
1975	Monoclonal antibodies	Milstein/Köhler	UK
1977	DNA sequencing	Sanger *et al.*	UK
1978	Polymerase chain reaction	Mullis	USA
1979	p53 Cancer gene	Lane	UK
1982	Cascade superfusion bioassay	Vane	UK
1985	DNA profiling	Jeffreys	UK
1988	H2-receptor antagonist	Black	UK
1996	Transgenic sheep	Wilmut	UK
1998	Antibody protein engineering	Winter	UK
1998	Nematode worm sequence	Sulston	UK

Source: Schitag *et al.* (1998), BioIndustry Association (1999).

TABLE 4: KEY INNOVATIONS IN DIAGNOSTICS

Innovation	Date	Country of origin
Enzyme labels (ELISA)	1972	Netherlands
Flow-through membranes	1976	UK
Time-resolved fluorescence	1979	UK
Enzyme amplification	1980	UK
Chemoluminescence	1980	UK
Biosensors	1980	UK/Sweden/USA/Japan
DNA fingerprinting	1984	UK
PCR amplification	1985	UK
Immunochromatography	1986	UK/USA
DNA chip	1991	UK/USA
Lab on a chip	1993	UK/USA

Source: DTI (1999), British In Vitro Diagnostics Association.

especially in places like Silicon Valley and Boston where VCs were clustered because of the earlier history of VC pioneers connected to IT start-ups.

Much the same can be said about the growing field of biotechnology application in *diagnostics* although originator countries other than the UK and USA enter the frame here. As the DTI (1999) report on which Table 4 is based rather poignantly states:

> many of the fundamental discoveries that have led to the development of diagnostics as a business sector were made by UK scientists. However, the UK has failed to exploit the R & D, with the consequence that the large companies which dominate this sector are now foreign-owned. (DTI 1999: 16)

Exactly the same has occurred with inventions. The key question, therefore, is what mechanisms caused exploitation for the market to be so effective in the USA, especially in California, but also Boston and, more germane to the analysis from the European perspective, what cultural or institutional barriers prevented exploitation from developing as effectively in the UK and Germany, in particular? Finally, what if anything, has been learned and implemented through governmental or private institutional action in respect of exploitation? We can start with a brief outline of American first-mover advantage, not least because excellent accounts such as Prevezer (1998) have already helpfully explored this.

Companies such as Sequoia Capital, Sierra Ventures, Mayfield Fund, New Enterprise Associates and Technology Venture Investors are relatively unknown by comparison with the firms they have invested in, but one of them, the largest VC, Kleiner, Perkins, Caufield & Byers (KP) is rather less obscure. It also happens to be the firm that launched the first biotechnology company, Genentech. In Kaplan's (1999) study of John Doerr and KP, of whom he is the fifth partner, it is pointed out that since its founding year of 1972, KP has raised $1.4 billion in capital and founded more than 300 companies. In 1997 these companies were claimed to be worth $125 billion in share value, produced $61 billion in revenue and employed 162,000 people. It is difficult to compare, but this is probably a higher rate of systemic innovation than many regional and some national systems have achieved in an equivalent period.

Regarding biotechnology KP associate Robert Swanson realized that genetic engineering was a different version of information technology and, wanting to start up such a business, asked KP for $1 million, in 1975 an eighth of the total KP fund, to start a firm. Turning him down, KP began scouring the universities and found Herbert Boyer of San Francisco Medical School who, unlike other, UK-based discoverers, had patented his discovery, with Stanley Cohen, of recombinant DNA in 1973. Swanson agreed to invest $100,000 from KP in return for 25 per cent of Genentech, established in 1976 as the first biotech firm. The systemic dimension of the process involves the first KP decision to encourage Swanson to subcontract parts of the genetic engineering process rather than paying for a total in-house solution, the involvement of public, including university, labs and early use of the patenting system. Subsequently Genentech was encouraged by KP to subcontract separate parts of the experimental work to three university or medical foundation research labs. As none of the contractors were able to see the big picture, confidentiality about a first-mover product—*somatostatin*, a human brain hormone—as well as experimental risk spreading were achieved. Later, a comparable model was followed when KP partner Brook Byers launched antibodies firm Hybritech in San Diego. KP earned $188 million for $1.4 million investment when these two made their IPOs in 1980–81. This was the start of the huge fund growth KP experienced from this time to the present. It dated from the 1980 Bayh–Dole Act that allowed a commercial return on research exploitation to be earned by universities in which the research was conducted.

A further dimension of this model of university-generated discovery being induced by VC into firm-formation, subcontracting and commercialization, was added by Hall (1987) and Prevezer (1998) when discussing the role of Eli Lilly & Co. in sponsoring a conference on the coming crisis of diminishing supply and escalating demand for insulin. Recombinant DNA was hypothesized to be a possible solution. Competition and co-operation ensued. Lilly funded a collaboration at the UC San Francisco Medical School which produced human insulin synthetically, giving rise to Chiron, while the genetic variety was subsequently originated at Harvard under Walter Gilbert, founder of Biogen and contracted to Novo Nordisk, Lilly's key competitor in insulin. The Genentech team of Boyer and the somatostatin collaborators, also backed by Lilly, had, by 1977 manufactured human insulin. Its base in synthetic chemistry meant it avoided regulatory controls on human genetic material of the time. Subsequent research has shown how localization of intellectual capital (Zucker *et al.* 1998), knowledge spillovers (Jaffe *et al.* 1993; Audretsch and Feldman 1996) and the creativity of knowledge networks (Powell *et al.* 1996) contribute to innovation. But there is a tendency for this literature to underplay the animator role of VC and contracts from pharmaceuticals firms, perhaps because the science is more beguiling than the mere money and management that make it commercializable.

In the UK at this time, such was the concern at being left behind that, as in other European countries, government induced a response while the pharmaceutical industry, unlike that in the USA, sought to develop strands of biotechnology in-house rather than collaborating with start-ups or universities. That there were few start-ups is testified by the role of the Labour government in establishing Celltech, rather as it had done in chip technology with Inmos. Crucially, as Shohet (1998) states, development of a small-firm sector was hampered by the virtual absence of VC. Moreover, the strong networking among private and public research funders, universities and specialist firms found in the USA, to some extent orchestrated through VC presence, was largely absent in the UK. There was no evident incentive structure for academic entrepreneurship, indeed disincentives included career-path erosion attendant upon joining industry and the regulatory "jungle" associated with new business formation. Industrial partnership or support was not required in research grant applications. This helps explain but not justify the failure of Milstein and Köhler, the Medical Research Council (MRC) or their Molecular Biology Laboratory to patent monoclonal antibodies. Realization of the aftermath of that failure had repercussions on the learning experience of institutional science in the UK, and could be said to have marked the first step in a change of culture that is still evolving today.

The first response came, as noted, not from the pharmaceuticals industry, banks or pension funds but from the 1974–79 Labour government which established Celltech as a biotechnology firm with first refusal on MRC-funded discoveries. The political repercussions of the lack of foresight shown by those involved in the loss of patenting rights are said to have contributed to the locational stand-off between Celltech, sited in outer London and the Molecular Biology Laboratory at Cambridge 60 miles away. By the 1980s and 1990s, however, many biotechnology start-ups had come into existence, especially at university cluster-sites like Cambridge and Oxford, as well as looser concentrations in Surrey, Scotland and Wales. Specialist VCs, notably Merlin Ventures established by Welsh biotechnologist and founder of Chiroscience, Dr (in 2001, Sir) Chris Evans, also include Biotechnology Investments Ltd and Apax Partners. Merlin Ventures now has a £155 million investment fund with Rothschild and is a large presence in the developing German biotechnology market. In 1999, Celltech and Chiroscience merged and subsequently acquired pharmaceuticals firm Medeva, the first such downstream integration, reversing the historic relationship whereby pharmaceutical firms acquire biotechnology firms as Roche did with Genentech. Recent research (e.g. Cooke 1999, 2001a) shows the UK with at least 270 biotechnology firms and pressure being placed on pension funds to raise their rate of VC investment from 1 per cent to closer to the government's perceived US rate of 5 per cent (Targett 2000).

Research funding and pump-priming in German biotechnology is largely at public sector funding behest. Traditionally, the Ministry responsible for earmarking developmental support, the Ministry of Science and Technology (now Federal Research Ministry), had become, in effect, "captured" by large German multinationals which stifled the growth of biotechnology because they did not understand its potential and they were much more attuned to the long and hitherto successful evolution of German synthetic chemistry than biology. Both academic and industrial research expertise pressed a shared interest that disfavoured the development of biotechnology. Unlike, for example, the National Institutes of Health in the USA, the German Ministry had no internal research competence in biotechnology. It was only a grant-allocating agency to meet external applications for programme or project funding, and relied too heavily on outside advice from chemists. This was reinforced by cultural and historical antipathies to genetic engineering. Other rigidities in the German case include a traditionally strong division between basic and applied research funding, the weak commercialization associated with programmes linked to the latter, and the clearly observed orientation of German pharmaceutical firms interested in biotechnology to look to the USA for innovations and innovative firms to partner or acquire.

The German innovation system (no more than the UK) had no piece of government legislation comparable to the US Bayh–Dole Act of 1980 that allowed universities to take a commercial return resulting from the exploitation of ideas and inventions discovered and developed in those universities. Thus German university researchers have had no incentive to file and exploit patents because, under German law, universities funded by the public purse had no right to intellectual property generated there. German IPR is assigned to the individual so if researchers wish to register patents this has to be done privately at the cost and risk of the individual researcher acting as a private citizen. A further point is that, unlike their counterparts in the USA or UK, German researchers and academics are civil servants and, as such, are not allowed to found their own enterprise or even take a second job as a member of a university. Thus, it continues to be the case that, say, a professor at a public university would have to leave that post to found a company. In countries where this is not the case such as the USA, UK, Netherlands and Sweden, academic entrepreneurship and one of its key supports, venture capital, were traditionally much higher (see Table 5).

Hence it is not surprising that until recently there were few biotechnology companies in operation as spin-outs from academic research. Technology transfer offices are generally not commercially minded, and, although there has been an increasing interest on the part of industry in funding biotechnology research and co-operating more generally, the realization on the part of the research community of the role they can play to help nurture future businesses, maybe founded and run by

TABLE 5: SHARE OF VENTURE CAPITAL INVESTMENT IN GDP

Country	VC/GDP ratio (%)
UK	0.39
Netherlands	0.24
Sweden	0.17
EUROPE	0.13
Norway	0.12
Finland	0.11
France	0.10
Belgium	0.08
Iceland	0.08
Portugal	0.07
Germany	**0.07**
Italy	0.06
Ireland	0.06
Spain	0.06
Switzerland	0.02
Greece	0.02
Denmark	0.02
Austria	0.01

Source: European Venture Capital Association (1998).

former researchers, has been slow to take root. Only very recently has the publicly funded German Society for Biotechnology Research begun to provide access for entrepreneurs to laboratories and equipment that might assist them in developing commercialization opportunities. Key to this was *BioRegio*, a Federal Research Ministry initiative from 1995 to generate biotechnology clusters at regional level by supporting public and private VC investments in start-up firms. Seventeen regions sought this funding (valued at DM 150 million) that was eventually by 1997 shared among three winning regions, centred on Cologne, Heidelberg and Munich (with a consolation prize for Jena). Hence, until the successful launch of *BioRegio*, this federal biotechnology cluster-building and commercialization contest (Dohse 2000), it could be said that, almost in spite of Germany's corporatist political culture, close co-operation and clear communication channels between government, industry and academia were severely hampered and to some considerable extent, non-existent (Giesecke 1998).

In terms of learning to change, something testified by *BioRegio* and *BioFuture*, a successor initiative in 1998, as well as many other public, federal and *land* initiatives, the sight of the German pharmaceuticals industry losing market share and investing in American biotechnology start-ups was the shock to the system that led to early initiatives, always led, however by the public sector, unlike the US case but rather similar to the early days in the UK. Thus while German pharmaceutical firms occupied a major position in the world market up to the 1970s, when 17 per cent of turnover derived from that source, it had declined to 8 per cent by 1993. Hoechst, for example, had declined from first to tenth position in the global market by 1994, recovering somewhat only by virtue of merger with Rhone Poulenc Rorer and Marion Merrel Dow in 1996 (since 2000, Aventis). When the relative decline was recognized in the early 1980s, the German business response was, in the main, to seek to buy into, form alliances with or seek closer supply relations with US firms, especially the newer, biotechnology firms that had started up in the 1980s. Hoechst, for example, were initiators in the move to conduct off-shore R&D in the USA when they signed a $70 million research contract with Massachusetts General Hospital in 1982. This event caused a reaction in the policy, academic and industrial fields of Germany and gave impetus to an effort to imitate the US model of technology transfer through the combination of research and venture capital to build successful biotechnology start-up firms.

These initiatives failed to raise commercialization of biotechnology in Germany, partly because large pharmaceutical firms often accessed funding to help make US acquisitions, partly because of the absence of VC, partly because of low research and academic entrepreneurship. The Gene Centres programme of 1984–89 was no more successful in enhancing exploitation though they were successful in regionalizing centres of excellence in basic research which subsequently proved to be valuable regional infrastructures into which the expressly regional cluster-building aspects of the 1995 *BioRegio* programme fitted. By 1997 there had occurred some quite significant growth, albeit from a dismal level, in VC, though most of it remained accessible mainly with public co-funding, minimizing private risk. Role-model firms like Qiagen, Morphosys and Lion Bioscience had grown to prominence, Qiagen being Europe's largest biotechnology firm by 1998. Ernst and Young (1999) found 220 biotechnology firms in Germany in that year, a big increase from the 170 in 1995. Most remain in platform products like diagnostics and reagent supply and there are, as yet few therapeutic drug firms among that group. So the German industry is immature in biotechnology, pharmaceutical firms still look to American acquisitions or partners for drug discovery and while VC has grown, it is less completely market-facing than in the USA or UK.

VENTURE CAPITAL

Venture capital is still small in Germany by comparison to the USA and UK. In 1998 US venture capital was some $50 billion, of which biotechnology took $1.3 billion. The equivalent totals in Germany were $6.6 billion and $180 million, respectively. Germany has fewer shareholders in general at 6.5 per cent of the population compared to 21 per cent in the USA. Even the venture capital that is invested in Germany is largely placed in traditional technologies and services with only some 7 per cent invested in new technologies of any kind (Schitag *et al*. 1998). Furthermore, German investors are more risk-averse than Americans in respect of the seed-corn funding and start-up stages of company development, with only 3 per cent of the above-mentioned 7 per cent of new technology funding going into these early, risky phases. A rise in VC since the active onset of *BioRegio* in 1997 has been accompanied by a rise in biotechnology start-up firms. However, both these events were kick-started into being by this first successful, federal commercialization programme because it spread *risk* for both VC and entrepreneurship (one VC D-Mark attracted at least one each from both federal and *land* funds) and risk-averse investment practice was the proximate cause of low commercialization.

If we explore what has been called a "venture capital revolution" in Germany, we find that most early and many subsequent firm development investments are made by "bootstrapping", with reliance on project-based funding, milestone payments and so on still the norm. A telling statistic is contained in Table 5, showing Germany's proportion of venture capital investment in total GDP in Europe.

So, although, as Table 6 shows, the German venture capital market is growing rapidly, it is from a very low base. Moreover, as Table 7 shows, venture capital investments in new technologies are generally minuscule compared to the USA and UK. Further added to this only marginally strengthening position is the fact that much of the available venture capital comes from banks and many of the funds and investing

TABLE 6: TOTAL VENTURE CAPITAL INVESTMENTS, US$ MILLION

	1995	1996	1997	Growth 1996–97 (%)
USA	7,566	9,535	12,791	34
Europe	7,043	8,575	10,910	42
UK	3,344	3,776	5,004	48
France	1,081	1,078	1,410	41
Germany	856	908	1,498	85

Source: European Venture Capital Association (1998).

TABLE 7: VENTURE CAPITAL INVESTMENTS IN NEW TECHNOLOGY FIRMS, US$ MILLION

	1995	1996	1997	Growth 1996–97 (%)
USA	4,045	5,952	8,487	43
Europe	1,676	1,688	2,607	74
UK	800	696	1,253	72
Germany	181	242	379	82

Source: European Venture Capital Association (1998).

firms have public origins. Also, as noted above, little of it goes to the most high-risk parts of the company development process.

Thus regarding the first point, concerning sources, German banks account for 58 per cent of venture capital funds, compared to 16 per cent in the UK, whilst institutional investors (pension funds and insurance companies) account for only 23 per cent compared to 53 per cent in the UK. On the second point, the public or quasi-public nature of venture capital firms, some 60 per cent of all venture capital investments in small and medium-sized enterprises requiring seed and start-up financing are made by MBGs (*Mittelständische Beteiligungs Gesellschaften*). These are public venture capital funds formed by *länder* in partnership with business and chambers of commerce because of the limited availability of private venture capital in Germany.

Although Germany has been the focus in making these venture capital comparisons, this is warranted both to demonstrate the surprisingly small amounts of private VC until very recently present in the German innovation system, and to open up some discussion about the nature of VC investment priorities. Clearly, even now, a very small amount of a relatively small total of private VC investment goes to technology firms and a negligible amount goes to biotechnology. Yet, it is believed that VC is now not a problem in Germany (Schitag *et al.* 1998). That judgement is based on the large amounts of public sector VC available in Germany, much more than in the USA and UK proportionately speaking. Evidence from the rate of new business start-ups in the three main *BioRegios* of Cologne, Heidelberg and Munich, which vary from 11 to 17 to 18, respectively, over 5 years, i.e. an average rate of nine per year in the most favoured locations, suggests strongly that caution is the watchword on the part of the joint bank–pharmaceutical firms–government–VC partnerships that decide which firms to fund. This is admitted by the managers of these key intermediaries, as reported in Cooke (1999).

The reasons for Germany's low venture capital investments, especially in new technology firms are partly cultural, partly regulatory. Founders do not welcome handing company stakes over in exchange for venture capital. Tax laws, too, had been quite restrictive because of their complexity, but from 1997 proposed changes in tax law for venture capital may have eased the position somewhat. A variety of tax incentives were also introduced and may have further improved the regulatory climate. However, the German Venture Capital Association is of the view that there remains a lack of comprehensive tax exemption from capital gains (Schitag *et al.* 1998). This contrasts markedly with the abundance of VC in the USA and to a lesser extent the UK. It also contrasts with capabilities in the last two economies to find the large sums needed for lighthouse companies to gain the large amounts of funding necessary to turn trial possibilities into marketable products, a sum estimated for the UK at between £800 million and £1.8 billion by 2004. VCs now habitually only look for investment opportunities in late stage firms about to go to market and seek an IPO giving the VC an exit strategy. Few will seriously entertain investments under £0.75 million in either the UK or USA, so Business Angels tend to be the source of high-risk capital for early stage firms.

Moreover, VCs put in management, which enables scientists to focus on science and technology issues rather than administering the firm, which most are ill equipped to do. This has become a highly efficient form of private induction of innovation from the science base and into the market, though not, of course, without its risks. Germany's VC stance still remains relatively over-wedded to a public-led sectoral innovation system in biotechnology and much else (Casper *et al.* 1999). It is almost certain that such sums as those cited for UK therapeutic products firms to develop could not be funded by German VC, leaving only a reluctant federal or state purse or, most likely, niche markets funded by large pharmaceutical firms, with little hope of escape to independence of the kind enjoyed by Amgen (market capitalization at £70 billion, larger than Eli Lilly and Schering-Plough) or at a smaller scale Celltech–Chiroscience, with an early 2000 market capitalization of $5 billion. In a paper on the subject, Casper *et al.* (1999) admit that Germany's recent improvement in performance with respect to biotechnology start-ups is confined to the incremental innovation segment of platform technologies (i.e. the tools to enable gene coding and therapeutic drug development) because it is less risky, less VC demanding and, interestingly, less based on flexible labour practices than drug discovery. This suggests a strong 'lock-in' effect caused by the German regulatory and institutional regime that is well attuned to medium rather than high-technology industries. The aforementioned Qiagen, Europe's leading biotechnology firm, falls precisely into this pattern as a producer of kits for DNA filtering.

Hence learning from global sources about ways of stimulating innovation, especially of the more radical kind which UK basic science and US technological applications and commercialization skills have produced seems confronted, to a great extent in the German case, to a lesser extent in the UK case, by important institutional and cultural barriers. In the German case its traditions of stable industrial relations based on long-term if not lifetime employment norms and co-determination make it hard to be innovative either in radical terms within specific industries or in inventing new industries. In high technology, it is a system more appropriate to incremental improvement of established technologies, lacking even today, a strong, independent and market-facing VC industry. In the UK case, regulatory barriers may have impeded commercialization, as for example, R&D has only recently begun to be seen as a tax-credit earning investment rather than a normal business cost, and share-options were highly taxed when traded, unlike the US position. More important was the culture imbuing university life, associated particularly with Cardinal Newman in the 19th century, that research as the dispassionate pursuit of knowledge was a virtue in its own right. This has been hard to change except by various waves of political attack on academic innocence. These carried with them the sometimes small, sometimes larger stick of withdrawal of public funding for failing to engage with an "enterprise culture" or "knowledge-driven economy".

THE CLUSTER CULTURE

This brings us to the third and final main section of this analysis of key elements in learning commercialization of science, examined through the lens of biotechnology, which is the curious manner in which, despite the market power of the large pharmaceutical firms, amongst whom are some of the largest firms of any kind in the world, biotechnology is controlled by essentially publicly funded research scientists and their institutions, on the one hand, and entrepreneurial start-up firms, on the other. Just as venture capital was first attracted to, or as Kaplan (1999) says invented in, Silicon Valley when Arthur Rock moved to San Francisco from New York to invest in Fairchild and then Intel (then *Rolling Stone* magazine), so the locational form and character of VC investments took the geographical shape of the cluster.

There are three key reasons for this. First, the science base is a magnet, even if only indirectly, for information technology and biotechnology business. Those universities with a high rate of generating radical innovations like University of California Medical School, San Francisco in medical research and Stanford in IT and biotechnology, act as bases upon which commercialization of new knowledge occurs. Second, because basic science output has an economic value it attracts VCs who have an interest in both exploiting the knowledge but also protecting their investment by installing their managers in the start-ups or, nowadays, pre-IPO candidates. Thus they locate "where the action is" as Rock referred to the reason for his re-location. Third, small firms, especially in highly knowledge-driven sectors, depend heavily on social capital (Putnam 1993; Fountain 1998; Cooke and Wills 1999). That is, they benefit from intellectual, technological and social "spillovers" based on network interactions with other entrepreneurs, other scientists, financiers and people in the same business and with comparable mindsets to themselves. Even if there are not, as often presumed to be, "free knowledge goods" or "untraded interdependencies" readily available, nevertheless proximity to potential knowledge-assets and opportunities for commercialization, even if as principally the case in biotechnology, at arm's length, acts as a great stimulus to entrepreneurship, especially around "star" scientists or entrepreneurs (Zucker *et al.* 1998).

Hence, those who are least dependent upon large business organizations in their everyday lives gain psychic and economic income from coalescing in geographical proximity to small firms, many similar to their own, some at the leading edge. Subsequent analysis, many years after the first of these modern clusters of "rootless community-seekers" had developed, showed knowledge-transfer, measured by patent-citation, remarkably circumscribed to a 50-mile radius (Jaffe 1989). Further economic analysis showed such clusters to be the sources of dynamic externalities or "spillovers" (Feldman and Audretsch 1999) though whether because of specialization or diversification economies (Griliches 1992) remained unclear. Meanwhile, Porter (1998) found clusters superior to large corporations on at least three indicators of competitiveness. They were more *productive* because up-to-date knowledge and technological as well as organizational improvements could be quickly learned and applied due to the "open-systems architecture" they displayed. They were more *innovative* because of the opportunities for trustful tacit-knowledge exchange made possible by the absence of bureaucratic watchdogs, corporate administration "silos", and confidentiality constraints typical of slow-moving corporate structures. Accordingly, the more collaborative atmosphere also made competition through *new business formation* from start-ups and spin-offs more common than in other settings, because new business opportunities and market niches could be spotted early, infrastructures for enterprise support, like VC, were available, and the value of their services understood.

In biotechnology, these characteristics seem to be heightened even more than in IT. The early US clusters were in or near San Francisco, San Diego and Boston, and there was, according to Prevezer (1998) a good deal of mobility between these locations by new firm founders. The importance of networking in Silicon Valley was recognized in San Diego where the leading biosciences university, University of California at San Diego (UCSD) set up the CONNECT network as a university–commercial partnership in 1985. Apart from the earlier leader firms noted above, key start-ups established by scientists in proximity to their research facilities include: Hybritech, San Diego; Genetics Institute, Cambridge; and Chiron, San Francisco. Some individuals created several firms, Genentech was linked through one of its founders to Creative BioMolecules, near Boston, then to Creagen back in California. Creative BioMolecules also gave birth to Codon, subsequently Berlex BioSciences (now owned by Schering AG), co-inventors with Chiron, in California, of Betaferon, the multiple sclerosis treatment. There are numerous instances of firm formation activity such as that described, including continuing new start-up and spin-out developments in each of the main American centres, as well as new ones in Maryland, North Carolina and Texas, amongst others. In every case the industry is clustered around major bioscience or biotechnological research facilities, mainly on or near campus science or technology parks.

In Cambridge, Massachusetts, and beyond the resurgent Route 128 (Best 2000) as far as Worcester and the I-495, biotechnology businesses can be observed evolving almost in cluster life-cycle terms. From small beginnings in rented, sub-let space on MIT science park or some former industrial or newer office building, 20 or so new firms, often launched with the backing of MIT Technology Liaison Office support, form each year. But clusters, as we have seen, are more than firms and buildings. The science base is exceptionally strong in the Massachusetts Institute of Technology (MIT), Harvard University, Boston University and Massachusetts General Hospital. Each year some $770 million in basic research funding flows through the system. Leading scientists and academic entrepreneurs, one of whom has been involved with some 350 patent applications, are present. Massachusetts has at least 150 venture capitalists, most of them in Boston or Cambridge. There are 132 biotechnology firms in the Greater Boston area (59 in Cambridge), 86 outside, employing 17,000 people in total. Finally, there are numerous intermediary bodies supporting the industry at state level, one of which, the Massachusetts Biotechnology Council is an industry association which organizes common purchasing and other services such as promotion, educational placement and careers development for its 215 member firms. The geographical breakdown, bearing in mind the 59 firms in Cambridge, is as follows: 132 firms are located east of Route 128 (59 in Cambridge, 16 in Boston, the remainder between there and Route 128), 58 are located between Route 128 and Route 495 (including 11 in Bedford and 6 in Wilmington) and 25 are located west of Route 495 (including 11 in Worcester) (Cooke 2001b). Many of these, especially in the outer locations, are based in incubators or technology parks, as are many start-ups on the technology park campuses of the key universities.

The market segment breakdown is that 34 per cent of firms are in the therapeutic products sector (meaning they have grown beyond the early stages, typically in platform technologies, including diagnostics); 20 per cent are in scientific equipment or supplies; 15 per cent are in scientific services; 14 per cent in human diagnostics; 10 per cent are in environmental and veterinary and 7 per cent are in agricultural biotechnology (animal, plant, diagnostic and transgenics). Perceived industry growth areas are: in medical therapeutics (genetically produced protein, vaccines, gene therapy, human growth hormones); human diagnostics (monoclonal antibodies, biological imaging, DNA probes, biosensors and polymerase chain reaction); ag-bio (nutraceuticals, rapid diagnostic testing and transgenics) and BioInformatics (biological discovery, patient databases, etc.). Seventy-nine firms were founded in the 1980s including (> 300 employees) Biogen, Genetics Institute and Genzyme. A further 88 began between 1990 and 1997; the remainder are more recent start-ups or inward investments. Employment grew from 7,682 in 1991 to 16,872 in 1998. As the industry matures, the number of start-ups is decreasing annually. Between 1996 and 1999 seven mergers and acquisitions occurred. Financing of companies in biotechnology is high risk and analyses show that public investment is present at the risky process or product development stage, often in the form of Small Business Innovation Research grants (Lerner 1999), competitively bid for and assessed by the National Science Foundation.

Some key elements in the innovation system in the Cambridge biotechnology sector would also include various public and private organizations such as the Massachusetts Economic Development department, which is responsible for R&D tax and capital investment credits, and provider of seed-corn subsidies to start-ups. In the academic sphere are MIT, for leading edge biotechnology research and commercialization, through campus incubators, technology park, MIT Entrepreneurship Centre, and MIT Technology Licensing Office which links trained entrepreneurs, through patenting, to VCs. Also of major importance are Harvard University with its numerous biosciences, genetics and medical research, and graduate training programmes, Boston University with its BioSquare incubator, and Massachusetts General Hospital for research and a large patient-base, invaluable for trialling therapeutic treatments. Leading the research field is the Whitehead Institute of Biomedical Research. This is an independent research and teaching institution (affiliated to MIT in teaching), a global research leader in genetics and molecular biology. With the Sanger Centre at Cambridge (UK), it was the international co-leader in the Human Genome project, source of comprehensive, published genome data. The institute also possesses a technology licensing programme and start-up scheme. Networking organizations include the Massachusetts Technology Collaborative, a state-founded, independent body to foster technology-intensive enterprise and cluster-building strategies. Finally, as noted, the Massachusetts Biotechnology Council is the trade association representing biotechnology firms (162 full and 83 associate members). It provides educational, careers, and promotional information to the industry and conducts common-purchasing contracting for biotechnology firm members.

In conclusion, firms exploit scientific research findings by transforming them, often over time periods extending over 10 years of trials, hence leading *exploitation* firms such as Genzyme, patenter and inventor of the therapeutic product that controls the genetically caused Gaucher's disease, are closely intertwined with this generation and diffusion system. Reinforcing the system are partnerships like the one with Genzyme as a founder member, of the Partners Healthcare System, with Brigham and Women's Hospital, and the Massachusetts General Hospital, on research funded at $400 million by the National Institutes of Health. Along with Biogen and Genetics Institute, plus other internationally known firms such as BASF, Corning and Quintiles and a host of SMEs and start-ups, this means the Greater Boston region is supported by the generation and diffusion organizations and associations already noted, and clearly functions as a well-integrated regional innovation system based on a cluster of leading-edge biotechnology businesses.

In Cambridge, UK, by contrast, starting its Science Park 20 years after Terman started Stanford's, there are 25 biotechnology firms in and around it, including neighbouring St. John's Innovation Centre. As in Boston, but a scale of magnitude smaller, firms are growing on a number of new incubation and technology parks to the south of the university city down the main highway links to London and its Stansted and Heathrow airports. There are also comparable private and some public enterprise and innovation support systems making Cambridge (like Oxford) relatively private New Economy Innovation Systems. In 1998 there were some 37,000 high-technology jobs in the area comprising 11 per cent of the Cambridgeshire labour market. South Cambridgeshire had about 66 per cent of these jobs while Cambridge city accounted for most of the remainder. The main high-tech activity is R&D, supplying 24 per cent of total high-tech employment; electronics has 17 per cent, computer services, 13 per cent, scientific instrumentation, 8 per cent, and next comes biotechnology, fifth in line at 7 per cent. Probably the estimate of some 2,600 employees in biotechnology for the county is a not unreasonable figure. This would give a Cambridgeshire figure of around 50 core biotechnology firms. The growth in number of biopharmaceutical firms has been from 1 to 23 over the 1984–97 period, an average of just under two per year, but the rate was more like four per year in the last 2 years of that period. Equipment firms grew from 4 to 12 in 1984–97, and diagnostics firms from 2 to 8. Table 8 shows the distribution of biotechnology firms and support services.

Thus, it is clear that Cambridgeshire has a rather diverse biotechnology processing and development as well as services support structure, even though the industry is relatively young and small. Some of the service infrastructure and perhaps the equipment sector benefits from the earlier development of IT businesses, many also spinning out with VC support from university research in Cambridge.

In Germany, attempts to replicate these US and UK experiences have been made via *BioRegio*. Three clusters, in Cologne, Heidelberg and Munich have been encouraged and others are growing independently. But unlike the US and UK ones these are strongly public-funded for reasons that have already been given. A good example is the Heidelberg cluster in Baden-Württemberg. Heidelberg is Germany's oldest university and has one of the best science bases for biotechnology. Two Max

TABLE 8: SHARES OF BIOTECHNOLOGY FIRM AND SERVICES FUNCTIONS IN CAMBRIDGESHIRE

Biotechnology firm distribution		Biotechnology services distribution	
Biopharmaceuticals	41%	Sales & marketing	29%
Instrumentation	20%	Management consulting	23%
Ag-food bio	17%	Corporate accounting	15%
Diagnostics	11%	Venture capital	15%
Reagents/chemicals	7%	Legal & patents	8%
Energy	4%	Business incubation	10%
Total	100%		100%

Source: Eastern Region Biotechnology Initiative (1999).

Planck Institutes, for Cell Biology and Medical Research are in the region, as is the German (Helmholtz) Cancer Research Centre (DKFZ). The European Molecular Biology Laboratory, and European Molecular Biology Organization are there, along with one of Germany's four Gene Centre, the Resource Centre of the German Human Genome Project, two further medical genetics institutes and two plant genetics centres. Three other universities, Mannheim, Ludwigshafen and Kaiserslautern and three polytechnics complete the research and training spectrum. There are a number of Germany's leading big pharma firms nearby, such as BASF/Knoll (Ludwigshafen), Boehringer Mannheim Roche Diagnostics (Mannheim), and Merck (Darmstadt). But the heart of the *BioRegio* is the Heidelberg-based commercialization organization, the Biotechnology Centre Heidelberg (BTH). This is a three-tiered organization consisting of a commercial business consultancy, a seed capital fund and a non-profit biotechnology liaison and advisory service. Central to BTH's functioning is Heidelberg Innovation GmbH (HI) a commercial consultancy that takes company equity in exchange for drawing up market analyses, business and financing plans, assisting in capital acquisition and providing early phase business support for start-ups. It is a network organization, relaying information, partnering organizations seeking contact with local biotechnology companies and linking to research institutes and local authorities.

The key initial financing element of BTH is BioScience Venture, which was established by local pharmaceutical firms and banks, managed by HI and acts as a seed fund and lead investor in early start-ups. It also seeks international venture capital to finance second round developments. Assessments of project viability are made with advice from HI and *BioRegio* Rhine-Neckar e.V., the third element of BTH. The last named seeks out commercial projects and recommends the most promising for *BioRegio* public funding support. Business proposals have run at some 50 per year since 1996, but between 1996 and 1998 only nine start-ups had been established, a figure that had risen to 17 (including biochip and biosoftware firms) by July 1999. The total number of biotechnology SMEs (excluding start-ups) was 20 in July 1998. Most are in the healthcare sector, with some in plant genetics. The main location for this cluster of some 37 biotechnology firms is the Heidelberg Technology Park for SMEs and the adjoining Biopark on the university's science campus. This has 10,000 square metres of laboratory and office space plus a further 6,000 on the Production Park nearby, where start-ups move to once they have grown beyond the research phase. A joint venture by local firms and universities has been to establish the Postgraduate BioBusiness Programme. This is designed to provide scientists with hands-on experience of business administration through 3 months' coursework and 9 months of practical training in industry (König 1998).

Once more, key ingredients for successful clustering are present, including close proximity for firms on the technology park to both pharmaceutical firms in Ludwigshafen and Mannheim and leading-edge science in Heidelberg. The *land* of Baden-Württemberg has a biotechnology initiative but also distributes its funding among the Freiburg BioValley (one of Germany's most dynamic *BioRegios*), Ulm, and Tübingen-Stuttgart as well as Rhine-Neckar region. As we have seen elsewhere *BioRegio* funding is principally used for start-ups, most of which are currently making losses. But through the network-like character of BTH, lead investor capital from BioScience Venture can be tripled by leveraging both *BioRegio* funding and *land*/corporate venturing funds. Thus reasonable sums of start-up capital can very easily be raised at low risk to the essentially public lead investor. The *land* helped fund Heidelberg Technology Park, subsidizes a patenting support initiative, providing grants to universities for making patent applications, and funds a Young Innovators pre-start-up funding programme for university and research institute personnel.

Some examples of firm practices and specialities give a flavour of activities in this *BioRegio*. Three cases show a variety of firm origins; the pharmaceutical firm partnership, the research institute start-up, and the "rent-seeker" entrepreneur. The rent-seeker is Dr Seeger the founder of Molecular Machines and Industries (MMI), former holder of a chair in biochemistry at Regensburg near Munich, but doctoral student at Heidelberg where he established his first start-up SL Microtest in 1993. This company (optical cell tweezers) has grown into a well-known optical bioinstrumental firm. Funding was self-generated but, to grow, the firm was moved to Jena (former East Germany) where a more favourable grant régime operated and optics is a famous local speciality. There, Seeger developed a new fluorescence-screening device with nanosecond protein detection time. He approached HI, which advised on a business plan, contracts were signed in early 1998 and space found in the Heidelberg Biopark. 'Lion' Bioscience is the acronym for Laboratories for the Investigation of Nucleotide Sequences, aiming to be a European leader in genomics and bioinformatics. Six Heidelberg scientists and F. von Bohlen, an automotive industry entrepreneur, raised funding of DM 4.5 million privately. *BioRegio* co-funded with DM 2.5 million. Technology was transferred from the European Molecular Biology Laboratory, the German Cancer Research Centre in Heidelberg, and the European Bioinformatics Institute at Cambridge. The company's key bioinformatics tool is bioSCOUT a powerful bioinformatics management system. Established in 1997, the firm had 100 employees by 1999. BASF-LYNX AG is a German–US joint venture, the LYNX end being a therapeutics firm. *BioRegio* funding facilitated the partnership, while an overall company investment of DM 100 million ($55 million) secured the joint venture. Activities include treatment of epilepsy in collaboration with the local Max Planck Institute for Medical Research, in receipt of a *BioRegio* grant, screening for toxicity detection, and development of micro-organisms for production of amino acids and vitamins. When start-up funds are exhausted, an IPO may be sought, or continued third-party collaboration.

CONCLUSIONS

In this contribution an attempt has been made to show that learning on a global basis regarding the formation of new forms of industrial organization in advanced, high-technology, science-based innovation systems is feasible and, up to a point, replicable. However, national, and to a lesser extent, regional innovation systems play an intervening role affecting the extent to which learning gains can actually be implemented. It was shown, initially, how the liberal market-led regulatory system in the USA made early exploitation of knowledge gains from outside the country, in Europe, remarkably effective. Though the public and private funded *basic* research system in California and Massachusetts was significantly less effective than the largely public biosciences innovation system in the UK in generating inventions, it was far superior in generating innovations, i.e. biotechnology products on the market.

More recently, this private exploitation advantage has been significantly enhanced in the USA with a new round of more aggressive search and selection by a powerful venture capital system, typified by, but not limited to, Kleiner Perkins, Caufield & Byers. From a position of relative power over start-ups, which has been extended by the development of intra-cluster *keiretsus*, not only by KP, but emulated also by non-VCs like Intel (Jackson 1998) and, some would say, in a different, growth-by-acquisition model approach, by Cisco Systems (Bunnell 2000) business growth has led to some species variation, at least in IT. It is possible to see the power of VC being equalized somewhat by VC auditions arranged by the biggest and most powerful serial start-up entrepreneurs such as Jim Clark, founder of Silicon Graphics, Netscape and Healtheon, but for most start-up firms VCs remain important not least because of the abundance of capital available for venturing, mostly taken recently by dot.com businesses (Lewis 2000).

Learning along these lines will probably occur in Europe, with the UK in the vanguard because of its possession of Europe's largest VC industry, though KP-like activity is in its infancy, especially in biotechnology, with Merlin the nearest equivalent on a very much smaller scale. In Germany, VC has grown, but remains wedded to a public–private partnership model which, combined with its regulatory character seems likely to condemn it for the foreseeable future to the role of medium-tech and high-tech-input incremental innovator rather than radical innovator. The power of VC finance in the New Economy Innovation System seemingly emerging in the USA is capable of sustaining and enhancing leading edge innovation. Until Germany disengages from the risk-averse institutional culture it has inherited and the UK develops a VC industry with the financial power and aggressiveness of the current Californian model, it seems that the apparent levelling up that has come with European learning about exploitation, venture capital and clustering may, yet again be placed in the shade by the US backlash.

Interesting questions remain to be explored in respect of New Economy Innovation Systems, given the experience of many "new economy" businesses (especially dot.com and telecom firms) following euphoria and misplaced faith by VC in their capabilities. Noteworthy among the errors of over-investment were the massive overvaluation of stocks and the disastrous practice of floating firms on stock markets well before they showed any sign of profitability. That European investors were not immune to a certain loss of touch with reality is testified by overvaluations and bankruptcies or cheap sales of briefly highly valued 'new economy' firms. Biotechnology is a special case of this phenomenon, and it is possible to see it as a progenitor of the overvaluation tendency in the 'new economy' in general, based on biotechnology's 'promise' of wonder-cures for intractable diseases. Thus far, and despite the emergence of European biotechnology firms, a minority of which has therapeutic treatments in drug-trials, the absence of European-originated biotechnological drugs on the market continues to be a major cause for concern. It can be argued, as the paper has shown, that clustering and the importance of VC in New Economy Innovation Systems settings are being learned. Attention now needs to focus on the quality of exploitation. Kettler and Casper (2000) point to weak and inexperienced management as a common feature of UK and German biotechnology, exacerbated by their plethora of start-up businesses, and advocate consolidations like Chiroscience–Celltech–Medeva which would create firm-based critical mass of management expertise. But this was not the route chosen by successful US biotechnology firms, for whom small-firm clustering clearly works. The key feature of VC in New Economy Innovation Systems, as the paper has tried to show, is not so much financial investment, important as that is, but quality, informed business management of commercialization of science. Until learning about this becomes more diffused and practised, and a new and better hybrid emerges, built essentially on Europe's abiding advantages in basic bioscience research, and a quicker exploitation capability than has traditionally been evident, then Europe's biotechnology innovation gap with the USA may grow significantly rather than, as can appear from evidence of many new UK and European drugs in late-stage trials (but still not on the market), diminish.

REFERENCES

Audretsch, D. & Feldman, M. 1996: Knowledge spillovers and the geography of innovation and production, *American Economic Review*, 86: 630–640.

Best, M. 2000: Silicon Valley and the resurgence of Route 128: systems integration and regional innovation, in J. Dunning (ed.), *Regions, Globalization, and the Knowledge-based Economy*. Oxford: Oxford University Press.

BioIndustry Association 1999: *BioScience UK: Fundamental, Influential, Exponential*. London: BioIndustry Association.

Braczyk, H., Cooke, P. and Heidenreich, M. (eds.) 1998: *Regional Innovation Systems*. London: UCL Press.

Bunnell, D. 2000: *Making the Cisco Connection*. London: John Wiley.

Casper, S., Lehrer, M. and Soskice, D. 1999: Can high-technology industries prosper in Germany? Institutional frameworks and the evolution of the German software and biotechnology industries, *Industry and Innovation*, 6(1): 5–24.

Cooke, P. 1999: *The German Biotechnology Sector, The Public Policy Impact and Regional Clustering: An Assessment*. Report to DTI, Cardiff, CASS.

Cooke, P. 2001a: Biotechnology clusters in the UK, *Small Business Economics*, 17: 43–59.

Cooke, P. 2001b: *Knowledge Economies: Clusters, Learning and Co-operative Advantage*. London: Routledge.

Cooke, P. and Wills, D. 1999: Small firms, social capital and the enhancement of business performance through innovation programmes, *Small Business Economics*, 13: 219–234.

Cooke, P., Boekholt, P. and Tödtling, F. 2000: *The Governance of Innovation in Europe: Regional Perspectives on Global Competitiveness*. London: Pinter.
Department of Trade and Industry 1999: *Genome Valley*. London: DTI.
Dohse, D. 2000: Technology policy and the regions: the case of the BioRegio contest, *Research Policy*, 29: 1111–1133.
Doran, A. & Bannock, G. 2000: Publicly sponsored regional venture capital: what can the UK learn from the US experience?, *Venture Capital*, 2: 255–286.
Eastern Region Biotechnology Initiative 1999: *Background Information for Cambridge and the Eastern Region Biotechnology Cluster*. Cambridge: ERBI.
Edquist, C. (ed.) 1997: *Systems of Innovation*. London: Pinter.
Ernst & Young 1999: *European Life Sciences 99: Sixth Annual Report*. London: Ernst & Young International.
Feldman, M. and Audretsch, D. 1999: Innovation in cities: science-based diversity, specialization and localized competition, *European Economic Review*, 43: 409–429.
Fountain, J. 1998: Social capital: a key enabler of innovation, in L. Branscomb and J. Keller (eds.), *Investing in Innovation*. Cambridge, MA: MIT Press.
Giesecke, S. 1998: *The Contrasting Roles of Government in the Development of Biotechnology Industry in the US and Germany*. Munich: Technical University (mimeo).
Griliches, Z. 1992: The search for R&D spillovers, *Scandinavian Journal of Economics*, 94: 29–47.
Hall, S. 1987: *Invisible Frontiers: The Race to Synthesise a Human Gene*. London: Sidgwick & Jackson.
Jackson, T. 1998: *Inside Intel*. London: Harper Collins.
Jaffe, A. 1989: Real effects of academic research, *American Economic Review*, 79: 957–970.
Jaffe, A., Trajtenberg, M. and Henderson, R. 1993: Geographic localization of knowledge spillovers as evidenced by patent citations, *Quarterly Journal of Economics*, 108: 577–598.
Kaplan, D. 1999: *The Silicon Boys and their Valley of Dreams*. New York: Morrow.
Kelly, K. 1998: *New Rules for the New Economy*. London: Fourth Estate.
Kettler, H. and Casper, S. 2000: *The Road to Sustainability in the UK and German Biotechnology Industries*. London: Office of Health Economics.
König, G. 1998: Nurturing biotech in the regions, *Pharmaceutical Forum*, 9–11.
Lerner, J. 1999: The government as venture capitalist: the long-run impact of the SBIR program, *Journal of Business*, 72: 285–318.
Lewis, A. 2000: *The New New Thing: a Silicon Valley Story*. New York: Norton.
Lundvall, B. (ed.) 1992: *National Systems of Innovation*. London: Pinter.
Micklethwait, J. and Wooldridge, A. 2000: *For a Perfect Economy*. London: William Heinemann.
North, D. 1990: *Institutions, Institutional Changes and Economic Performance*. New York: Cambridge University Press.
Norton, R. 2000: *Creating the New Economy: the Entrepreneur and the U.S. Resurgence*. Cheltenham: Edward Elgar.
Porter, M. 1998: *On Competition*. Boston: Harvard Business School Press.
Powell, W., Koput, K. and Smith-Doerr, L. 1996: Interorganizational collaboration and the locus of innovation: networks of learning in biotechnology, *Administrative Sciences Quarterly*, 41: 116–145.
Prevezer, M. 1998: Clustering in biotechnology in the USA, in P. Swann, M. Prevezer and D. Stout (eds.), *The Dynamics of Industrial Clustering*. Cambridge: Cambridge University Press.
Putnam, R. 1993: *Making Democracy Work*. Princeton, NJ: Princeton University Press.

Schitag, Ernst & Young 1998: *Germany's Biotechnology Takes Off in 1998 (First German Biotechnology Report*). Stuttgart: Schitag, Ernst & Young.

Shohet, S. 1998: Clustering and UK biotechnology, in P. Swann, M. Prevezer and D. Stout (eds.), *The Dynamics of Industrial Clustering*. Cambridge: Cambridge University Press.

Targett, S. 2000: Pension fund chiefs to link up with venture capitalists, *Financial Times*, 11 May.

Teece, D. 1988: Technological change and the nature of the firm, in G. Dosi, C. Freeman, R. Nelson, G. Silverberg and L. Soete (eds.), *Technical Change and Economic Theory*. London: Pinter.

Tödtling, F. and Sedlacek, S. 1997: Regional economic transformation and the innovation system of Styria, *European Planning Studies*, 5: 43–64.

Zucker, L., Darby, M. and Brewer, M. 1998: Intellectual human capital and the birth of US biotechnology enterprises, *American Economic Review*, 88: 290–306.