INSTITUTIONS FOR INDUSTRIAL COMPETITIVENESS IN THE INTERNATIONAL PHARMACEUTICAL INDUSTRY

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Introduction

JORGE MESTRE-FERRANDIZ

One of the main characteristics of the pharmaceutical industry, including biotechnology, is the important role played by public institutions. Their role is not only focused on encouraging research and development (R&D), but also on regulation of the final product market. The special characteristics of the pharmaceutical industry and its economic importance for many nations imply that governments have a strong interest in supporting the efficient functioning of the industry.

Many, different, economic agents are involved. Public authorities and institutions interact with a wide variety of firms in this sector. Both public authorities and firms deal with universities and other research institutions. We need to understand these interactions because how they work and are structured raises important questions of particular interest to policy makers as well as economists.

Competencies and incentives are key words. The aim of this collection of papers is to analyse how the role of public institutions can help provide both the correct competencies and the right incentives for the pharmaceutical industry to be competitive and innovative and so promote economic growth.

Focusing on incentives and competencies helps to explain differences between the US and the EU pharmaceutical industries. The US is considered to have one of the most, if not the most, developed pharmaceutical and biotechnology sectors. Conventional wisdom sees the EU as lagging behind, but what are the reasons for the poorer performance? What role do public authorities play? Are competencies and incentives so different in these regions?

Of particular relevance is how and where the science is done, but moreover, what is done with the science. Is it better to undertake research in a public institution, or rather in a private firm? How are incentives rewarded in these two settings? As a consequence of the differences between these two sectors, a trade-off between patenting (private-oriented) and publication (public-oriented) emerges. But

what of the competencies? How good is the supply of scientists in the US compared to the EU? Are they actually better educated and trained? Is the quality of research better in the US?

On December 15th 2000, the Office of Health Economics hosted a seminar entitled 'Institutions for Industrial Competitiveness in the International Pharmaceutical Industry' and chaired by Professor Richard Nelson of Columbia University, which set out to debate these questions, drawing on the expertise of representatives from many different areas. This volume of papers draws on the presentations made at that conference. The participants presented a broad range of information, analyses and views but a number of key themes did emerge.

There is a general consensus that the pharmaceutical industry in the EU is lagging behind the US. Orsenigo (Chapter 1) explains in detail how the US system functions, and suggests why it is working better than its EU counterpart. He highlights the importance of the National Institutes of Health (NIH) as a well resourced national body that allows competition for funding, but at the same time integrates the entire research system. He argues that incentives faced by the actors involved in undertaking research are well developed. Moreover, the interactions between university and industry are well established in the US. For example, new scientists get quickly involved with the industry, and the degree of mobility between academia and the commercial world is higher in the US than in EU. Still, Orsenigo argues that incentives need to be coupled with competencies: and the US system has been spending huge amounts of money in order to create these competencies. Orsenigo then raises an interesting question: will the American system kill the goose that laid the golden eggs? If the US research system changes from a facilitator to an inhibitor of innovation as a result of information staying in the private domain rather than becoming public knowledge, barriers to innovation may arise. Orsenigo argues that the trade-offs between private information and common knowledge have to be better understood.

Pammolli (Chapter 2) offers reasons why the EU pharmaceutical industry as a whole is lagging behind the US's. He argues that the

structures of companies in the two regions are different. In the EU, companies are much more labour-intensive than in the US. This leads EU firms to produce medicines of lower added value on average. Moreover, the way in which final product markets are regulated may also contribute to the problem. Pammolli argues that EU markets are too local, fragmented and heavily regulated with less room for firms to innovate than in the US. Hence, the incentives to innovate are stronger for the American industry. It seems that US firms are also more efficient at doing their job. Is this because competencies are also better developed in the US? One cannot dispute the fact that the US has been spending huge amounts of money on basic research. And this helps create the right competencies.

Pammolli also looks at how the interactions between the different agents involved in the pharmaceutical industry are working. Like Orsenigo, he highlights the role of the NIH as one major determinant explaining the US success. It appears that both the incentives faced by agents and the competencies available are better in the US than in the EU. There is no pan-European R&D at university level. This is important because if we look at the US case the NIH plays a very powerful role as an integrator. In the US, there is a core of generalist universities which work closer together than in the EU, where there is only a set of specialist, and isolated, institutes. Hence, Pammolli argues that the EU system does not allow integration between different entities. European firms are not involved enough in networks, so they are not implicated in too many deals.

Casper and Kettler (Chapter 3) present a detailed analysis of two interesting cases, the UK and Germany. They have Europe's two most important biotechnology industries. Using the US as a reference point, Casper and Kettler try to explain recent trends and future policy implications for the biotechnology industry in these two countries. The roles of public institutions and institutional arrangements are once more highlighted. German authorities tried to change the incentives faced by the players in the late 1990s, but at the same time, tried to improve the competencies available for the nation. As a result, new firms have been increasingly entering the sector, although they have mostly been in the area of more general, platform technologies.

Is this because the competencies needed to have specialised firms are simply not there? It might seem so.

The UK case is somewhat different. The biotechnology industry in this country is more mature, and the public authorities were involved many years before. The UK is considered to be similar to the US in that the right incentives for the growth of its biotechnology industry appear to exist. However, the outcome has not been as good as expected: there are few success stories. One possible explanation given by the authors is that there is a problem with staff and management for the biotechnology industry. Casper and Kettler argue that not only is the number of scientists in the UK insufficient, but also that there has been an underinvestment in basic research. Hence, again it seems that not all the needed competencies are present.

McKelvey and colleagues (Chapter 4) provide an interesting case study: the Swedish pharmaceutical-biotechnology industry. They focus on the issue of co-location. Rather than assuming that there are interactions between the agents involved in this sector, they actually test them, to see whether co-location matters for knowledge collaboration. The results show that co-location does matter, but to a lesser extent than predicted within systems of innovation. In fact, close collaboration occurs but only about as commonly as all other types of deals. By building a non-English language database, McKelvey and colleagues find that we must be cautious about how databases are used. They argue that the traditional, English-language-based databases can lead to biased results, because they underestimate the interactions of organisations in non-English language countries, such as Sweden.

In the last chapter, Owen-Smith analyses how the reward system has affected the distinction between public and private sector research. Traditionally, while patents are the characteristic outcome of private research, scientific publications are generally the outcome of public research. These are two different ways of putting knowledge into the world. Owen-Smith focuses on the different incentives faced by firms and universities. Through an empirical analysis of the US system, he finds that this private-public distinction is starting to blur. Universities

are starting to patent while also remaining grant receivers and publishers. In short, public science success criteria (reputation through publications) starts to influence private activity (patenting). Does this imply that incentives faced by firms and universities are now converging? If this is so, what can we expect about the future organisation structures of universities?

The answer to the last questions is particularly interesting if the EU plans to import the American system of research incentives. When nations import an incentive scheme from a different region, but have different competencies, they must be very careful. Europe may be able to import the incentive structure, but what about the competencies? It might be wrong to use the American incentive structure with the European system of competencies: they might simply not work together. Incentives and competencies are inextricable, and there is no reason to expect them to be the same everywhere.

Chapter 1

The Interactions between Scientific, Institutional and Organisational Change in the US Pharmaceutical Industry

LUIGI ORSENIGO

Introduction

This paper addresses the question of why the US system of innovation for pharmaceuticals has out-performed its European competitors in the period since the late 1970s. This is an especially interesting question because it is not at all clear that Europe always lagged behind. In fact, evidence in Gambardella et al. (2000) suggests that Europe used to be one of the leaders of the pharmaceutical industry. Nevertheless, since the take-off of molecular biology in the late 1970s, Europe seems to have lost this advantage. So what has gone wrong?

The interaction between a number of different variables and events has driven the US industry forward. Nonetheless, should we summarise in a word what has taken the US so far ahead, then 'science' seems to be the key. The US system has taken control and used science in ways above and beyond pure research. Science is the language that is spoken in the US between pharmaceutical companies, regulators, policy-makers and representatives of patients. They discuss business as well, of course, but their first common language is science. This is a significant difference between the US and Europe.

'Science' – reasons for US leadership

To understand the US's lead in science, one must first take into account the fact that enormous investments have been made in basic scientific research since the late 1940s. By the early 1970s these investments had produced a number of blockbuster discoveries and, perhaps more importantly, a well structured and funded research system. The role of the public sector in this needs to be highlighted.

The US public research system has a number of characteristics. First, an amazing amount of money has been invested, and a significant

number of people employed, in basic research. There is little question that the sheer amount of resources devoted to biomedical research in the US in the post-war era goes a long way to explain US leadership in life sciences. The US expenditure is also concentrated on centres of excellence, thereby providing critical masses of researchers. This spending on basic research has had a significant effect on the productivity of the large US firms able to take advantage of its outcomes.

Second, the research is decentralised but integrated at the same time. When the funding of biomedical research began in earnest in the US, the original idea was to replicate the approach used for the Manhattan project (for developing the atom bomb) within the National Institutes for Health (NIH). But the NIH quickly found it impossible to run such a large-scale, centralised program given the many anomalies and wide range of potential research areas involved. As a result, the NIH started funding what they deemed to be critical research projects in many different research centres all over the US, instead of conducting all the priority research in-house. These research centres, and hence the projects, were and are geographically dispersed. However, they are still integrated by way of the NIH, especially those pursuing complementary areas of research.

The third characteristic of the US system is that most of the research is conducted in universities. This science is based on peer review and publications, which has not always been the case in Europe. A significant portion of US funding goes to universities and an important fraction of this support goes towards basic or fundamental science that is widely disseminated through publication in the refereed literature. Furthermore, US universities conduct research across complementary departments and integrate the progress and results into the teaching curriculum, medical practice, and developments in the industry. One example that illustrates this point is the discovery of restriction enzymes at the University of California, Los Angeles (UCLA) and Stanford University in 1973. The research involved was done in the medical schools. However, in Europe there were no molecular biologists working in medical schools in the early 1970s. Consequently, no research on theoretical issues was being undertaken.

An important related point is how new scientists, who have been exposed to basic research projects in medical schools, relate to the pharmaceutical industry. When these new scientists get involved with the industry, a transfer process occurs. In the US, this transfer process is more developed than in Europe. This means that the transfer of personnel, ideas and research between universities and industry has been, and still is, a critical component of the industry development process in the US. The organisation of research and teaching in the US has characteristics that facilitate both the production of high quality research and high degrees of mobility between academia and the commercial world. In Europe, however, it seems that this transfer process is not happening.

Intellectual property (IP) rights and the incentive schemes that exist to commercialise basic research from universities and other public research centres are also important factors. The US has both strong IP rights and incentives for this commercialisation to occur. Since the mid-1970s, the drive towards an increasing commercialisation of the results of research accelerated dramatically and took a variety of forms. Academic institutions and scientists have been directly involved in commercial activities. Increasingly, universities have been assuming, and were asked to assume, the role of direct engines of (local) economic growth. These factors have helped to spur the creation of new biotechnology firms and, more generally, develop pharmaceuticals research. They are also important reasons for the US's dominant position.

The US's IP system raises some critical issues. Is this system changing from a facilitator to an inhibitor of innovation and development? Will it eventually kill the goose that lays the golden eggs? The answer to these questions is not straightforward. On the one hand, the incentives to commercialise science and the results of science foster new technology firms spinning off from publicly funded research. On the other hand, however, there are concerns in the industry about whether or not the arrangement of such entrepreneurial behaviour may have gone too far. With such strong incentives to commercialise basic research, whereas a large pharmaceutical company might allow some information to become common knowledge, it may instead be

kept in the private domain by small technology firms that have spun out of a university or even by NIH scientists. There are trade-offs that must be considered as a result. However, we do not have a clear picture yet as to the trend or the implications.

Other types of regulation beyond those concerned with IP are also helping the move of the US's strong science base and companies into the world's leading positions. The pharmaceutical industry is a strongly regulated industry for good, and perhaps in some cases also for bad, reasons. The motivations of governments imposing price controls on pharmaceuticals, for example, are complicated and go beyond cost-containment goals. But, in any case, the US has a freer environment in terms of price regulation than Europe. Pharmaceutical companies are afforded a relatively high degree of pricing flexibility in the US, which in turn contributes to the profitability of investments in R&D. This allows US companies to have more funds for R&D and they have indeed spent more on R&D in the post-1980 period than their European counterparts.

It is important, however, not to focus on any single aspect of regulation, as it is a combination of regulations that drives the relative competitiveness of the US system. The 1962 Kefauver-Harris Amendments concerning approval of medicines are a good example of influential regulation in the history of American industry. These amendments came about as a result of public concern about the large profit margins that US drug firms were earning. Also, the thalidomide case gave rise to a concern for existing procedures for product approval. In the late 1950s, the drug thalidomide was taken by pregnant European women to relieve morning sickness, and its use resulted in about 8,000 deformed babies.

The main outcome of the Kefauver-Harris Amendments was the introduction of tougher procedures for product approval, without any direct intervention in the pricing of medicines. The provision of efficacy controls, in addition to safety, was a result. The reaction of the industry was quite hostile to such reforms. However, the creation of a stringent drug approval process in the US may have also helped to create a strong competitive pressure favouring really innovative

strategies. Although the amended process of development and approval increased costs, it also significantly increased barriers to imitation, even after patents have expired. These amendments prompted strong competition in the US marketplace. They were a tremendous shock to the industry as they significantly raised the cost of R&D of new medicines. They also provoked major restructuring of the industry, forcing several players out and causing the rest to re-evaluate their strategies. The most innovative companies came out on top. Hence, an overall outcome of this stringent regulation was to improve competitiveness of the US pharmaceutical industry.

These regulations also link back to the point that science is central to the US story. One of the outcomes of the introduction of the Kefauver-Harris Amendments was that companies and the regulatory authorities were forced to consider scientific issues more. Companies had to produce evidence based on science. The consequence was that both the regulatory authorities and the companies had to broaden their science base in order to understand, evaluate and discuss the outcomes of their clinical trials.

This development may have helped to make the US industry's transition to molecular biology in the 1970s and 1980s much faster than in Europe. In general, companies in the US pharmaceutical industry became more accustomed to dealing with science as compared with the European industry. UK companies can perhaps be considered as the one European exception. The British system of regulation and innovation has more in common with the US system than elsewhere in Europe. Introduction of a tougher regulatory environment in the UK followed the US 1962 experience. The strongest British firms gradually reoriented their R&D activities towards the development of more ambitious, global products. The agents involved in the UK were in a better position to learn and respond to the research being undertaken by molecular biologists in medical schools. Such responses involved, firstly, an organizational change, especially a move to greater use of alliances and external collaborations with universities. Secondly, new biotechnology companies were then able to integrate and utilize the new scientific developments.

Conclusions

To conclude, two words help our understanding of the recent performance and growth trends in pharmaceuticals. One is an important word in economics; the other is not yet but should be. They are 'incentives' and 'competencies'. Standard economics shows that people react to incentives. This is very true. On the other hand, in order to react to these incentives, competencies must be in place or be created: while you can offer me the biggest incentives in the world, I will not become a surgeon tomorrow morning; I do not have the competencies; I do not have the capabilities.

Strong incentives can create virtuous circles when they are coupled with strong competencies, but they might be ineffective and even dangerous when competencies are insufficient. The opposite is also likely to be true: competencies without adequate incentives will probably be underutilised and wasted.

In order to understand the diverging performance and evolution of the US and European pharmaceutical industries, the tremendously complex interplay between the development of competencies and the development of incentives must be analysed. The two things need not complement each other. Incentives may or may not help in the development of appropriate competencies. As economists, we are trained to think that competencies without incentives would produce a world where people do nothing, but incentives without competencies can provoke havoc and disaster. How the two co-evolve is a major conceptual issue for everyone, however, not only for economists.

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Chapter 2
Global Competitiveness in Pharmaceuticals: A European Perspective

FABIO PAMMOLLI

Introduction

It is now a widespread perception that the European pharmaceutical industry is losing ground vis-à-vis the US. Against this background, the European Commission commissioned a report examining the competitive position of the European pharmaceutical companies and industries, comparing them with their counterparts in other parts of the world, particularly the US. The first part of this paper summarises the results obtained in this report (Gambardella et al. 2000). The second part introduces additional research being undertaken on one particular aspect raised by the report.

We analyse the pharmaceutical industry in Europe, based on the Competitiveness Report prepared for the European Commission (Gambardella, et al. 2000). This is done firstly by defining the industry as a system of complex relationships. We then present the findings from the empirical analysis, the main results of which are that:

1. the European pharmaceutical industry as a whole is more labour intensive than the US industry. This was especially true in the 1990s. This labour intensity is associated with a larger presence of lower value added activities;
2. the European industry has slower rates of growth than the US industry;
3. if we look just at new products and entities, the growth in sales of European new chemical entities (NCEs) was less significant in the 1990s than for US NCEs;
4. there is a comparative lack of effective division of innovative labour and a lower degree of diversity within the European industry. This industry also lacks the distinction (more common in the US) between two different types of firms collaborating within

the industry: what we call 'originators', that is small firms that start new projects and then sell them to the established firms, and large 'developers';

5. European markets are local and relatively protected national markets. There is weak competition in the final market, with national companies still nurtured by the specificities of national regulatory regimes within the industry. I feel that this lack of competition in the industry and the fragmentation of the market are important possible explanations of some of the results previously mentioned: lower productivity and growth and higher labour intensity in the European industry.

Europe's industry is losing out to the US

The first major finding is that the European pharmaceutical industry is more labour-intensive than that in the US, and this higher labour-intensity is associated with lower value-added activities. Table 2.1 gives evidence that supports these findings. It reports the share of pharmaceutical labour costs in total production value in the EU-15, the US and Japan. 'Non-labour' inputs are computed by subtracting labour costs from the total value added. The table also reports the share of total value added (which is the sum of the two shares) as a proportion of the total value of production. This provides a measure of the extent to which the industry relies on internally generated inputs vis-à-vis inputs purchased from third parties. The shares are averages across 1986-1991 and 1992-1997.

As illustrated in Table 2.1, the share of labour costs out of the total value of production is higher in Europe than in the US. Table 2.1 also shows that the share of value-added net of labour costs in total production value is significantly higher for the US. The US industry relies more than Europe on 'non-labour' inputs, such as capital or, most likely, R&D. The overall share of total value-added in production is higher in the US than in Europe. This suggests the presence in Europe of a relatively larger group of fringe companies that are specialised in low-value added activities, which include manufacturing and commercialising products licensed from other

Table 2.1 **Shares of labour and non-labour inputs, and value added, in total production value, 1986-1991 and 1992-1997 averages**

	1992-1997			1986-1991		
	Share of personnel costs	Share of non-labour inputs*	Share of value added	Share of personnel costs	Share of non-labour inputs*	Share of value added
EU-15	23.21%	16.58%	39.78%	24.92%	15.64%	40.56%
United States	13.50%	57.55%	71.05%	15.58%	55.32%	70.89%
Japan	12.57%	53.60%	66.17%	12.90%	53.31%	66.21%
Denmark	26.50%	26.99%	53.49%	26.99%	21.78%	48.77%
Germany	33.11%	9.36%	42.47%	31.81%	12.00%	43.81%
Spain	23.00%	14.33%	37.33%	27.73%	10.56%	38.29%
France	18.87%	14.00%	32.87%	20.18%	13.22%	33.39%
Ireland	10.69%	42.18%	52.87%	14.11%	33.06%	47.17%
Italy	22.74%	13.99%	36.73%	23.46%	13.50%	36.96%
Netherlands	18.43%	14.91%	33.33%	22.86%	11.18%	34.05%
Austria	23.17%	17.80%	40.97%	Na	Na	Na
Finland	26.44%	21.68%	48.12%	24.12%	25.14%	49.26%
Sweden	18.42%	30.59%	49.01%	Na	Na	Na
United Kingdom	21.69%	28.40%	50.09%	23.60%	30.23%	53.83%

Na=not available.

*Value of non-labour inputs computed as total value added minus personnel costs.

Source: Author's calculations from Eurostat data.

companies, or simply of low-value added medicines. We also observe that the growth of pharmaceutical markets in Europe has been lower during the 1990s than in the US. Table 2.2 shows that in 1999 North America represented 40% of the total world market, compared with 34% a decade earlier. Over the same period Europe's share of the world market fell from 31% to 27%.

We can show that industry growth is likely to depend to a good extent on what we call 'receivables', that is factors other than traditionally measurable ones, such as R&D and capital investment. Table 2.3 uses

Table 2.2 **Pharmaceutical markets, 1989-1999, US$billion**

Markets	1989	1990	1995	1996	1997	1998	1999
World	153.3	165.8	280.3	290.8	296.1	304.7	337.2
Regional shares	%	%	%	%	%	%	%
North America	34.0	32.4	31.2	33.0	35.9	38.1	40.2
Europe	31.0	26.5	29.6	30.7	28.8	29.1	26.7
Rest of World	35.0	41.0	39.2	36.3	35.2	32.7	33.0

Source: IMS.

Eurostat data to decompose the growth in production value in the EU-15, the US and Japan during 1986-1991 and 1992-1997. We employ the typical growth accounting procedure, which divides the growth in sales into the part explained by the growth of its measurable inputs (typically labour and capital) – weighted by their cost shares – and the residual growth not explained by the growth in inputs. This last element of overall output growth is commonly referred to as total factor productivity (TFP).

Two results can be extracted from this table. Firstly, Europe experienced the highest average growth rate in the value of pharmaceutical production compared with the US and Japan during 1986-1991, but this declined in 1992-1997. The effect is reversed for the US, whose industry became the fastest growing in the 1992-1997 period. We not only observe lower rates of growth in Europe than in the US but also a higher variance, i.e. greater volatility, in rates of growth.

Secondly, in both periods, the growth of production in Europe is accounted for largely by the residual total factor productivity. In the US, in both periods, production growth is explained mostly by the growth in non-labour inputs i.e. capital and R&D assets. Not only is the growth of the industry in Europe likely to depend significantly on factors other than R&D, capital or labour, but it is more prone to 'exogenous' factors. Such factors include regulatory regimes, licences from international companies, the pricing policies or peculiarities of public regulatory and health care systems in individual European countries. Therefore, growth is more erratic in the EU than the US.

Table 2.3 **Decomposition of pharmaceutical growth – contributions of labour and non-labour inputs and total factor productivity (TFP), averages for 1986–1991 and 1992–1997**

	1992-1997				1986-1991			
	Total growth	Labour	Non-labour inputs	TFP	Total growth	Labour	Non-labour inputs	TFP
EU-15	5.81%	0.14%	1.32%	4.35%	9.14%	0.62%	1.39%	7.13%
United States	8.44%	0.40%	4.84%	3.20%	7.18%	0.31%	4.43%	2.43%
Japan	4.71%	–0.08%	2.65%	2.15%	6.82%	0.04%	4.40%	2.39%
Denmark	6.43%	1.77%	1.90%	2.76%	8.72%	0.72%	4.54%	3.46%
Germany	2.25%	–0.49%	–0.74%	3.48%	7.74%	0.82%	0.89%	6.03%
Spain	3.16%	–0.23%	0.97%	2.42%	13.36%	0.56%	1.66%	11.14%
France	5.28%	–0.10%	1.30%	4.08%	9.61%	0.61%	1.43%	7.57%
Ireland	22.89%	1.64%	11.62%	9.63%	10.40%	1.11%	2.68%	6.61%
Italy	2.02%	0.22%	0.67%	1.12%	10.28%	0.49%	0.82%	8.98%
Netherlands	11.94%	0.46%	3.93%	7.54%	8.46%	0.26%	–0.45%	8.66%
Austria	1.93%	0.11%	0.94%	0.87%	Na	Na	Na	Na
Finland	6.95%	2.53%	0.12%	4.30%	10.32%	0.31%	4.26%	5.75%
Sweden	14.24%	0.80%	3.35%	10.09%	Na	Na	Na	Na
UK	7.04%	0.05%	1.72%	5.28%	7.72%	0.66%	2.55%	4.51%

Note: Contributions of labour and non-labour inputs were computed by the usual growth accounting procedure, namely $g_S = w_L \cdot g_L + w_K \cdot g_K +$ residual, where w_L is the share of personnel costs in production value and w_K is the share of value of non-labour inputs in production value. The value of non-labour inputs is the difference between value-added and personnel costs; g_S, g_L and g_K are respectively the growth rates of production value, number of employees and non-labour inputs. The residual, or TFP, is the difference between g_S and the first two terms in the expression.

Source: Computations based on Eurostat data.

We now focus on performance at the level of individual firms and individual major innovative products. We find apparently broadly similar performances in R&D in the US and the EU. Differences in the number of NCEs developed by EU and US multinationals during the last 15 years are not great, as is shown in Table 2.4.

Table 2.4 also illustrates another important point. Sales for major innovative products are higher in the US than in Europe and,

Table 2.4 **Top 50 NCEs by nationality of main producer corporation***

	Number of NCEs	
	1985-1989	**1995-1999**
US	17	24
Japan	20	3
Switzerland	3	6
EU-15	10	16
UK	3	8
Germany	7	4
Netherlands	0	1
France	0	3
	Sales(%)	
	1985-1989	**1995-1999**
US	41.5	69.1
Japan	37.3	3.9
Switzerland	2.9	7.8
EU-15	18.3	18.5
UK	6.5	9.4
Germany	11.8	3.3
Netherlands	0.0	0.8
France	0.0	5.0

*By location of headquarters.

Source: IMS.

moreover, sales of 'top-50' NCEs increased more significantly in the US than in Europe in the period 1985-1999. The US share, in terms of sales of global top-50 NCEs launched by its corporations as a percentage of the total sales generated by the top selling 50 NCEs on the world market, rises dramatically in the 1990s to reach almost 70%. One of the reasons for these differences in performance is the faster growth rate of the US multinationals' sales on the domestic US market. For the period covered, the rate of growth of the national market in the US was much higher than the European market's rate of growth. A large proportion of US multinational firms' sales is still in

their domestic US market, so US firms are benefiting from the exceptional growth of the US market. This is an important factor.

It therefore appears that differences in industry growth rates are due, at least in part, to differences in local market growth rates. However, there are two important qualifications to be made. First, if we control for the share of globalised products among the NCEs produced in Europe versus the US, we find that the share of NCEs that are sold across the world in a very homogenous way is higher for US companies than for European companies. Secondly, we find that the product portfolio of the major European companies tends to be older than the portfolio of their US rivals. Hence, even if past performance can be explained mostly by different rates of growth of domestic markets, there are still signals that show that big companies in Europe are losing ground vis-à-vis US firms.

Another important qualification is that even if we can currently observe many European-based pharmaceutical companies within the core of the industry, these firms tend to have survived in this core by going through a wave of mergers and acquisitions. On the contrary, a few US companies are in the core of the industry by means of their internal growth, based on innovation. We might think that European firms in the core of the industry are doing alright, better than the overall average picture of the industry. However, at industry level, there are signs even of the big EU multinational companies also losing ground vis-à-vis their US rivals.

I now focus on R&D, innovative capabilities and opportunities. An important point that arises from our analysis is that there are different degrees of vertical specialisation in the European and US industries. Europe does not have a structured system of transactions; but in the US there is an important role for an industry of specialised technology suppliers, which has emerged within the last ten years. This sector has been able to generate new technologies that are then developed by established pharmaceutical companies. The US has extensive vertical specialisation between an industry that is specialised in the 'exploration' of new technologies and innovation opportunities, and another industry that is specialised in their

'exploitation'. We observe a higher level of fragmentation of the European network of R&D collaborative agreements, not only as far as industry relationships are concerned but also in the role of the public research system. I will return to this point later in the paper.

US companies also show a higher probability of success than their European counterparts in all the phases of clinical trials. Division of innovative labour and use of markets for technology can allow companies to gain access to external knowledge and increase the productivity of their research. European companies should rely more on the market for technology, in order to help compensate for their lower in-house capabilities.

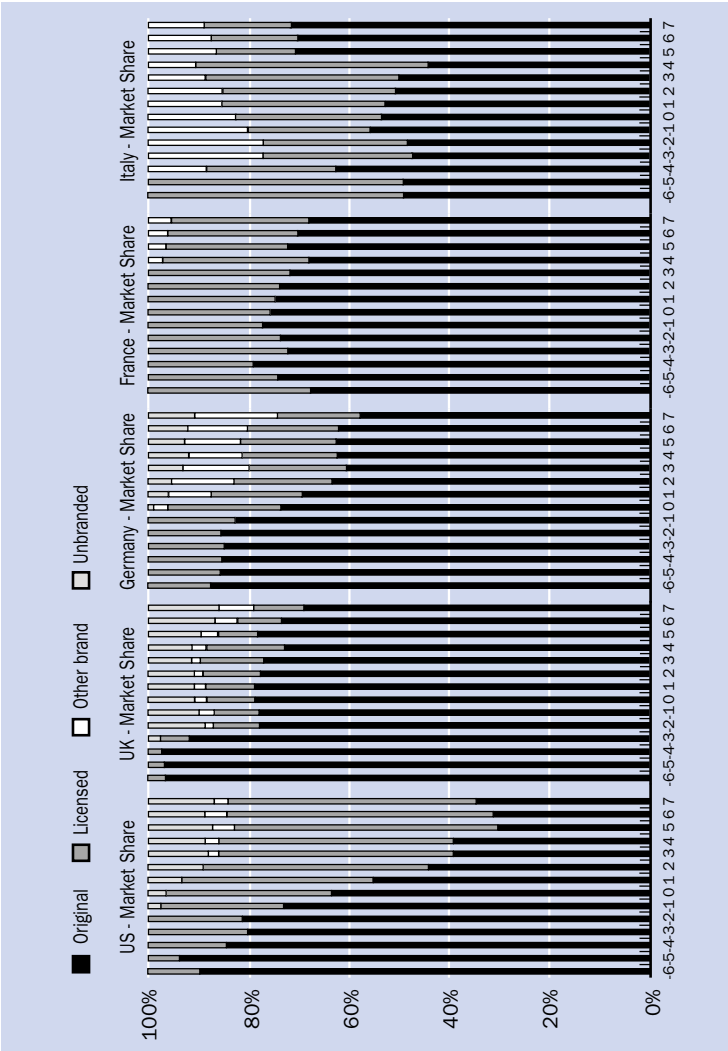
There is an area where Europe apparently has a potential competitive advantage: new tools based on chemistry or derived from technologies that are traditionally very strong in Europe. However, even in the area of new research tools we are now observing an increasing competitive advantage for the US system as compared with Europe.

The implications of these differences in the organisation of the industry upstream are not only relevant to the growth of the downstream industry, that is, the competitive advantage of the European multinationals vis-à-vis US multinationals. They also impact on economic growth and social progress in the European environment, because of the number of jobs that have been generated in the US by the new biotechnology industry; far more than in Europe.

Finally, if we analyse five different countries (the US, UK, Germany, France and Italy) we find a lack of competition in some major European markets. The results, even though not based on a direct comparison of trends across countries but on the dynamics that are in place in each of them, are very similar in spirit to the results obtained in the analysis of price comparisons across countries for pharmaceutical products.

One important result is that we observe big differences between these five countries. From the level of variation in terms of prices and market shares after patent expiry, a clear pattern emerges depending

Figure 2.1 **Market shares in the years before and after patent expiry (=year 0)**



Source: Pammolli et al. (2002).

on the pricing system in operation (see Pammolli, et al. 2002). Those countries that rely more on administrative pricing systems, i.e. on the direct regulation of prices, promote a less competitive environment within the industry. Local firms are able to benefit from the higher stability, in terms of prices and market share; and there is a less clear distinction between innovators and imitators, in terms of the premiums that they earn. Systems that rely more on price competition, i.e. market-based competition, after patent expiry promote a clear distinction between the innovators and the imitators. They have a high level of switching between originator products and generic copies after patent expiration. This can be seen from Figure 2.1. The differences in regulatory systems between the US market and some major European markets constitute an important factor explaining differences in productivity for the pharmaceutical industry.

The role of public research vs. industrial sources of innovation

The final part of this paper focuses on the preliminary findings of a study undertaken with Walter Powell, Jason Owen-Smith and Massimo Riccaboni (Owen Smith, et al. 2002). This analyses the relationships between public research systems – the non-industrial sources of innovation – and industrial sources of innovation. We focus on the institutional differences at that level and how they affect the flow of patents.

The conclusions presented here are based on more than 100 research institutes world-wide. We have analysed patents in terms of therapeutic micro classes and pharmacological mechanisms and biological actions, in order to have a clear understanding of these institutes in terms of their competencies. We follow their activities through the pipelines of their R&D projects, which implies moving from discovery through the development process, and their interactions with private firms. One of the objectives is to distinguish the roles of public R&D institutes as originators of new projects rather than as developers of projects started by someone else.

The first finding is that US and European university-industry ties are geographically clustered in different ways. Clusters exist at a national level in Europe, so we do not observe international clusters in terms of collaborative agreements and signing of patents among and between European universities and institutes. Something similar appears to apply in the US but with an important distinction and qualification: the powerful role of integrator played by the US government and the public National Institutes of Health (NIH) complex. In the US, most of the funding for biomedical research is administered by the NIH, with:

- substantial integration between the production of biological knowledge on the nature and mechanisms of human diseases, clinical research, medical practice, and the discovery and development of new therapeutic treatments;
- significant support for basic or fundamental science in universities and public research centres, widely disseminated through publication in the peer-reviewed literature.

Secondly, in the US there is a core of what we call generalist universities and institutes, especially the NIH. Generalist in this sense refers to the micro level analysis of therapeutic classes and sub-classes, where we are able to see which areas are more central in terms of the number of projects that are carried out there; for example cancer, infectious diseases and AIDS. On the other hand, in Europe, there is a set of specialist research institutes that act as top quality institutes, but in an isolated way. Examples that illustrate this point include the Institut Pasteur, the National Centre for Scientific Research (CNRS), or Max Planck. These institutes are very good in specific areas but are isolated from the European network and play alone. In Europe there is no generalist platform that enables integration between these different entities.

Thirdly, the level of vertical integration of the US universities and institutes tends to be higher. In some cases these organisations act both as originators and as developers. In some specific areas, they have capabilities that range from molecular biology to clinical competencies. They are also integrated through their relationships with local medical schools thereby forming a common package. This

represents an important difference from Europe. Hence, we can say that the relative propensity of these US institutes to form relationships is greater than in Europe.

Summarising the relationships between institutes and the pharmaceutical industry, we can see that the flexibility of the US academic system, the high mobility of the scientific labour market and, in general, the social, institutional and legal context that makes it relatively straightforward for leading academic scientists to become involved with commercial firms, have been major factors in the development of the US industry. However, in Europe the links between academia and the industry have been weaker.

There are some institutes in the US that act both as originators and developers, and there are a huge number of inter-connections between them. From preliminary work, we have obtained two important results. First, the complex of the NIH agencies acts both as an originator and as a developer. It starts projects that are then developed by other institutes, while at the same time it licenses projects that are generated by firms outside. Moreover, it is able to contribute to the clinical development of these projects. This is not a surprising result. What is surprising, however, is the scale of the role of the government linkages within the system. If we remove these nodes, the overall number of connections is greatly reduced.

The second result is that US universities also play a role both as originators and developers. Examples in Boston include Harvard University, the Children's Hospital and Massachusetts Institute of Technology (MIT). US institutions seem to have a high level of coherence between upstream and downstream capabilities, as compared to European institutes. In fact, the only three European institutes that we are able to monitor moving from the upstream to the downstream are three British institutes: the Cancer Research Campaign, the British Technology Group and ISIS.

We feel that this analysis has been underevaluated hitherto, but that it is part of an important dimension in the analysis of US and EU competitiveness. We are planning to carry out further, deeper research to improve our knowledge of this area.

Conclusions

The European pharmaceutical industry has been losing competitiveness as compared to the US, although there are large differences and trends across individual European industries. The analysis of the dynamics on the R&D side reveals that the gap with the US is becoming larger, especially in biotechnology and among the most innovative, globalised, profitable, and best selling drugs, i.e. at the frontier of innovation. The observed concentration of research and innovation in the US is worrying. Europe risks being relegated to the fringe of the industry, surviving, and possibly even thriving, through imitation and generics but giving up a large share of the value added and becoming dependent on the US for the development of new products.

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Chapter 3
Institutional Frameworks and the UK and German Biotechnology Industries[1]

STEVE CASPER and HANNAH KETTLER

Introduction

This paper examines the nature and origin of the differences between the biotechnology industries in the UK and Germany. We combine industry dynamics with an understanding of what is going on at the firm level. We analyse how differences in national institutional frameworks influence the competence, structure and strategies of firms in these two countries.

The UK and Germany are the European leaders in biotechnology in terms of number of companies, employment and investment. The two cases present an interesting puzzle for institutional theory. They exhibit rather different development paths and strategic profiles and both countries have yet to create a critical mass of viable biotechnology companies.

We argue that whether biotechnology firms in aggregate succeed or not in different countries, depends on whether they have available to them the types of institutional resources needed to resolve the organisational dilemmas they face. This is where national institutional frameworks come in.

Our micro-level analysis of the two countries' biotechnology industries highlights the links between institutions and performance in this sector. National institutional arrangements play a pivotal role in UK and German companies' growth trajectories and strategic choices. The four issues discussed are:

- technology transfer;

1 This chapter draws on 'The Road to Sustainability in the UK and German Biotechnology Industries', 2000, London: Office of Health Economics, by the same authors.

- performance incentives within the firm;
- competency destruction risks; and
- financing.

Starting with technology transfer, there is a sizeable debate over intellectual property roles. The question we want to pose is whether or not firms and universities in Germany and the UK have incentives to commercialise technology and spin it off from the universities.

Secondly, biotechnology firms need to have high-powered performance incentives within the firm in order to get both managers and scientists to exert high levels of effort.

Competency destruction risks relate to labour markets. In particular, many biotechnology firms fail and those that do not fail change the competency structure or the structure of R&D within the firm fairly regularly, especially in therapeutics. As a result, we argue that biotechnology firms need to be of the 'hire and fire' type. Employees working in these firms need to be able to readily switch from firm to firm. Flexible labour markets would allow a great deal of competency destruction or asset recycling to take place, so reducing the riskiness of working within one of these biotechnology firms.

Finally, we address the problem of financing. This is especially relevant in biotechnology due to the long-term nature of R&D and the high failure risks. Hence, venture capital financing is needed, which links back to the general structure of capital markets.

Germany: is the industry changing?

The German story has two distinct phases. Germany was doing very poorly in biotechnology until the 1990s, with very few firms in the sector. In the second half of the 1990s, however, things started to change, with a big expansion in the numbers of biotechnology firms.

One difficulty for the German biotechnology sector is that intellectual property created in the academic sector is owned by professors in Germany, not by their universities. This system was set up to help accommodate long-term applied research links between large firms

and academic researchers. Professors nevertheless tend to turn to their universities to commercialise their patent rights. However, this has proved difficult in biotechnology and new sciences, where commercialisation is mainly undertaken by small firms, which need to work closer with universities. Since the intellectual property is owned by professors, universities do not have any incentives to organise technology transference as they will obtain no reward from doing so. This is an important obstacle.

Let us now focus on incentives. The German industrial relations system and finance laws make it difficult to use individually tailored performance incentives within firms, although this picture is improving. For example, stock options were illegal in German companies until 1998. Furthermore, the industrial relations system is based on long-term consensus style approaches. Workers' councils do not favour individual performance incentives in terms of bonuses, or unilateral decisions about how people are promoted. This implies that in Germany it is hard to establish the type of internal organisation required by hi-technology, entrepreneurial firms.

What can we say about competency destruction? The issue here is not just hiring and firing, although that is a problem in Germany. Rather, large firms in Germany tend to have long career tracks for their employees, expecting people to work within the same firm for a long time to develop their careers, rather than changing employer frequently. Hence, there is not a flexible labour market for highly skilled staff, especially mid-career level scientists and managers. This makes it hard for biotechnology firms in Germany to engage in competency destruction type areas of activity. Instead, they are basically competency preserving, in line with the rest of the economy.

The last core issue relates to the availability of finance. We will see later that this is the area that has changed the most. Germany has a credit-based system, making it difficult for venture capital to appear, especially since there exists no exit option for venture capitalists. In the investment banking community and the follow-on market for initial public offerings of shares, it is harder than in other countries to diversify venture capital risks and to have an effective exit option.

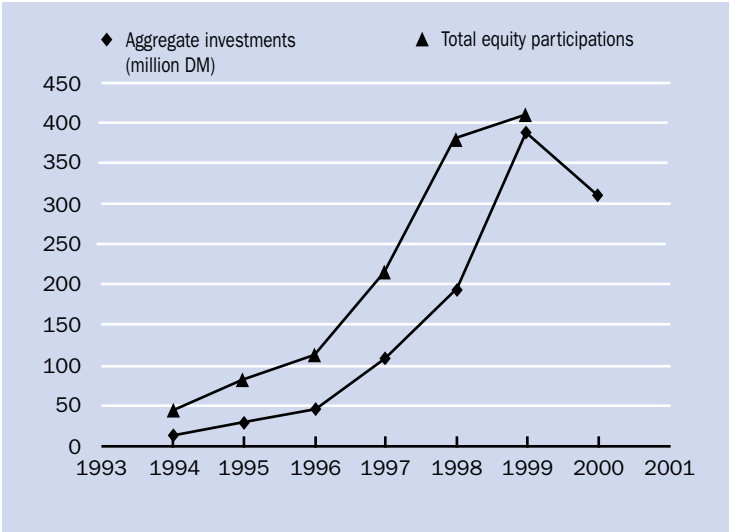
All of these things could and did cause big problems in the German biotechnology industry. Why then has there more recently been a big turn-around that appears to contradict our arguments? There were well over 200 German biotechnology companies at the end of 2000; 13 of them quoted on the public stock market. Most are less than five years old. The vast majority are in platform technologies. However, there are not many success stories yet. The interesting question is why is it that, all of a sudden, German institutions are able to support and develop large numbers of biotechnology companies while there are zero products in the market being produced by them?

We argue that one reason for this change is the creation of a sectoral support system that specifically supports biotechnology in Germany. Rather than changing general laws, an alternative technology transfer system just for biotechnology has been set up, outside the universities. Public policy has created 'BioRegio' offices with enough money to aid technology transfer by, for example, carrying out paper patenting for professors, organising computer laboratories and hiring consultancy advice. This has been done at a local level, but with federal government support. Hence, there is now an alternative technology transfer system, and most German biotechnology firms have come out of it.

Secondly, a number of public venture capital programmes have been established and these have also spurred the private venture capital market. Moreover, there has been financial reform to legalise stock options for employees, so enabling biotechnology, and other, companies to provide high powered incentives for their employees.

Figure 3.1 shows data on public venture capital. The upper line is the number of companies in all sectors and the lower line is the amount of public venture capital invested in them. About 28% of public venture capital has gone to firms in the biomedical technology sector, more than any sector, as illustrated in Figure 3.2. It is active government policy to push new firm creation in high technology sectors. However, it is important to point out that the new firms are generally not in areas of therapeutic research. The pattern of sub-sector specialisation by German biotechnology firms is dramatically

Figure 3.1 **German 'public venture capital'**



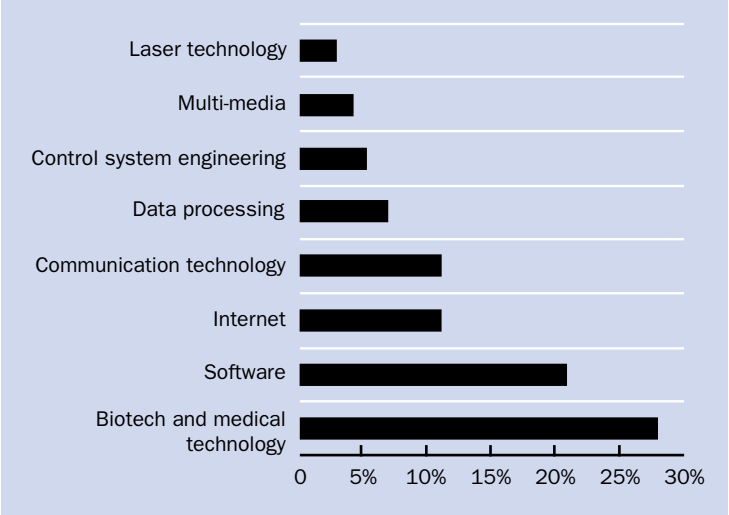
Source: tbg; 2000 figures up to August.

different from that in the US and UK. As shown in Figure 3.3, most German biotechnology firms are in contract research and manufacturing, platform technologies or diagnostics, rather than therapeutics.

Figure 3.4 illustrates an important point about differences between biotechnology patents in Germany and the US. The graph shows the scientific intensities of patents in the two countries as measured by the average number of scientific citations referred to in each biotechnology patent in application. The US in 1998 had about 24 scientific citations supporting each patent, and Germany had about nine citations. This implies that a difference exists on the kinds of work being undertaken by these two biotechnology sectors.

There is a common presumption, especially in Germany, that Germany has created another Silicon Valley. We disagree. Certainly,

Figure 3.2 **German 'public venture capital' by sector**

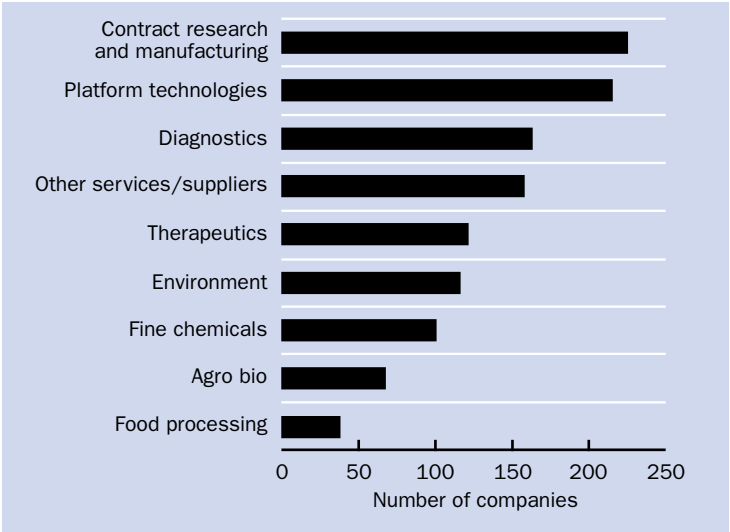


Source: tbg as of August 2000.

there are German biotechnology firms that are based on high-powered employment incentives, but they are different to the US's in many ways. In particular, German firms do not 'hire and fire' to the same extent; and the corporate governance system is relatively untested as much investment is partially funded through public venture capital finance. The corporate governance role in venture capital in these firms is weaker than in the US (and even the UK). Cultural factors are also important, but more difficult to quantify. Why have German firms concentrated on platform technologies? Is it because the German business community is more risk averse, because these are less risky forms of biotechnology?

We have interviewed managers in many of these platform technology firms and found that their innovation trajectories are basically incremental. They tend to have one basic technology, such as a DNA test kit, or some kind of service for companies, that has been spun out over a range of different areas. They have follow-on assets in terms of

Figure 3.3 **Areas of specialisation of German biotechnology SMEs***



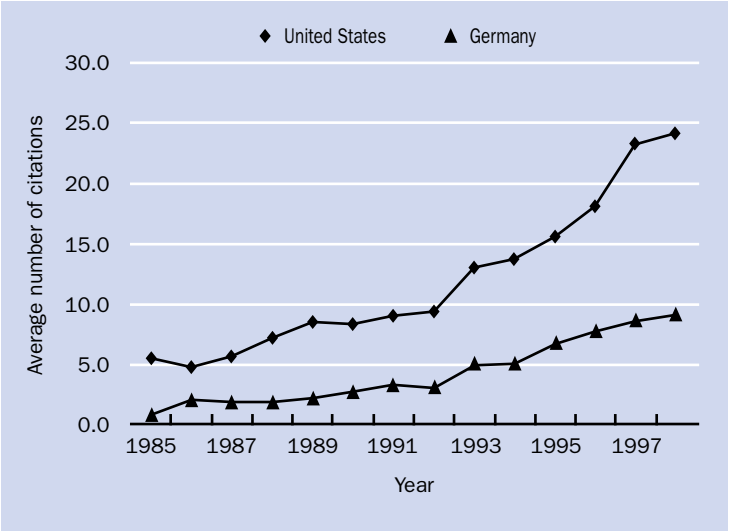
*Small and medium-sized enterprises.

Source: Schitag Ernst and Young (1998).

consultants or technicians or companies, or people doing R&D in other niches in the same technology, and they sell these to firms. Most platform technologies are, in effect, making people in biomedical laboratories unemployed because they rationalise testing and other laboratory procedures. This is the business that the German firms are in. We argue that these firms require a lot of long-term knowledge investments that would tend to be more passive and certainly more firm-specific than in the therapeutics area.

German firms might have an advantage where competency development in staff over the long term is required. This differs from the US, Silicon Valley, model. Due to the technological volatility and the failure rates of US firms, their staff, however efficient and hard-working, could be out the door the next day. That means it is very hard to get firms and their staff to invest in long-term career tracks within the Silicon Valley model. In platform technologies, however,

Figure 3.4 **Scientific intensity of US and German biotechnology patents**



Source: Casper and Kettler (2001).

institutions tend to be competence-preserving. This enables managers of such firms to make a credible commitment that staff are not going to be 'hired and fired'. Hence, it is safer to make longer-term, firm-specific knowledge investments.

In general, Germany is not on the road of mimicking the US in biotechnology.

The UK: less successful than expected?

The UK provides an interesting contrast to Germany. The UK biotechnology industry is closer to the US model than the German. The UK arguably has more flexible institutions than Germany, better developed financial markets and more deregulated labour markets. However, if you look at the sustainability of the UK industry and the performance of its firms, there have been major challenges and

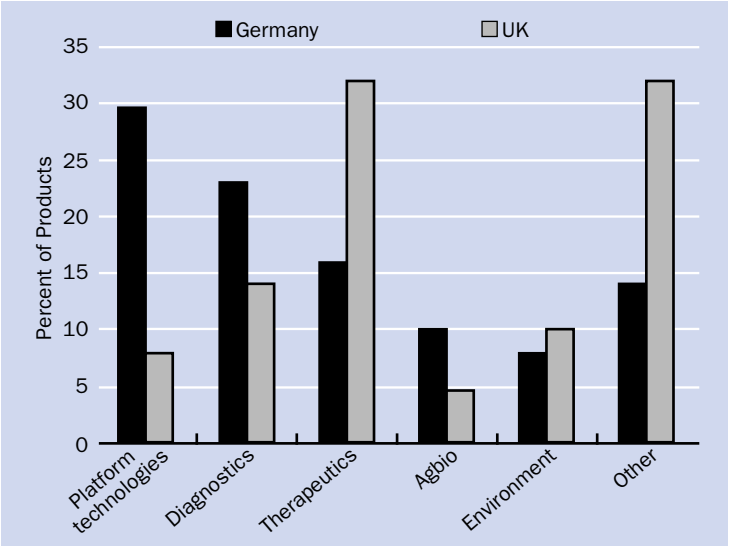
problems in the UK. UK biotechnology performance falls short of that in the US despite the apparently similar models employed.

The UK biotechnology industry is still the largest and most mature in Europe. Institutional policies and arrangements introduced in the early 1980s prompted the development of a biotechnology industry with a large number of new companies. So why do we have a large biotechnology industry in the UK and yet a lack of success stories in that industry? Although Celltech is developing to a scale that approaches some of the leading US companies in the biotechnology industry, it has taken 20 years to get there, and it has been done via mergers rather than endogenous growth. There are now one or two British biotechnology products on the market, but no blockbusters. So we still have a 'stumbling along' industry in the UK.

If you look at sub-sector specialisation, the UK biotechnology industry is much more like the US than Germany. Figure 3.5 shows the sub-sector specialisation of biotechnology products in 1999 for the UK and Germany. A third of UK products are in therapeutics, which is twice the proportion in Germany, where platform technologies are comparatively much more important. The 'other' category includes hybrid companies which do both therapeutic and contract research. Hence, the UK's sub-sector specialisation structure is similar to the US's, and this is also reflected in the institutional arrangements that exist in the UK. Similarly, the UK is the only country in Europe that has any therapeutic biotechnology products in the market. This is partly the result of being around in biotechnology for 10-15 years longer than any other European country.

Although the UK has the institutions and companies, and some products in the pipeline, it does not have many biotechnology success stories to tell. This can be explained in terms of the following four factors: technology transfer, finance, the quality of science, and the ability of personnel to move easily between companies. We analyse whether the relatively poor performance of the UK biotechnology to date, compared with the US, is due to institutions not working quite right, a lack of incentives, or a problem of scale i.e. there are just not enough resources devoted to biotechnology in the UK.

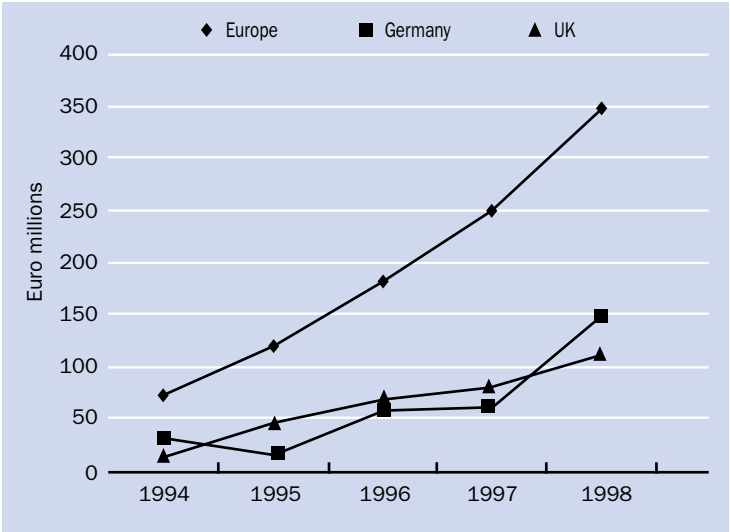
Figure 3.5 **Sub-sector specialisation of biotechnology products, 1999**



Sources: Arthur Andersen (2000), Schitag Ernst & Young (1998).

With respect to technology transfer, the UK government became involved in active promotion of university-based spin-offs in the early 1980s. They have copied the US Bayh-Dole Act, but the results of these technology transfer policies have lagged behind the US's because of differences in the financial arrangements at US and UK universities. UK universities generally lack large private endowments, but such endowments have proved crucial to fund the staffing of technology transfers offices in US research universities, and to provide seed money to university-based venture capital funds. In the long term, UK technology transfer offices hope to generate substantial revenues from the licensing of intellectual property, but in the short run they must rely on funds provided by the university. The inability to pay a reasonable salary to staff in the key area of technology transfer is a major obstacle in the UK.

Figure 3.6 **Venture capital investments in biotechnology**



Source: BVK (1994-1998).

Turning to finance, there has been a lot of venture capital available in the UK. Figure 3.6 shows venture capital investments in Europe as a whole, Germany and the UK for biotechnology. It shows that venture capital investments were rising quite rapidly at the end of the 1990s throughout Europe. However, in the UK biotechnology sector a lot of venture capital is going into buy-outs, which implies a totally different risk structure than for biotechnology venture capital in the US. Important follow-up questions arise: is this because there are no other projects to invest in; are UK venture capitalists right to see the only place to make money as in buy-outs; is there a different type of risk arrangement and incentive structure in the UK that encourages this kind of investment?

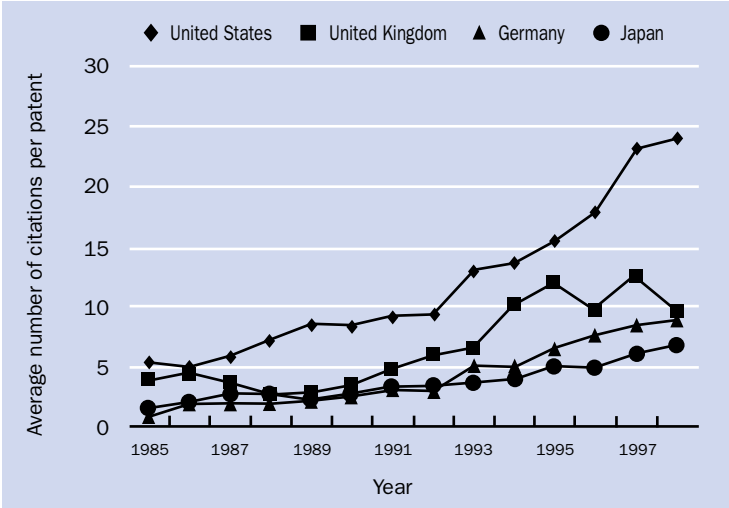
We find considerable differences in the extent to which the financial systems of the UK and US have worked to support biotechnology companies. In general, investors in the UK seem more risk-averse

compared to the investors in the US. In the biotechnology industry, while US venture capitalists were quick to invest in new start-ups, UK venture capitalists initially stayed away. Initially, the lack of an exit option was a deterrent to private investors in biotechnology in the UK. Reforms in the 1990s aimed to improve this situation. The Alternative Investment Market (AIM) was established in June 1995, which improved biotechnology companies' access to public equity. Moreover, the London Stock Exchange requirements allowing listings from companies were eased. This creation of new exit options did draw some venture capitalists towards the biotechnology sector, although investments for early stage biotechnology have remained scarce. A lack of obvious success stories, coupled with recent disappointments in the largest UK public biotechnology companies, means that it has in recent years also become difficult to raise money for biotechnology through an initial public offering of shares. UK companies do not have access to the kind of public seed money available in Germany, and communication between companies and existing business angels could be improved.

Another important point with regard to the circumstances and situation in the UK is whether or not the science is as good as the US's. Is the quality of the projects and the research going on in UK companies comparable with the US? The UK's strategy is similar to that in the US, i.e. concentrating on therapeutic, high-risk areas. However, as Figure 3.7 shows, while the UK was tracking the rate of increase of US biotechnology patents' scientific intensity in the early 1990s, the UK then stagnated while the US continued to rise. By 1998 the scientific intensity of UK biotechnology patents was no higher than in Germany, and less than half the US level.

Table 3.1 shows biotechnology sector performance in the UK and Germany relative to the US, in 1997, adjusted for GDP. If we look at the number of companies, employment and revenues, relative to GDP the figures for the UK are similar to or better than the US. However, the problem arises in the R&D figures: 36 to 100. UK R&D spend in biotechnology as a share of GDP is much lower than in the US, albeit still much higher than in Germany. We are not concluding that the UK's lack of success is just explained by this figure, but if the

Figure 3.7 **Scientific intensity of biotechnology patents**



Source: Casper and Kettler (2001).

strategies followed by the UK biotechnology sector do depend heavily on R&D and interactions with universities, it is a topic that should be explored further.

The last factor to discuss is labour market structure in the UK. The UK has labour and company laws that are more conducive than in Germany to the development of the labour markets and employee motivational schemes suitable for entrepreneurial biotechnology firms. UK labour markets are relatively deregulated and open, while company law imposes few restrictions on owners and top managers in creating performance-based incentive schemes. Despite a seemingly favourable institutional climate, however, a consistent theme in our UK interviews was that recruiting high quality staff remains an important problem in the UK biotechnology industry. We suggest three factors that may contribute to this problem:

- the overall size of the UK labour market for scientists might not be sufficient;

Table 3.1 **Biotechnology performance, adjusted for GDP (1997)**

Index US = 100	US	UK	Germany
Number of companies	100	144	79
Number of public companies	100	99	1
Employment	100	175	12
Revenues	100	94	6
R&D expenditure	100	36	15

- critics have charged that the UK government has not invested sufficiently in basic research; and
- cultural factors might mean that top UK managers are more risk averse than in the US, preferring to work within large companies rather than in risky start-ups.

Conclusions and policy implications

From a comparison of the UK and German industries, it is clear that any policy package to promote the biotechnology industry must not only respond to a set of industry-specific demands but also be tailored to reflect specific national institutions. Our paper highlights a number of key findings. Firstly, we have identified important differences in the structure and performance of the German and UK industries. The German industry is relatively young, while the UK's is more mature. The range of sub-market sectors represented is broader in the UK's industry than in Germany's.

Second, using information about the industry's dynamics in the UK, Germany and the US we have identified three key competencies that companies must have in order to innovate and grow:

1. the ability to access and commercialise new technology;
2. the ability to access sufficient finance; and
3. the ability to recruit and retain capable and experienced research scientists and managers.

Third, our research of Germany and the UK suggests that government policy plays an important role in shaping a country's industry development. However, we caution against attempts to directly transfer or borrow policies from one country to another, especially when the countries involved have highly dissimilar institutional structures.

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Chapter 4
Does Co-location Matter? Knowledge Collaboration in the Swedish Biotechnology-Pharmaceutical Sector[2]

MAUREEN MCKELVEY, HÅKAN ALM and MASSIMO RICCABONI

Introduction

This paper assesses the validity of assumptions about the importance of co-location for innovation, by analysing whether or not co-location matters for formal knowledge collaboration in the Swedish biotechnology-pharmaceutical sector. In addressing this question, we provide an empirical overview of the population of Swedish biotechnology-pharmaceutical firms, including their patterns of regional, national and international collaboration with other firms and with universities. This work leads onto the second aim of this article, namely to compare and contrast the adequacy of alternative data sources.

Within the systems of innovation literature, innovation is argued to result from a collective process of knowledge development.[3] Existing information infrastructures influence the creation and diffusion of knowledge throughout a population of actors (Smith 1997; Foray 1997; OECD 1997). This population of actors may include private firms or public organizations like universities and government, and may be defined at the regional, national, sectoral or technological levels. The studies of innovation systems differ in arguing which level of interaction should be considered most important for explaining innovative outcome and, by extension, economic development. Two assumptions underlie the majority of innovation systems analyses:

- that interactions occur among the chosen population of actors; and

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3 Research funded by the Merck Foundation (EPRIS Project) and by the European Union research project 'Sectoral Systems in Europe – Innovation, Competitiveness and Growth (ESSY)' under the Fourth Research and Technological Framework Programme, Targeted Socio-Economic Research, TSER. [Contract no: SOE1-CT 98-1116 (DG 12-SOLS)]

- that these interactions influence innovations, and thereby economic growth (Edquist and McKelvey 2000).

There are also often strong assumptions about the importance of co-location.

We analyse formal knowledge collaboration which involves at least one Swedish biotechnology-pharmaceutical firm. Our aim is to identify the relative frequency of regional and national interactions, as opposed to international, sectoral interactions across the population of firms. By formal knowledge collaboration we mean activities such as co-development, co-authorship and collaborative R&D[4]. The population of Swedish biotechnology-pharmaceutical firms is defined as firms located in Sweden which invest in R&D nationally, and are involved in the broad knowledge area of biotechnology-pharmaceuticals.

Sweden is an example of a small country with a high domestic knowledge base (OECD 1999). Domestic, multinational firms finance the majority of the total Swedish R&D investment, as opposed to government financing of basic science. Still, Sweden as funded through Swedish research policy has traditionally been a strong player within medical science research (Archibugi and Pianta 1992). These facts taken together imply that some national knowledge infrastructure exists in medical research, making it possible for nationally based firms to collaborate with national research scientists. The Swedish biotechnology-pharmaceutical sectoral system can be used to exemplify some of the opportunities, and challenges, for other sectors and other small countries with high knowledge intensive activities.

The current debate concerning sectoral systems of innovation is whether the pattern of collaboration among partners ought to reflect co-location in a geographic area (regional or national) or whether it should instead

4 Our indicators should be contrasted with 'informal' collaboration or social interaction that is not reported, such as when a larger community of practitioners meets informally. Informal collaboration for knowledge development requires a different method to identify how systematically, and how frequently, it occurs across the population.

be expected to be international. This is an important question because much of the existing empirical literature on systems of innovation simply assumes that linkages and interactions are (or ought to be) close geographically, sometimes without critically questioning the relative impact of close linkages as compared to international ones.

Concepts such as 'social capital' and 'associative governance' are used to explain why regional development occurs in certain geographic areas but not others (Cooke 1998; Porter 1990, 1998). People know each other and they move around. These informal interactions are argued to facilitate trust among the group and thereby also the diffusion of knowledge (Saxenian 1994). This perspective emphasizes the importance of informal linkages among a population of actors. Such interaction is in turn assumed to depend on co-location in a geographic area. National (or regional) institutions, information infrastructures, and government policy are other elements which are often formed relative to specific geographic locality (Nelson 1993; Lundvall 1992).

Other research puts more emphasize on the sectoral – especially international – dynamics of knowledge development, and thereby focuses on when and why firms may gain access to new and/or relevant knowledge, which is crucial in economic competition. Nelson (1989, 1996) and Mowery and Rosenberg (1998) emphasize the interactions between basic science and economic growth to explain differential patterns in national and sectoral growth. In this process, there are important productivity effects, which come from the translation of scientific knowledge into products, routines, and processes, which are of economic value. The economic benefits from new knowledge accrue not only to the innovating firm but also more widely across the economy.

Cantwell and Santangelo (2000), Dosi (2000) and Pavitt (1991) put more emphasis on the importance of specific firms in organising and consolidating scientific and technical knowledge within specific sectors. A diversity of firms in terms of technical and market knowledge bases should be visible, although the population of competing firms in a sector may also share some common knowledge bases. Nelson and Mowery (1999) and Malerba (2002) provide

evidence of the similarities and differences between different sectoral systems of innovation. These theoretical arguments lead to a view that while individual firms will differ, special characteristics and features of knowledge development may run internationally by sectors, rather than being nationally dominated.

Sweden's biotechnology-pharmaceutical sector

This section of the paper identifies the basic population of Swedish biotechnology-pharmaceutical firms and their characteristics. It also provides an outline of the methodology and definitions we used to create a new database, BioSweden.

The Swedish population of firms in the biotechnology-pharmaceutical system of innovation is defined as including any firm which has (modern) biotechnology-related research in this health-care area within Sweden.[5] Examples of firms included under this definition include: contract research organizations and diagnostic firms; genomic firms; firms developing biological material in this area; small biotechnology firms involved in pharmaceutical development; and existing (large) pharmaceutical firms.

Rather than only including small dedicated biotechnology firms, all firms engaged in R&D in the appropriate knowledge areas and in the geographical locality are included. Including both large and small firms is particularly important because some US definitions focus specifically on small, specialized firms. But to focus only on such firms misses much of the knowledge and economic dynamics of the sector. Biotechnology firms are often a link between universities and large pharmaceutical firms, where each type of organization has respective specialized techniques and knowledge. One would miss at least a third of the dynamics by excluding large firms. Large firms influence innovation both by engaging in collaboration with others and by funding extensive in-house research (McKelvey 2002). A single large firm can have disproportionately large effects on the orientation and existence of a national system of innovation

5 Firms involved in medical devices are excluded if they do not develop biological materials.

(Verspagen 1999). For these reasons, large firms doing research are included in our population of firms.

Subsidiaries and research centres of multinationals and foreign-owned biotechnology firms are included in our population. The firms are not necessarily Swedish owned, nor organically started in Sweden. The marketing or sales divisions of international companies are excluded from our definition, however, as we only include firms with active R&D or search activities in Sweden. The formal knowledge collaborations analysed by us have to involve at least one of these Swedish biotechnology-pharmaceutical firms, but only one of the partners needs to be located in Sweden[6].

Using the above definitions to define the Swedish biotechnology-pharmaceutical sector, we developed a new database: BioSweden. This identified 105 relevant firms as existing in 1998.[7] This population thus includes all firms that 'survived' until 1998. The founding dates of these firms are shown in Table 4.1. From 1982, the rate of entry of firms into the sector fluctuates some but is fairly steady at a low level. Given that modern biotechnology research really took off from the late 1970s, this indicates that these biotechnology-pharmaceutical firms originate from innovation opportunities within modern biotechnology and/or related pharmaceutical/health care activities.

6 The rationale is that this allows us to identify whether such collaboration is occurring within one defined region or national context and/or crossing international boundaries.

7 This is a new database, built up through the ESSY project and through parallel research. This database has been built up to include datapoints about the firms at the years 1975, 1981 and 1995-1998. The material used relies on intensive and systematic search of existing sources of literature, including the previous Nordic Biotech Directory, NUTEK reports, questionnaires sent to all Swedish firms suspected of being involved in biotechnology in any way, and searching the Swedish language business and technical press. NUTEK (2000) and Vinnova (2001) also identified firms which were active in the biotechnology area in Sweden 1998. They found 116 so-called biotechnology firms using somewhat different boundaries of the biotechnology-pharmaceutical sector. The NUTEK (2000) study excludes some of the largest firms in the sector and includes firms that produce, but do not develop, biotechnology-related technologies.

Table 4.1 **Founding dates for the 105 Swedish biotechnology-pharmaceutical firms existing in 1998**

1998	4	1988	6
1997	5	1987	8
1996	8	1986	3
1995	6	1985	3
1994	4	1984	8
1993	2	1983	4
1992	3	1982	3
1991	7	1981	1
1990	5	1980	0
1989	6	Before 1980	19
		All years	105

Source: BioSweden.

Many of the 105 biotechnology-pharmaceutical firms are small. Very few are large or even medium sized firms. Table 4.2 shows that only five firms had more than 500 employees in 1998. Moreover, 57 firms, more than half of the total number, had fewer than 10 employees. Of these very small firms, 19 apparently had zero (full-time) employees. These 19 firms were most likely consulting companies developed by individuals (presumably university researchers) with other full- or part-time jobs.[8]

The importance of geographic locality within Sweden is visible in the database, with a clear concentration of firms in the four major regions of scientific medical research. 101 of the 105 firms are located in the dominant four major regions: Stockholm-Uppsala (48 firms); Skåne, which is the southern region including Lund and Malmö (31); Gothenburg (13); and Umeå (nine). Thus, a clustering effect between university and biotechnology-pharmaceutical firms is visible.

8 University researchers have the rights to both own their own patents individually and to consult for up to 20% of their total work time. Both of these rights are conferred to the individual researcher, and neither provides intellectual property rights (IPR) or financial returns to the employing university directly.

Table 4.2 **The size distribution of Swedish biotechnology-pharmaceutical firms in 1998***

Size of firms	Number of firms
0 employees	19
1-9 employees	38
10-49 employees	25
50-499 employees	15
> 500 employees	5

**Note:* Unfortunately we were unable to obtain information about employee numbers in 1998 for 15 of these firms. For 12 of them we have used data about numbers of employees for the years 1995-1997. For the other three firms we have not been able to obtain any information about employee numbers at any time in 1995-1998.

Source: BioSweden.

Collaboration between firms and universities

Basic research is particularly important in the biotechnology-pharmaceutical sector. Nilsson et al. (2000), Sandström et al. (2000) and Vinnova (2001) examined the publication of scientific, biotechnology papers, including where there was co-authorship between Swedish universities, Swedish firms, and/or international partners (universities or firms). Note that co-authorship of scientific papers similarly requires active participation by both parties.[9] Publication is a result of interaction which can be counted, however, rather than an intention to collaborate. While Nilsson et al. (2000)

9 Nilsson et al. (2000) thus present a bibliometric analysis from 1986 to 1997 about the science base for the Swedish biotechnology-pharmaceutical sectoral system. Their definition of the biotechnology innovation system is: 'The actors that develop, produce, analyse or use biological systems on a micro-, cellular or molecular level and the public and private institutions that affect their behaviour' (Nilsson et al. 2000:8). This source differs from the other two in that: it uses a different indicator for alliances; it only gives a picture of Swedish to Swedish alliances; and it covers a longer time period. Bibliometerics are based on the publication of scientific papers as an indicator of output (through quantity) and as an indicator of quality (through citations and impact analysis).

mostly analyze the Swedish perspective (and Swedish collaboration) in their study, we re-examine their results in a wider, international perspective. The following five trends are then evident:

1. the subset defined as 'smaller firms which also write scientific papers' tend to co-author with regional actors (e.g. universities located nearby geographically) although this result requires some further testing. One explanation for this trend could be close personal and work relationships as small Swedish firms include researchers who work both at a university and at that firm and/or researchers who recently left a university department;

2. two large pharmaceutical companies have dominated co-authorship of papers with universities in Sweden. The multinational companies of Pharmacia & Upjohn and AstraZeneca emerged from the two Swedish pharmaceutical companies of Pharmacia and Astra (which each resulted from earlier mergers within Sweden);

3. these two large pharmaceutical companies mainly co-author papers with researchers at those few Swedish universities which have major medical research and/or related biochemical or chemical engineering, principally: the Karolinska Institute (Huddinge/Stockholm); Uppsala University; Gothenburg University/Sahlgrenska; and Lund University;[10]

4. the two large pharmaceutical companies reduced their co-authorship of scientific papers with Swedish universities in the period 1986 to 1997, relative to the pre-1986 period. According to the NUTEK/Vinnova data, the two companies are not necessarily moving their biotechnology related scientific research abroad, but rather are simply doing less co-authorship of scientific papers with universities;[11]

10 These universities are located in the same geographic regions, with the exception of Umeå, as those where the biotechnology-pharmaceutical firms are concentrated.

11 The indicator may be picking up a trend whereby firms put less time and effort into scientific papers with universities because this has less value than previously. Or the firms' behaviour may have changed such that they still work with universities but choose not to publish.

5. while these two large pharmaceutical firms have reduced their direct co-authorship with Swedish universities, numerous smaller biotechnology-pharmaceutical firms have started to co-author, especially with geographically close universities. Still, the total number of co-authored articles between Swedish universities and Swedish firms is decreasing over time.

However, the importance of interaction between Swedish firms and Swedish universities should not be over-emphasized. In fact, the partner of a university in authoring a paper is most likely to be another university.

To what extent does inter-firm collaboration involve geographically close partners?

This section compares data from three different databases which report collaborations between pharmaceutical firms and biotechnology firms. Much of the existing literature on collaboration and innovation relies on one database to draw conclusions. Our suspicion, however, was that non-Swedish databases would not adequately represent Swedish to Swedish interactions. Thus, the BioSweden database can be used in order to test the validity of existing data sources and in order to get a more nuanced picture of Swedish to Swedish collaboration.

We looked first at the Recombinant Capital database, which specifically focuses on alliances between biotechnology firms and their partners, especially in the US context[12]. The second database, the PharmaDeals international database, specifically focuses on the pharmaceutical industry and is oriented towards European firms[13]. PharmaDeals might be more reliable for our purposes than

12 The Recombinant Capital database is available at www.recap.com

13 The PharmaDeals database reports alliances involving European firms in pharmaceuticals. It thus differs from those that only focus on biotechnology industry and/or involving deals with US firms. Information is based on Pharma Ventures news services, public domain information and company press releases.

Recombinant Capital, since the former focuses on Europe rather than the US. Finally, our newly developed 'BioSweden' database provides a separate source based on systematic examination of relevant literature[14].

By analysing the PharmaDeals database, 100 agreements between January 1996 and March 2000 were identified which involved at least one Swedish firm. Of these, 33 agreements involved co-development and collaborative R&D and hence could involve joint work with another firm or university, as shown in Table 4.3. Table 4.3 indicates the frequencies of different types of agreements, but any one agreement may be double counted as it may include elements of more than one agreement type[15]. The two multinational corporations – AstraZeneca and Pharmacia & Upjohn – are identified separately from all other Swedish firms[16].

The newly developed Swedish database, BioSweden, only reports agreements related to development or sales of technology, techniques and knowledge, and covers the period January 1993 to May 2000. BioSweden thereby differs from information shown in Table 4.3 (which also includes marketing and supply and manufacturing) and covers a somewhat longer period. In Table 4.4, as in Table 4.3, any one agreement may be classified in two ways, which can lead to double counting. The purpose of doing so is to identify the frequency of certain types of deals among the population of biotechnology-pharmaceutical firms – not to classify each specific deal. Note that the three largest Swedish-located firms are excluded from this BioSweden

14 BioSweden is focused on Swedish biotechnology-pharmaceutical firms and was built up from Swedish language specialist technical and/or business press. The database includes number, type and the partners in collaborative alliances.

15 The most common types of double agreements involve both marketing and supply & manufacturing (11).

16 In calculating the figures for Astra or Pharmacia, data for the current multinationals were used as well as historical data. However, in the historical data, only those parts of the merged firm which had heritage from one of the Swedish pharmaceutical firms were included. Thus, for example, agreements by Zeneca before the merger with Astra were not included.

collaboration data[17]. BioSweden shows that co-development of technology is the most common type of agreement, followed by licensing agreements. This ranking of frequency is similar to that reported in Table 4.3.

Still, differences in the types of agreements reported in the two databases have some implications for interpreting the results. BioSweden indicates 102 reported deals, which is approximately the same number as the 100 reported by PharmaDeals. Because BioSweden is specialised towards research and technological development agreements, however, our database indicates a larger total number of deals. Moreover, BioSweden excludes the largest three firms as objects of analysis, which were major players reported in the PharmaDeals shown in Table 4.3. These differences confirm our suspicions that international databases may under-report the activities of firms which are from non-English speaking countries.

According to PharmaDeals, only 11 Swedish firms were partners in the 33 'co-development and collaborative R&D' agreements identified in Table 4.3. These 11 firms include few very small firms. Those Swedish biotechnology-pharmaceutical firms engaged in formal knowledge collaboration are larger than average of the total population identified, at least as reported in this international database.

We used the PharmaDeals and Recombinant Capital databases to see whether national biotechnology-pharmaceutical linkages are stronger

17 The three largest Swedish biotechnology-pharmaceutical firms (all with 500+ employees) were excluded as the object of analysis in these figures. This implies that they are included only to the extent that they collaborate with any of the other Swedish biotechnology-pharmaceutical firms, but not as independent objects. These three firms are AstraZeneca, Pharmacia & Upjohn and Amersham Pharmacia Biotech, which all have extensive international activities. The development of a Swedish language database is assumed to have fairly low returns in terms of yielding additional information about the very largest firms. Their activities are well reported and analysed in the international press. This implies that existing, commercial or freely available international databases can be assumed to cover their activities relatively well.

Table 4.3 **Agreements involving at least one Swedish actor, January 1996 – March 2000, by type of agreement and type of Swedish partner. PharmaDeals**

Type of agreement which involves:	Number	Of which, number involving at least one Swedish university	Of which, number involving at least one Swedish biotechnology-pharmaceutical company (excluding Astra and Pharmacia)	Of which, number involving Astra or Pharmacia (or their respective merged multinational corporations)
Co-development and collaborative R&D	33	2	17	17
Marketing	27	0	14	11
Changes affecting ownership in companies[a]	20	1	7	6
Supply and manufacturing	16	0	13	8
Property rights[b]	15	0	9	4
Termination of some business agreement[c]	11	0	3	6

Notes: Based on authors' calculations from PharmaDeals database. Categories defined to include:
a = joint ventures, divestment, mergers, business acquisition;
b = licensing, product acquisition, technology acquisition;
c = rights reacquisition, co-development termination, divestment, termination.
Some agreements may be double-counted as they include elements of more than one agreement type.

Source: PharmaDeals.

Table 4.4 **Agreements involving at least one Swedish actor (other than the three largest Swedish located firms), January 1993 – May 2000, by type of agreement. BioSweden**

Type of agreement which involves:	Number
Co-development of technology	48
Mergers and acquisitions	10
Licensing agreements	33
Acquisitions of technology	11
Clinical testing and contract research	8
Unknown	3

Note: Some agreements may be double-counted as they include elements of more than one agreement type.

Source: BioSweden.

or weaker than international linkages for collaboration for knowledge development. In the PharmaDeals database, only five of the 32 agreements involved two Swedish partners. In the Recombinant Capital database, only two of these five alliances identified by the PharmaDeals are reported, plus one other (different) Swedish to Swedish collaboration. Taken together, this indicates that co-location in Sweden is not very important for such deals.

Moreover, in line with Nilsson et al.'s (2000) analysis of co-authorship of scientific papers referred to earlier, the majority of international alliances were with US partners. In some cases, even though the 'Swedish partner' still has headquarters and/or research activities in Sweden, the bulk of its business activity is in the US or UK. Thus, the international linkages are not randomly or evenly spread across all possible partners, nor are they even oriented towards Europe. The linkages instead run towards the US and UK, which are also the preferred collaborative partners for Swedish university scientists.

Our BioSweden database gives a somewhat different picture. Of the total population of 105 firms in the sector in Sweden, 31 had at least one collaboration with other organizations (firms, universities, etc.)

Table 4.5 **Total number of technology deals by Swedish firms, by partner. January 1993 – May 2000. BioSweden**

Number of interactions	With other firms					With universities				
	Swe	US	UK	Other	Total	Swe	US	UK	Other	Total
The 31 Swedish firms	32	21	7	11	71	23	4	3	1	31

Source: BioSweden.

to develop and/or sell technology-related products. In total, BioSweden shows that these 31 firms engaged in 102 agreements. This result shows a much higher number of firms than the PharmaDeals database (31 versus 10). Moreover, BioSweden reports a higher total number of reported deals as well as a higher number of firms engaging in such activities. Taken together, this indicates that collaboration for technological knowledge is more widespread among the Swedish biotechnology-pharmaceutical firm population and occurs more frequently than is reported in international databases.

Of the 102 deals reported in BioSweden, 71 were between two firms, while 31 were between a firm and a university. See Table 4.5. Furthermore, BioSweden shows that Swedish to Swedish interaction is more common than reported in international databases. Fifty-five of the 102 deals were between Swedish-based partners while 47 were between a Swedish-based firm and a foreign-based partner. Table 4.5 shows that more Swedish firms collaborate and they collaborate more often than otherwise reported in international, commercial available databases.

Nevertheless, this result indicates that even small and medium sized firms chose partners from the Swedish national context only about as often as from all other localities. After Sweden, partners are drawn firstly from US and then the UK, then everybody else, which is a result which replicates the patterns of co-authorship of scientific papers

found in Nilsson et al. (2000). Partner firms more often than not (39:32) are from outside Sweden. Partner universities are most often Swedish, however (23:8).

Conclusions

Much of the empirical material about biotechnology in general and biotechnology-pharmaceutical sectoral systems has been based on the US experience, with a few notable exceptions.[18] This paper has analysed data about formal knowledge collaboration in Swedish biotechnology-pharmaceutical firms from two international and one Swedish-language database. The comparison shows deficiencies in the international databases. As compared to BioSweden, the two international databases provide inconsistent data about individual firms, and they also under-represent both the total number of collaborations and the total number of Swedish firms engaged in collaboration. While we might expect such under-representation for smaller Swedish firms, more surprisingly, the two international databases were particularly inconsistent for the large multinational corporations: AstraZeneca and Pharmacia & Upjohn. This indicates the need for caution when interpreting results for small countries from international databases. Our results also demonstrate the value of new databases, which are compiled from home country sources and which provide systematic and large scale material.

As to the role of collaboration, the analysis presented here shows that a large number of Swedish biotechnology-pharmaceutical firms engage in formal knowledge collaboration to a greater extent and with greater frequency than would be expected based on international data. International firms are also coming to Sweden to find competent partners for technological development and/or sales, or to access the specialised knowledge bases of Swedish biotechnology-pharmaceutical firms of all sizes.

According to the analysis presented here, co-location of partners in the same region for formal knowledge collaboration is somewhat less

18 Such as Senker (1998).

common than might be predicted within the systems of innovation approach. Close collaboration occurs but only about as commonly as all other types of deals. The propensity to collaborate with geographically co-located partners differs depending on whether the collaboration is firm to firm, firm to university, or university to university. The overall finding is that geographical co-location is less important for firm to firm deals or for university to university co-authored papers than for firm to university deals.

After Sweden, the relative importance of Anglo-Saxon interaction for the biotechnology-pharmaceutical sector is visible in the results. Both Swedish biotechnology-pharmaceutical firms and scientific researchers appear to prefer US, followed by UK, partners to any other international partners. Many reasons could be speculated upon for this skewed distribution of collaboration.

Beyond these trends, one other result stands out which must affect our analysis of the 'Swedish-ness' of any overall Swedish biotechnology-pharmaceutical innovation system. The two large multinational corporations with strong Swedish heritages are not greatly engaged in formal knowledge collaboration with the rest of the national firm population, and they are also reducing their involvement with Swedish universities over time. This raises questions about the extent to which these particular firms can be said to interact with the national knowledge infrastructure as well as, more abstractly, how to interpret the interactions of these types of firms within a national or sectoral system of innovation. It also emphasizes the increasingly international nature of biotechnology-pharmaceutical sector.

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DATABASES

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Recombinant Capital (www.recap.com)

EU data sources:
BioSweden. Database about Swedish biotechnology-pharmaceutical firms. University of Linköping, Sweden.

PharmaDeals (www.pharmaventures.com)

Chapter 5

Accumulative Advantage across Public and Private Science: Explaining the Trends in US University Patenting[19]

JASON OWEN-SMITH

The aim of this paper is to explore two related issues:

- as intellectual property rights have moved upstream into US universities, why have some universities in the US been much more successful than others?
- what are the implications for the universities of this move into intellectual property?

Answering these questions for US universities will help us think about current attempts to import norms of US university – industry relations to European countries.

Public and private science: hypothesising about the relationships

There are two key concepts that need further discussion. One is cumulative, or first mover, advantage, in which success breeds success and the gap between winners and losers increases over time. This is taken from Robert Merton's (1968) description of the impact of reputational rewards in science. It was called the Matthew effect after the passage in the Gospel of St Matthew: 'For whosoever hath, to him shall be given, and he shall have more abundance ...'

The second concept is that of realm separation and realm overlap. One view is that intellectual property and privately driven or commercial science represents a fundamentally different realm from public or academic basic science. This distinction is drawn in part from Dasgupta and David's work (1987, 1994). They argued that the

19 This chapter has been edited from the transcript of the seminar presentation on 15 December 2000. More detail is available in an article by Jason Owen-Smith in Research Policy, 2003 (forthcoming).

difference between (public) science and (private) technology cannot be seen in day to day laboratory activities. Should you walk into a laboratory in a biotechnology firm or major pharmaceutical firm or university, and look at what people were doing at the level of reagents, questions and problems, you would not see a difference. The major distinction between the 'republics' of science and technology is cultural – arising from differences in the respective norms of information disclosure and in the reward systems. They argued that:

'What matters is the socio-economic rule structures under which the research takes place, and, most importantly, what the researchers do with their findings' (Dasgupta and David, 1994).

The basic distinction between public and private science is that patents are characteristic of private science whereas publications are the characteristic outputs of public science. These represent two distinctive ways to put knowledge out into the world. Patents mean limited exclusivity rather than the full disclosure that is characteristic of publications, and patents trade pecuniary rewards against the greater reputational rewards associated with full disclosure into the public domain via publication.

A point by point comparison, which suggests that patenting and publishing are two very different and possibly conflicting activities, is set out in Figure 5.1. This view suggests that importing patenting and commercial logics into academia seats two potentially contradictory reward systems within the same institutional mission – that of research. This raises some potential difficulties for universities and has the potential for a host of unintended and academically interesting, but perhaps policy-wise frightening, outcomes. It is something that should be considered when we think about bringing these norms into the European university system.

US evidence on university patenting

Patenting by 'research 1' universities, which are the 89 most research intensive universities in the US, has increased several times over between 1976 and 1998. This is shown in Figure 5.2.

Figure 5.1 **Rewards differ across public and private science**

Patents	**Publications**
• Patents are 'fences of interest' (Rip 1986)	• Publications are 'funnels of interest' (Rip 1986)
• Patent rewards are pecuniary	• Publication rewards are reputational
• Patents characterize commercial science	• Publications characterize academic science
• Bureaucratic judgments of veracity are based on a legal fiction	• Peer judgments of veracity are based in author's status
• Must meet legal standards of novelty, usefulness and non-obviousness	• Quality standards established by sceptical peer experts

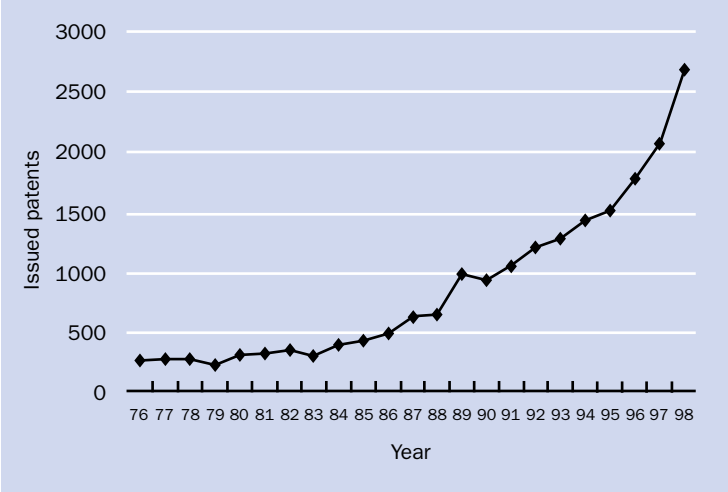
Patenting is very concentrated by institution. Figure 5.3 shows that in 1998 the top ten patenting universities in the US averaged nearly 100 patents per university, while the overall mean for all 'research 1' universities was 30 patents per university. Fifty per cent of the patents issued to all 'research 1' are issued to the top ten institutions. This relationship holds true for all academic fields. The gulf between high volume and low volume patentors is growing – in line with the theory of cumulative advantage. There is a lot of concentration, with a small number of universities dominating patenting in the US.

Figure 5.4 shows the results of a matching between US patent classifications and SIC industrial classifications for the top four classes of patents. They account for about 70-75 per cent of all US university patents. You can see in later years, 1996-1998, that the biotechnology and pharmaceutical industries drive the growth in patenting.

Realm separation versus realm overlap

Which universities are the high volume patentors? This is where the issue of realm separation versus realm overlap becomes important. High volume patentors come from all levels of the public science

Figure 5.2 **'Research 1' university patents 1976-1998**



Source: United States Patent and Trademark Office.

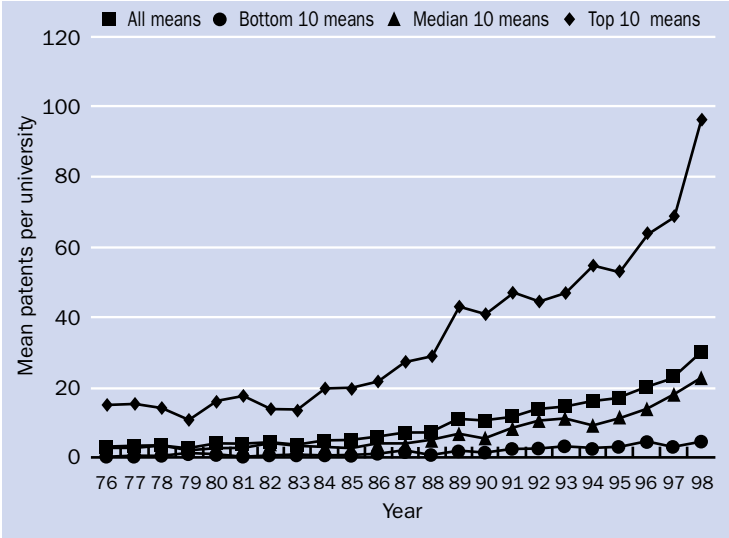
hierarchy. Table 5.1 shows the most prolific patentors among US universities over a 23-year period (1976-1998).

There are three possible ways to think about what would drive universities to patent frequently:

1. universities could patent because of resource scarcity. As they fail to win federal grants, they could turn to patenting intellectual property to keep their R&D budgets in the black;
2. patenting and publishing could be completely interlocked, in which case we would expect the highest prestige universities with the most successful, well-funded science to patent the most;
3. something else could be going on – and this is what I want to argue.

To put this issue in perspective, we need to return to an important distinction between the US and Europe. Not only do the US National Institutes of Health and the US federal government play roles as

Figure 5.3 **Patents issued per 'research 1' university**

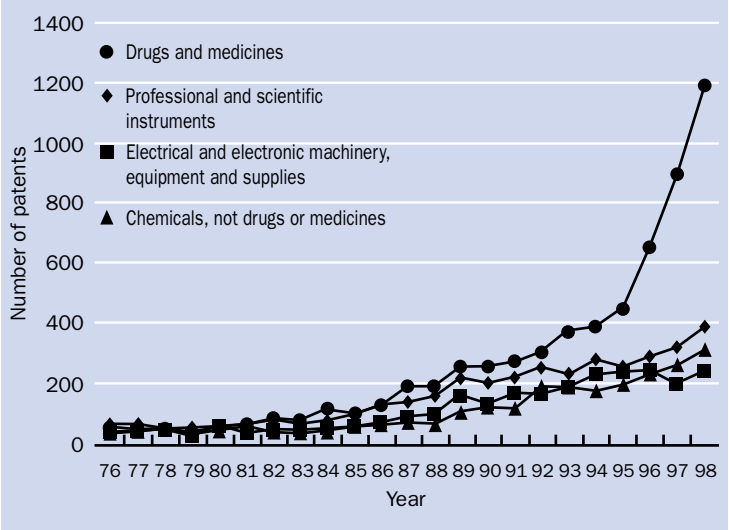


Source: United States Patent and Trademark Office.

integrators in research collaborations, but they are also a central and dominant source of academic research funding. In the post-war era, the US federal R&D funding architecture has allowed the creation of a national stratification order among universities. It is well understood among universities that your position in this rank determines the probability of success in funding applications.

The US National Research Council (NRC) grades universities according to their 'impact'. Thus three different measures of university research standing are implied: patents, federal grants received and NRC 'impact'. There are some universities, e.g. MIT and Stanford, which rank highly on all three measures. But there are also high patentors who do poorly on other measures, e.g. Iowa State. There are also universities with high public science ratings but a more volatile patenting performance. The fact that all three kinds of universities exist suggests that the drive to patent is not fully explained by either of the first two hypotheses listed above.

Figure 5.4 **Life science patenting drives the aggregate trends**



Source: United States Patent and Trademark Office.

We should note that the 1980 Bayh Dole Act, which is credited as being a major reason for these results, came into force in July 1981, which is after the most successful universities had already appeared on this list. Bayh Dole allowed universities (plus other non-profit organizations and small firms) to retain ownership of intellectual property developed with federal government funds. But universities were patenting far earlier than the Bayh Dole Act. Thus Bayh Dole did not create university commercialisation in the US. Instead it encouraged all the universities to do it, rather than just some of them, and accelerated the marketing and related activity of those that were already patenting.

The next point to argue is that the aggregate increases in patenting by the 'research 1' universities, and the growing gulf between universities, both result from increasing overlap between public and private science over time. The reason some universities are successful

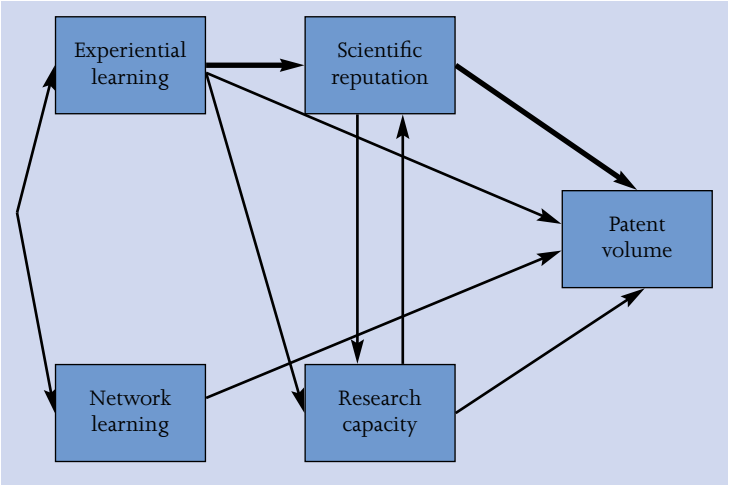
Table 5.1 **'Research 1' universities ever in the patenting top ten, 1976–1998**

University	Years in top 10	First year
MIT	23	1976
UCB/SF	23	1976
Wisconsin/Warf	22	1976
Caltech	21	1976
Cornell	21	1976
Stanford	20	1976
Iowa State	19	1976
Florida	13	1984
Minnesota	10	1979
Purdue	9	1978
Hopkins	9	1978
SUNY	7	1984
Utah	6	1976
U-Penn	4	1993
U-Chicago	3	1980
Harvard	3	1982
UT-Austin	3	1985
USC	2	1979
UC-Davis	2	1979
Michigan	2	1990
Case Western	1	1976
Ohio State	1	1977
Missouri	1	1982
Rockefeller	1	1992
NC State	1	1995
Duke	1	1996
Michigan State	1	1998

Source: United States Patent and Trademark Office.

and others are not depends on whether they manage to balance these two conflicting institutional missions within a single organisational unit. There is also evidence of first mover advantage (the Matthew principle). Together these two concepts suggest that the top group of patentors are likely to pull even further away from the pack and it will be harder for other universities to catch up.

Figure 5.5 **A conceptual model of the relationship between public and private science**



I have investigated this hypothesis using 18 years (1981-1998) of panel data for 'research 1' universities. The estimation model is built on a conceptual model of the relationship between public and private science which is illustrated in Figure 5.5. The dependent variable here is volume of patents. I argue that the volume of patents is a function of:

- learning by doing, or 'experiential' learning, measured by lagged prior patenting success;
- learning from networks, measured by co-assignments to firms in patents, and also by the length of time since the university began investing heavily in a technology transfer office for patenting and licensing activities;
- scientific reputation, measured by federal funding and by citations; and
- research capacity, measured in terms of total R&D expenditure, also industry-funded R&D expenditure, and institutional wealth,

measured by the book value of endowment assets.

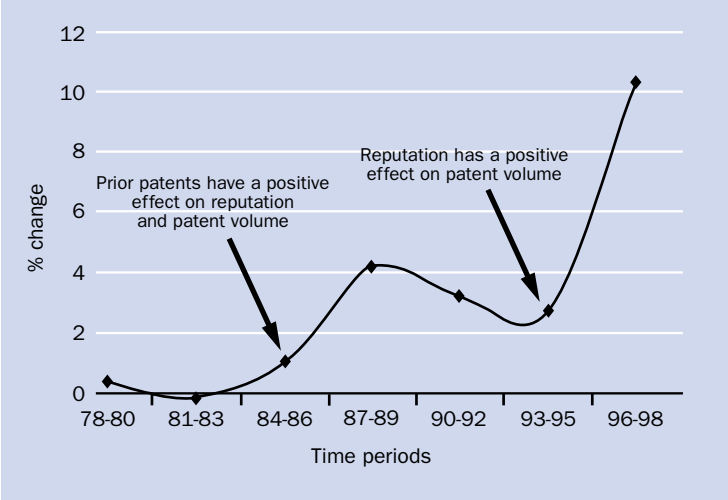
The first two of these explanatory variables can be taken as private science success related, and the remaining two as public science success related. If, however, boundaries are blurring, then public science success criteria, such as scientific reputation, will show a positive relationship with patenting success, and the two bold arrows in Figure 5.5 should move over time from negative or non-significant linkages to significant and positive ones.

In my analysis I have used the 18-year time period from 1981-1998. The Bayh Dole Act passed in December 1980, so 1981 is the first meaningful year for it to have an impact. I separate the 18-year period into six three-year time periods. I then estimate a five equation model with a set of equality constraints (Owen-Smith, 2003, explains this analysis in detail).

Initially (from 1981 to 1983) there were no significant linkages between patents and publication impact, suggesting that the realms of private and public science were separate. The number of patents held by universities was explained almost entirely by their research capacity and number of ties to firms (learning from networks). In this early period it looked as though universities that were good at patenting had put a lot of money into research – each patent comes out at 'costing' about $2 million to $2.5 million of R&D spending in a major US university – and had a lot of collaborations with firms. However previous patenting (experiential learning) became significant as a determinant of patent volume from 1984 onwards.

In the late 1980s we see a positive link emerging between the number of prior patents (which is our measure of experiential learning) and scientific reputation. The realms are overlapping to the extent that universities that patent a lot begin to see scientific benefits from patenting in terms of citations of their papers, and enhanced academic prestige. Finally, in 1993-1998 there was a connection from scientific reputation to patenting: scientific reputation has a positive impact on patenting activity. What seems to be happening here is that over time, at the aggregate level of all 'research 1' US universities, public and private science is beginning to overlap.

Figure 5.6 **Change in mean patents by three-year time period**



The structural shifts that drive the change in aggregate patenting can be shown as in Figure 5.6. The line is a poor man's derivative. It represents the change in mean patenting in each of the three-year time periods. The first time period, 1978-1980, shows the mean number of patents by universities in 1980, minus the number of patents in 1978. You see a straight, almost flat, line. There is an almost zero rate of change. Figure 5.6 then illustrates that there were two major accelerations in university patenting in the US, starting in 1984 and 1993 respectively. These took place in the same time periods where positive structural shifts in the relationship between public and private science occurred in my model. In 1984-1986 prior patents begin to exert a positive significant influence on scientific reputation, and in 1993-1995 scientific reputation begins to exert a positive significant influence on patenting activity.

This analysis suggests that public and private science now overlap for 'research 1' universities. The boundaries between public and private science are blurring; cumulative advantage now holds across the two

realms. It is no longer the case that you can play one game exclusively as a university. Increasingly, universities will be unable to be successful in a single realm. As public and private science become intertwined on 'research 1' campuses, success in one type of endeavour will require competence in both.

This may not be a good thing, but to a certain extent the genie is out of the bottle. There is no way to change this trend in the US. But as European nations make attempts to move towards it, lessons may be learned.

Public policy implications

Science matters and the relative success in life sciences of the US and Europe is much related to the role of universities. But there are concerns about what is happening to universities, and whether the commercialisation of academic R&D in the US is killing the goose that laid the golden egg. This has public policy implications for European systems.

There are major potential outcomes of this change. It re-works the post-war stratification order that has prevailed among US universities. It has effects on the lead universities that do not patent, suggesting that they may fall out of the elite. It also has effects internal to universities. As they become more oriented towards being cost centres rather than educational institutions, and the rationales for their administration change, there is a move towards concentration within the university on research areas that can be commercialised. This can explain the creation of biopharmaceutical juggernauts in medical schools at the expense of the rest of the university.

What can we say in conclusion on public policy implications? There are important things to consider if European nations want to import something like Bayh Dole and policies to support patenting and commercialisation of research by universities. Notice that the universities that drive most academic patenting in the US were active patentors prior to the policy changes. They play the role of incumbents; helping to create the rules of the game as they became successful. These universities jumped into the patenting game in my

model prior to the development of all the interconnections between public and private science. As a consequence, they made the rules, and later entrants struggle to succeed in a game that they cannot change all that much, that is still being dominated by the incumbents. Importing an established rule system from the US to a place like the UK, may have the negative implication of creating a system where there can be no incumbents, in which every single university participant is effectively a struggling 'new entrant'. We have to be careful. The transfer of practices from one national innovation system to another is fraught with risk.

At the level of Europe as a whole, the distinction between looking at individual national innovation systems and looking at Europe as a system of national innovation systems, is important for academic R&D. The national institutes in the US (principally the NIH) played a crucial role in structuring not only the academic prestige hierarchy but also approaches to R&D collaboration in the US. In Europe there is no centralised funding agency like the NIH, and consequently what may happen is that bringing in Bayh Dole and its policy mechanisms, will have the effect of further fragmenting European national innovation systems rather than integrating them.

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