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An international comparison of sectoral knowledge bases: persistence and integration in the pharmaceutical industry

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Abstract

This paper builds upon and extends existing studies of scientific and technological specialisation by proposing an analytical framework to compare sectoral knowledge bases across countries. It develops the concepts of knowledge persistence and knowledge integration as the relevant dimensions along which knowledge bases can be compared. Persistence is studied by analysing the evolution of specialisation over time. It hints at the cumulative, path dependent nature of learning processes. Integration is studied by analysing the evolution of specialisation across different typologies of research. It hints at the complex, non-linear interdependencies that link the scientific and technological domains. On the strength of an original database encompassing 630,000 peer-reviewed papers published between 1989 and 1996 in 11 chemistry and pharmacology-related fields across three types of research (i.e. basic, applied and development), it is argued that countries with high degrees of both persistence and integration (e.g. the US in pharmacology) are the most likely sources of useful research results for EU firms' innovative efforts in the pharmaceutical sector. Also, some doubts are cast on the existence of a European paradox in pharmaceuticals.

JEL classification: O3; L3; H4

Keywords: Knowledge; Specialisation; Integration; European paradox; Chemistry; Pharmaceuticals; NSI; Science and technology indicators

1. Introduction

This paper builds upon and extends existing studies of scientific and technological specialisation by proposing a unifying theoretical framework within which to compare sectoral knowledge bases across countries. In conducting this comparison, we elaborate upon the large body of literature that analyses National Systems of Innovation (NSI) (Lundvall, 1992; Nelson, 1993). An NSI is defined as 'being comprised of those elements of social organisation and behaviour, and the relationships among them, that are either located within or rooted inside the borders of a national state, and that interact in the production, diffusion and use of new, and economically useful knowledge' (David and Foray, 1995). The concept of NSI gained wide popularity that went beyond the boundaries of the academic community as it became (often unwillingly) entangled with 'techno-nationalistic' positions that have animated the industrial policy debate throughout the 1980s and 1990s. As stressed by David and Foray (1995), such

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positions are based upon two related (and nowadays widely-held) assumptions. First, technical capabilities lie at the core of a country's international competitiveness. Second, the development of such capabilities is influenced by issues of national localisation and can be managed via proper government action.

Recent research has challenged the relevance of the national dimension. In particular, it stresses that firms and researchers are entwined in thick networks of international relationships that cut across national boundaries. NSIs come under increasing strain, as the research and development (R&D) activities of large firms are progressively internationalised. Such internationalisation is caused by emerging imbalances between what a country's science base has to offer and the knowledge requirements of innovative processes. However, despite their undeniable increase, R&D linkages have not developed on a global scale; rather they involve mainly United States (US), European Union (EU) and, to a lesser extent, Japanese firms (Patel and Pavitt, 2000).

In this climate of internationalised R&D activities, it is very important to understand why specific countries are at the core of such international networks. Standard explanations refer to a number of factors considered to be key determinants of 'national competitiveness' (Porter, 1990). Following a well-established tradition (Fagerberg et al., 1999), this paper acknowledges that a country's specialisation pattern in specific scientific and technological fields plays a key role: firms establish R&D facilities where they perceive they can access relevant capabilities. However, most studies that empirically explore scientific and technological specialisation patterns at country level focus on a rather narrowly defined concept of specialisation. The emphasis falls squarely on the fields in which countries and/or firms patent. Classic specialisation studies focus on the cumulative evolution of countries' technological capabilities and, more often than not, scientific specialisation is not analysed. The stability of specialisation patterns over time (what we will term 'knowledge persistence') is well established; however, persistence and cumulativeness are not the only dimensions relevant to a study of knowledge bases.[1]

[1] Of course, economists have thoroughly analysed national trade and production specialisation patterns for a long time, starting with the Ricardian idea of comparative advantage.

It is well known that design and development activities capture a relevant share of the R&D funded by companies (Rosenberg, 1994). A country's knowledge base may have a strong science base but lack the engineering capabilities to embody scientific results in profitable products. Or, it might have strong development capabilities that are not supported by robust basic scientific knowledge. Different typologies of knowledge are complementary and interrelated. A strong presence in each typology of research induces an easier multidirectional flow of knowledge that can facilitate the production of successful innovation. Micro-level innovation studies strongly support this view, for example, Pisano (1997). Therefore, what type of research (for instance, basic versus engineering-oriented) is carried out in each field becomes a key issue.

The chief aim of this paper is to develop a framework within which to analyse knowledge specialisation both over time and across research typologies. We put forward this framework as a way to approach questions related to industry decisions to source knowledge internationally. In particular, we want to link these decisions to specific characteristics of the sectoral knowledge base that is drawn on. The paper identifies and operationalises, at sectoral level, the relevant dimensions that make the comparison of the knowledge bases of different countries a meaningful exercise. Particular attention is devoted not only to examining whether each country's specialisation is stable over time (knowledge persistence), but also to whether specialisation by field is similar across different typologies of research (knowledge integration).

The operationalisation of these two dimensions is based upon the design of a comprehensive data set of peer-reviewed papers that was obtained by combining the standard ISI classification by science field with the Computer Horizons Inc. (CHI) classification, which links scientific journals to specific types of research and development (i.e. Applied Technology & Engineering, Applied Research and Basic Research). The result is an original data set encompassing some 630,000 papers in 11 different sub-fields of chemistry and pharmacology published between 1989 and 1996. The limitations of peer-reviewed publications as an indicator of the knowledge bases are discussed. This data set will allow for a quantitative analysis of the characteristics and evolution of the specialisation profile of the four largest European countries (the UK, Germany, France and Italy), the EU as a whole, the US and Japan.

This data set is analysed in combination with the Policies, Appropriation and Competitiveness in Europe (PACE) survey (Arundel et al., 1995). The results of the PACE questionnaire pinpoint the pharmaceutical industry as being a highly internationalised industry. PACE data show that not only do EU R&D managers in the pharmaceutical sector value the results of public research, but also that they rely upon international research much more than those in the chemical sector and in other manufacturing industries. Also, PACE stresses that the pharmaceutical industry relies more on North American research than on EU research. The questions that demand explanation are why do EU pharmaceutical firms rely to such a great extent on North American research? What makes it attractive to EU firms? In attempting to answer these questions, we discuss some evidence related to the existence of a 'European paradox', i.e. a high quality science base, measured through the rate of publication, which does not correspond to a strong technological and economic performance, measured through patenting activity (European Commission, 1997) in the case of traditional pharmaceuticals. To do this, we compare sectoral knowledge bases across countries by developing a grid designed along the two dimensions identified above: integration and persistence.

The paper is organised as follows. Section 2 discusses the concept of knowledge persistence and integration. Section 3 presents an empirical exploration of the concepts developed in Section 2 in the case of the pharmaceuticals and chemicals knowledge bases. Finally, Section 4 offers concluding observations and raises a few policy issues.

2. Towards a theoretical framework of knowledge specialisation

Although the recent literature has devoted increasing attention to analysis of the economics of science and its implication for the innovation process (Dasgupta and David, 1994; Mansfield, 1991; Narin et al., 1997), the analyses of national science and technology specialisation profiles have remained so far largely independent. Despite token acknowledgement of the complexity and intricacy of the relationships between the science and the technology domains, specialisation studies tend to focus either on science or on technology. The former traditionally rely on bibliometric indicators; the latter on patent studies. The former are dominated by sociologists of science; the latter by economists who study technical change. The rhetoric of the linear model still determines the intellectual division of labour in this area of research. This paper represents a first step towards the redefinition of such division of labour.

This is achieved by complementing the analysis of knowledge specialisation over time with an analysis of knowledge specialisation across types of research. First, we briefly review a few classic specialisation studies developed in the historical, sociological and economic literature to stress the cumulative and path dependent process of knowledge production and accumulation. The concept of knowledge persistence (that is, of specialisation over time) is based upon these notions. Second, micro level analysis of technical change will inspire the introduction of the concept of knowledge integration (that is, specialisation across types of research).

2.1. Specialisation patterns over time: knowledge persistence

Research in the history of science has stressed the cumulative and social aspects of scientific endeavour. Historians have provided a number of accurate case histories that reveal how the accumulation of results over time influences the rate and direction of the discovery process. For instance, Conant and Nash (1964) describe the process of accumulation of quantitative results in physics that led to Lavoisier's revolution in modern chemistry. Such a process did not entail the substitution of inaccurate explanations with more accurate ones; rather, it involved the re-conceptualisation of existing findings to deliver a new, more general, explanation. In addition, it is particularly interesting that scientific advancement is often focused on a common frontier. The evidence for this is the incidence of multiple discoveries that Merton characterised as endemic rather than isolated features of science (Merton, 1965). The cumulative development of science has also been studied following the seminal work of Price (1963). Price sketches a macro 'growth of knowledge' approach that highlights the acceleration of scientific publication that accompanied the growth of the scientific community. This approach is probably more congenial to economists who are able to advance a number of established theoretical propositions to explain Price's empirical results. First, the increasing size of the scientific community would enable increasing division of labour and generate network externalities so that 'increasing returns' in scientific endeavour would be activated. Second, the growth of the scientific community stimulates the race for priority in discovery. This would create a powerful incentive to publish more prolifically in order to share some of the credit for 'discovery'. Scientific advance would then occur in smaller steps with greater overlap and duplication. Third, as the scientific community grows it becomes more difficult to assess individual contributions, which, in turn, provides an incentive to produce more publications in order to make claims about 'productivity'. As the three mechanisms are not mutually exclusive, cumulativeness is the most likely outcome.[2]

On the basis of the above mentioned literature, studies in the fields of bibliometrics and the sociology of science have analysed the scientific base of individual countries in terms of publication shares (Braun et al., 1995). However, the analysis of absolute shares does not allow for meaningful cross-country comparisons. It is only recently that the methodology used to analyse technological specialisation (based upon relative specialisation indicators) has been applied to the publication output of countries in an attempt to develop a comparative analysis of scientific specialisation patterns (European Commission, 1997; Geuna, 2001; Godin, 1994; OST, 1998; Pianta and Archibugi, 1991).

The work of Soete (1987), Pavitt (1989) and Cantwell (1989) provides the building blocks for the analysis of stability of technological specialisation patterns at the country level. Following these studies a large body of literature has been devoted to the study of technology and trade specialisation. The analysis of country-level technological specialisation patterns is nowadays a commonly used methodology to study the relationship between innovation and performance in terms of international trade and/or growth. In a nutshell, as technical change is a cumulative process that generates clusters of innovations, 'it is not indifferent to which technological areas countries are specialised' in (Meliciani, 2001). Different technical fields are characterised by different degrees of innovative opportunities and appropriability conditions (Carlsson, 1997; Malerba and Orsenigo, 1997). Furthermore, the learning processes that underpin technical change tend to be localised and cumulative (Pavitt, 1992): it is easier to learn in the proximity of what one already knows, so to speak. Therefore, if one is specialised in the 'wrong' (i.e. low opportunity) technical or scientific fields, one should not expect to be able to refocus one's own specialisation pattern in the short term. Trade and growth indicators will reflect such 'bad' specialisation. Scholars of technical change have therefore devoted much effort to matching technological specialisation indicators and countries' growth indicators (Fagerberg et al., 1999). Although there is some consensus about the importance of the knowledge base (or science base) of a country in the process of economic growth, the empirical and theoretical analyses have focused almost entirely on technology (especially patents) and generally do not attempt to provide measurements of the scientific base of the country. The work of Archibugi and Pianta in the early 1990s (see, for example, Archibugi and Pianta (1992)) is a rare example of the combination of patent studies and bibliometric analysis to examine national specialisation in the EU countries. Expanding upon the bodies of literature discussed above, we define knowledge persistence as the stability of the knowledge specialisation pattern over time.

2.2. Specialisation across research typologies: knowledge integration

Persistence and cumulativeness are not the only dimensions relevant to a study of the knowledge bases of firms or countries. Micro-level studies of technical change have highlighted how the integration of different types of research plays a crucial role in the process of innovation. Integration issues have been studied at length in the innovation management literature. Pavitt (1998) stresses that the key role played by modern firms is to map an increasing range of relevant disciplines into products. Integration efforts at firm level have been thoroughly discussed by a number of authors. Granstrand et al. (1997) studied the distributed

[2] We are indebted to Ed Steinmueller for the development of the discussion on the cumulativeness of science.

capabilities that enable firms to monitor and integrate technologies. Iansiti (1998) analysed integration issues in the mainframe industry. Prencipe (1997) studied similar aspects in the aero-engine industry. Engineering disciplines are commonly stressed as being powerful, although often overlooked, enablers of such integration. They provide the problem-solving techniques to handle complex problems by decomposing them into simpler sub-tasks, which can be solved and then integrated back into a consistent whole. For instance, Patel and Pavitt (1994) studied the pervasiveness of mechanical engineering skills across a variety of sectors. Landau and Rosenberg (1992) analysed chemical engineering as the key engine of growth in the modern chemical industry. Vincenti (1990) stresses the key role played by engineers and engineering sciences in solving the problems and finding the explanations that led to the birth of the aircraft industry. Pisano (1996, 1997) studied in detail a sample of pharmaceutical development projects in order to conclude that success is related to the capability to carry out, in a co-ordinated and timely manner, a number of activities that go well beyond the traditional boundaries of the R&D laboratory. The development of economically viable routes to produce drugs on an industrial scale is fraught with complex engineering issues, particularly where new untested routes are being explored.

Nevertheless, more aggregated studies continue to have a focus on indicators that do not make it possible to analyse whether the country possesses a strong knowledge base, that spans basic, applied and development research activities, in any specific sector. A country's sectoral knowledge base may have a strong science base but lack the engineering capabilities to embody scientific results within profitable products, or strong development capabilities but a not sufficiently robust base of scientific knowledge. In either case, firms may need to access those capabilities that are lacking, from where they exist, for example, from another country. This view is not based on a simple linear model that sees basic research as the source of the whole knowledge that is then transformed into technology. On the contrary, what we want to stress here is that the various typologies of knowledge are complementary and interrelated. A strong base in each typology of research induces an easier multidirectional flow of knowledge that can facilitate the production of successful innovation.

Such intuition is consistent with the theoretical framework developed by David and Foray (1995). They argue that 'an efficient system of distribution and access to knowledge is a sine qua non-condition for increasing the amount of innovative opportunities' (p. 40). Consistent with the results of micro-level studies of technical change, we argue that the successful exploitation of such combinations requires the existence of capabilities spanning a range of disciplines that go beyond the traditional boundaries of scientific endeavour. Knowledge bases that are too narrowly focused around core scientific disciplines (with no competencies in the related, but different, engineering sciences) may fail to close the feedback loop between the science and the technology domains. Such failure would seriously hamper the "distribution power" of the system (David and Foray, 1995, p. 46). In other words, in order to close the feedback loop between the science and the technology domains, countries (as well as firms) need to maintain distributed (rather than narrowly focused) competencies at sectoral level. As a national bias seems to exist in terms of the effectiveness of the linkages between business practitioners and academic research (Arundel and Geuna, 2004; Malo and Geuna, 2000; Narin et al., 1997), it is likely that such a bias exists also with respect to the linkages between the scientific and engineering communities. Thus, particular attention should be devoted not only to examining whether each country's sectoral specialisation is stable over time (knowledge persistence), but also to whether each country's sectoral specialisation cuts across different types of research (knowledge integration). A sectoral knowledge base with high knowledge integration would have similar specialisation by field across different typologies of research.

To conclude, what we propose is a simple analytical framework capable of combining the analysis of specialisation profiles over time with analysis of specialisation across type of research. This framework, built upon the notions of knowledge persistence and knowledge integration, should shed light on the 'morphological' characteristics of different countries' knowledge bases in certain sectors and thus help to explain firms' international knowledge sourcing decisions. Fig. 1 below summarises the above discussion. In what follows, we will argue that this typology can be usefully deployed to study a number of issues

		Knowledge Integration	
		Low	**High**
Knowledge Persistence	**High**	Country B	Country A
	Low	Country D	Country C

Fig. 1. Matrix of knowledge specialisation.

related to the characteristics and evolution of countries' sectoral specialisation profiles, as well as firms' decisions about where to source useful knowledge and capabilities.

With respect to any specific sector, a country can be positioned in one of the four quadrants of the 2×2 matrix of knowledge specialisation (Fig. 1). Country A, in the top right-hand quadrant is characterised by a persistent pattern of scientific specialisation and high level of knowledge integration. In the fields where it is positively specialised, Country A has developed capabilities in basic, applied and engineering research. Country B (top left-hand quadrant) would be persistently specialised in one or more fields, but its capabilities would be focused on, say, basic research only. Country C (bottom right-hand quadrant) would be characterised by integrated, although somewhat erratic, scientific and technological skills. Finally, Country D would be both erratic and unfocused in terms of research types: the fields of positive specialisation would change frequently and would be different in different types of research.

3. An empirical exploration of knowledge persistence and knowledge integration

We are interested in understanding the differences between patterns of internationalisation of knowledge sourcing activities pursued by different industries. Traditional explanations of this type of behaviour stress that firms go abroad whenever they (think they) can access 'better' capabilities relevant to their innovative and manufacturing efforts (Cantwell, 1995). Implicitly, these explanations assume that firms go abroad when their home knowledge base is not specialised in the 'right' fields. Second, the notion that a European paradox exists has gained wide support in the public policy arena (European Commission, 1996). According to this position, in some sectors EU firms would be very good at developing new ideas, but would tend to fail to exploit them commercially. Something would be 'missing' from the EU system of innovation (or its national components) that would leave EU firms at a disadvantage compared to their US counterparts. While the anecdotal evidence is abundant, rigorous empirical studies to prove (or disprove) the existence of such a problem are scant. Tijssen and van Wijk (1999) provide one of the few systematic efforts to solve this difficulty with robust empirical data in the specific case of the ICT sector. The use of the notion of knowledge integration can help to shed a better light on these types of issues.

We operationalise our framework in the case of the international pharmaceutical industry, using the chemical industry as a yardstick. The pharmaceutical industry is an interesting case for our purposes for a number of reasons. First, it relies heavily on basic, relatively codified research at the forefront of human knowledge; thus, the scientific and technological knowledge base contributes to the development of this industry in a crucial way. Second, the pharmaceutical industry appears to be one of the most internationalised manufacturing sectors, not only in terms of product markets, but also, specifically, in terms of the knowledge sourcing strategies pursued by the major players (Patel and Pavitt, 2000). Third, and consistent with the previous point, the results of the PACE survey (Arundel et al., 1995)[3] show that 'general and specialised knowledge' produced by public research institutes is particularly valuable to pharmaceutical firms (much more than to other manufacturing sectors), and that these firms consider scientific publications to be the key channel to internationally access this knowledge. Thus, publications can be used as a proxy for the measurement of the characteristics of persistence and integration of the knowledge base.[4]

Chemicals are used as a benchmark for establishing the divergence of pharmaceuticals. This benchmark is appropriate because the chemical industry, overall, behaves in its knowledge sourcing activities similarly to the other industrial sectors (see also Geuna, 2001). If all sectors are similar, why choose the chemical, and not some other, industry as a benchmark? The principal reason is that we wish to make inter-country and inter-sectoral comparisons *simultaneously*. Countries differ in the nature and extent of their development of specific industries. Since these differences are very difficult to capture, it is useful to choose industries that share a common knowledge base as the point of reference, but that rely on knowledge generated outside their home countries to different extents. Therefore, differences in sectoral behaviour may be related to the country-specific characteristics of the foreign NSI. Of course, the knowledge bases of the chemical and pharmaceutical industries differ greatly. The key difference is the increasing reliance of pharmaceuticals on biology and biotechnology, rather than chemistry (Gambardella, 1995; Orsenigo, 1989; Pisano, 1997). The chemical sector seems not to have seriously explored the potential of biotechnologies, although recent developments in combinatorial chemistry and biology provide evidence of the possibility for convergence (Malo and Geuna, 2000). By leaving aside the biotechnological knowledge base, the portion of the pharmaceuticals knowledge base that relies on the more traditional chemical processes can be analysed. This knowledge base is fairly similar to the knowledge base relied on by the chemical industry.

The results of the PACE survey reveal the sources of the public research activities most useful to EU R&D managers and the specific channels used to find out about such research activities. Brusoni and Geuna (2004) study the frequency with which EU firms source knowledge from different regions (with respect to various methods for learning about public research). Chemical firms obtain information from conferences in their own country and those in other European countries with the same frequency (about 88% of respondents). In the case of publications, informal contacts and hiring, respondents from the chemical industry reveal a clear 'home localisation effect', while attributing equally lower weights to other European countries and North America (exhibiting a lower EU-localisation effect than all industrial sectors combined). In the pharmaceutical industry, the home country localisation effect tends to vanish. Brusoni and Geuna (2004) report that, in seeking to source public research results EU R&D managers approach the North American science system, the EU and domestic sources with similar frequency. In particular, North American papers are used with the same frequency as home country publications (95%) and more frequently than papers from other EU countries (92%).

The behaviour of the pharmaceutical industry is of particular importance, if only because it is widely considered as one of the main areas of strength for the EU (Sharp et al., 1997). However, despite past

[3] The PACE questionnaire surveyed the largest R&D performing industrial firms in 1993 in 12 of the EU countries. The responses are from 414 large manufacturing firms across 9 EU countries (Belgium, Denmark, Germany, Ireland, Italy, Luxembourg, Netherlands, Spain and the UK).

[4] Before proceeding, an important caveat related to the use of publications as a descriptor of the knowledge base needs to be discussed. We fully acknowledge that by adopting peer-reviewed publications as a descriptor of a country's knowledge base we limit our analysis to the most codified (and codifiable) bits of this base. This limitation is determined by obvious data constraints (tacit knowledge is rather difficult to capture 'live'), and also by the responses to the PACE questionnaire, which pinpoint scientific papers as a key mechanism to locate relevant sources of knowledge. Hicks (1995) thoroughly discusses the role of scientific papers as signals of information about the presence of valuable 'hidden' tacit skills. This paper considers publications as elements of a signalling system whose morphological characteristics reveal something of the deeper structure of a country's sectoral knowledge base. Publications would be a sort of observable 'sufficient statistic' of the underlying unobservables. Finally, as publications represent a preliminary and incomplete proxy for the knowledge base, more inclusive indicators or combinations of indicators should be developed to operationalise the interpretative framework.

Table 1
Summary statistics for publication output by countries for the period 1989–1996

Country	Total number of scientific publications	Total number of publications in 11 chemistry fields[a]	Share of world total (%)	Share in chemistry fields (%)	Per capita total publications (1000 inhabitants)	Per capita chemistry publications (1000 inhabitants)
EU 15	1692165	212504	34	33	4.59	0.58
France	292025	35678	6	6	4.96	0.61
Germany	388945	51531	8	8	4.83	0.64
Italy	167952	23530	3	4	2.95	0.41
UK	446681	42179	9	7	7.75	0.73
USA	1916879	159890	38	25	7.47	0.62
Japan	413444	77236	9	12	3.32	0.62

Source: CHEMPUB database; Elaboration of SCI data.
[a] Only articles included; author fractional count.

successful performance, the EU industry seems to be rather pessimistic about the future (Sharp et al., 1997). Rising levels of R&D, decreasing profit margins and the struggle to refocus research efforts toward biotechnologies have been undermining the competitive position of the industry. US pharmaceutical companies are often considered to be way ahead of their EU competitors, particularly with respect to the adoption of biotechnologies.

It is often argued that the comparative success of the US industry is related to its capability to effectively transform the results of basic research into blockbuster drugs, rather than its ability to generate such results per se. In this respect, the European paradox is commonly evoked. While most observers seem to agree on this last point, explanations of its causes and empirical validation are in short supply. Generally speaking, the firms themselves are often blamed for not applying sensible management practices that would enable them to fully exploit the wealth of insights provided by the EU system of innovation and its national components. British firms are too short sighted; German firms are too slow in making decisions and pursuing new research routes; French firms are sheltered from the pressures of the global economy by a complacent state-managed health system, and so on.

While appealing, such propositions fail to consider the complementary possibility that there is something systematically different between the EU and the US knowledge bases that enables US firms to be more competitive and induces EU firms to look to the US scientific knowledge base to source new knowledge. In what follows, we operationalise our framework to interpret the results of the PACE survey and assess the anecdotal evidence about the European paradox.

3.1. Mapping and measuring countries' sectoral knowledge bases

We examined the publication profiles of different countries in the fields of chemistry and pharmacology. Following Geuna (2001) we used the science citation index (SCI) database of the Institute for Scientific Information to analyse the publication output of the four largest European countries, the EU, Japan and the US in the period 1989–1996 (see Geuna (2001) for a description of the resulting CHEMPUB database). CHEMPUB identifies eleven scientific fields relevant to the chemical and pharmaceutical industries.[5] Table 1 provides the summary statistics for publication output of the seven countries and the EU15. The chemistry and pharmacology fields appear to be an area of relative strength for the EU15 in terms of both level (Column E) and intensity (Column G) of publications. Moreover, the US exhibits a relatively low level of output in this area of research.

In order to operationalise the concept of knowledge integration, the journals in which each of the publications considered was published are classified according to the 'type' of research on which each journal focuses. To do so, we rely on the CHI journal

[5] C1: general chemistry; C2: analytical chemistry; C3: applied chemistry; C4: crystallography; C5: inorganic and nuclear chemistry; C6: medical chemistry; C7: organic chemistry; C8: physical chemistry; C9: polymer science; C10: pharmacology and pharmacy and C11: chemical engineering.

classification, which links scientific journals to specific types of research and development. Each journal is considered to belong to one of these four categories: Applied Technology (Level 1), Engineering and Technological Sciences (Level 2), Applied Research (Level 3), and Basic Research (Level 4).[6] For example, in the context of medical chemistry and pharmacology, Narin and Rozek (1988) propose that Level 1 is typified by the Journal of the American Medical Association, Level 2, by The New England Journal of Medicine, Level 3, by the Journal of Clinical Investigation, and Level 4, by the Journal of Biological Chemistry. Given the relatively small number of publications in Level 1 and Level 2 type research, these two categories were aggregated and labelled, for the sake of simplicity, as 'applied technology and engineering'. Godin (1994), who studied a sample of large innovating firms in order to analyse the complementarities between science and technology, proposed a similar approach. He developed a database of publications that were then divided into four groups in a spectrum that varied from very applied to basic ('untargeted') research. Unlike this paper, his work focused on firm-level activities, rather than sectors.

To develop a comparative analysis of the knowledge base in chemistry and pharmacology, the relative specialisation of a country was studied. The symmetric Relative Specialisation Index (RSI) (see Appendix A for methodological issues concerning the RSI) is calculated on the basis of data from the SCI database for six countries and the EU, 11 scientific fields and three research areas between 1989 and 1996 (Balassa, 1965; Soete, 1987). The statistical results are used to operationalise the theoretical framework of knowledge specialisation for the pharmaceutical and chemical industries.

3.1.1. Knowledge persistence (stability of specialisation patterns over time)

In the 8-year-period under examination the specialisation of the EU and the six countries considered has changed, in some cases quite substantially. To verify the stability (or lack thereof) of overall specialisation patterns we examined how all 11 specialisation indices had changed over time. Following the work of Pavitt (1989), we calculated the Pearson correlation coefficient for each country at the start and at the end of the period considered. Positive and significant coefficients would hint at the cumulative and path dependent nature of knowledge accumulation processes. We discovered that the knowledge specialisation in France, Germany, the UK, Japan and the US is positively correlated in the two periods, while no significant correlation was found for Italy and the EU.

Furthermore, in order to analyse the path of specialisation or despecialisation of a country, we regressed the symmetric specialisation index in 1996 on the 1989 value, country by country. Such a methodology was originally proposed by Cantwell (1989) and consists of a simple country-by-country regression at two different points in time. The dynamic path, therefore, cannot be studied. Also, nothing can be said about the determinants of the initial pattern of specialisation. Despite these limitations, this methodology has been widely used in specialisation studies. Its main advantage is simplicity. Given that the chief aim of this paper is to provide an example of how to operationalise the framework presented in Section 2, rather than develop an innovative quantitative technique, the advantages of simplicity counter balance its disadvantages.

If the β coefficient is equal to 1, then the country specialisation pattern has remained unchanged over the period. If $\beta > 1$ then the country is increasing its positive specialisation in fields where it was already specialised. If $0 < \beta < 1$, the country has decreased its non-specialisation in those fields where it was negatively specialised at the beginning of the period (or decreased its positive specialisation where it was positively specialised). In all cases, variations in specialisation occur in a cumulative way, as $\beta > 0$. In the case that β is not significantly different from 0, the hypothesis that changes in specialisation are either not cumulative or are random cannot be excluded. If β is negative we are witnessing a process of reversion in the specialisation. The case where $\beta > 1$ is often referred to as β-specialisation (Dalum et al., 1998).

Cantwell (1989, pp. 31–32) argues that $\beta > 1$ is not a necessary condition for increasing specialisation. Therefore, we have also analysed the so-called

[6] As noted by one referee, such a classification implicitly assumes a disjunctive linear sequence of 'basic-applied-engineering' research. While acknowledging this limitation of the CHI classification, we also wish to stress that in this paper we do not look at each typology of research in isolation, but at their interplay. The latter point will be clarified in the following sections.

Table 2
Fields of positive specialisation by type of research

	Applied technology and engineering	Applied research	Basic research
EU15	C10 C3 [C8]	C4 C7 [C10 C8 C2 C1]	C2 C5 [C4 C8 C6 C7]
France	C8 C4 [C6 C10]	C7 C4 [C8 C6 C9]	C7 C4 [C8]
Germany	C3 C4 [C11]	C1 C5 [C4 C9 C8]	C5 C4 [C8]
Italy	C10 C6 [C8]	C7 C6 [C10]	C2 C6 [C7 C5 C4]
UK	C3 C10	C4 C7 [C10 C3 C6]	C6 C4 [C5 C2]
US	C1 C2 [C9 C6 C10]	C6 C10 [C3 C1]	C6 C10 [C2 C8 C3 C7]
Japan	C4 C11	C10 C9 [C1]	C1 C10 [C7]

Source: CHEMPUB database; elaboration of SCI and CHI data. Top two positive specialisation fields out of brackets. C1: general chemistry; C2: analytical chemistry, C3: applied chemistry; C4: crystallography; C5: inorganic and nuclear chemistry; C6: medical chemistry; C7: organic chemistry; C8: physical chemistry; C9: polymer science; C10: pharmacology and pharmacy; C11: chemical engineering.

s-specialisation (Dalum et al., 1998). The dispersion of a given distribution does not change if $\beta = R$; if $\beta > R$ the specialisation increases (s-specialisation) and if $\beta < R$ the specialisation decreases (s-specialisation).

For each country we ran regressions on all fields, basic research only, applied research only, applied technology and engineering research only. For the most general regressions (*all fields*), we found that Germany was the country with the most stable specialisation pattern ($\beta = 0.96$, $R = 0.724$). Italy and EU do not have significant coefficients. All the other countries despecialised cumulatively (i.e. $0 < \beta < 1$) in terms of both β and s-specialisation, with the UK ($\beta = 0.843$, $R = 0.897$) being the most cumulative, followed by the US ($\beta = 0.779$, $R = 852$), Japan ($\beta = 0.659$, $R = 926$) and France ($\beta = 0.42$, $R = 799$). All coefficients are significant at the 1% level (2% for Germany). In the case of *basic research* alone, only the US, Japan and the UK have β coefficients with a significance level higher than 5%, respectively, 1.04 (1%), 0.95 (2%) and 0.44 (4%). The US, with both $\beta > 1$ and $\beta/R > 1$, increased specialisation in sectors where it was already specialised, and became less specialised where initially specialisation was low. Japan, with both $\beta \sim 1$ and $\beta/R \sim 1$, showed a high stability in its specialisation patterns. In particular, the US deepened its specialisation in fields related to the pharmaceutical industry: medical chemistry (C6) and pharmacology (C10). The four largest European countries saw an increase in the dispersion of their basic research specialisation. EU countries, especially Germany and France, show a tendency to remain more focused on traditional chemistry fields. No statistically significant results were obtained in the cases of applied research and applied technology and engineering.

3.1.2. Knowledge integration (specialisation across research typology)

Table 2 presents a summary of the relative specialisation of the EU and the six countries under consideration over the entire 8-year-period. It lists, by type of research, the chemical fields in which each country exhibited positive specialisation. The first observation that can be made is that there is some degree of overlap between the positive specialisation in applied research and that in basic research, while the area of applied technology and engineering tends to differ from the other two areas of research. If knowledge integration is defined as the presence of positive specialisation in the same scientific fields in the three typologies of research, it can be stated that the US has a much higher degree of knowledge integration than the EU. Indeed, the US has a positive specialisation in medical chemistry (C6) and pharmacology and pharmacy (C10) in all research typologies. Among the four largest EU countries, France has positive specialisation in crystallography (C4), organic chemistry (C7) and physical chemistry (C8) in all three research typologies. Similarly, Germany is positively specialised in all typologies in crystallography (C4) and inorganic chemistry (C5). Finally, Italy is consistently positively specialised in medical chemistry (C6) and organic chemistry (C7).[7]

A simple indicator of integration is calculated by dividing the fields in which a country is positively

[7] A problem emerged with respect to inorganic chemistry (C5) and organic chemistry (C7). For these fields, no publications are recorded in applied technology and engineering. Thus, for these two fields, we considered as integrated those countries that exhibited positive specialisation in applied and basic research only.

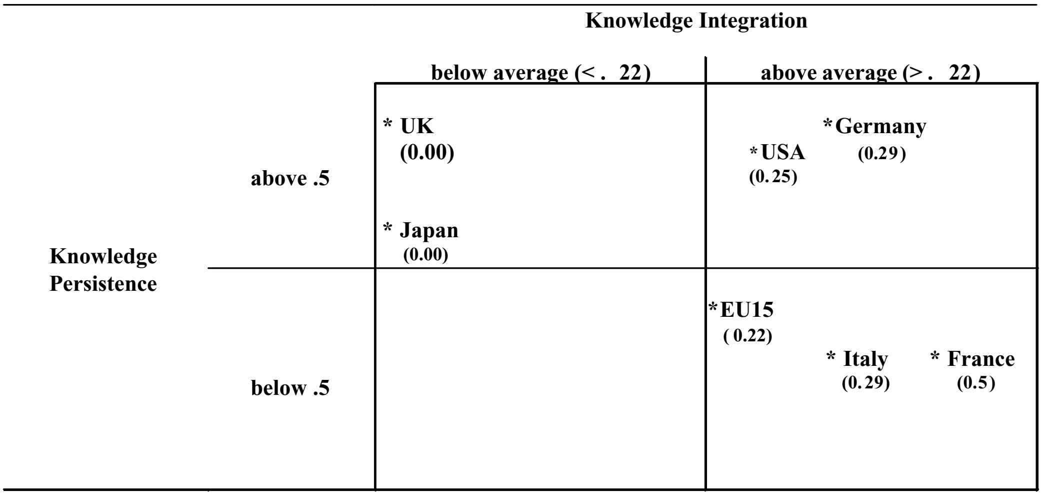

Fig. 2. Integration and persistence: a rough-and-ready map This figure maps the indicator of integration on the horizontal axis and the indicator of persistence on the vertical axis. For persistence, we have used the results of the regressions for all chemistry and pharmacology fields, first and last year, country by country. For integration, we have used the indicator discussed in Section 3.1.2. The threshold between high and low integration is given by the arithmetic average of the indicator (0.22).

specialised in all research typologies by the total number of fields in which a country is positively specialised. So, for each country we have

$$\mathrm{INT} = \frac{\sum \text{Number of fields of positive specialisation in all types of research}}{\sum \text{Number of fields of positive specialisation}}$$

This indicator varies from 0 to 1. It is 0 when the country considered does not exhibit any overlap between the three types of research. It is 1 when the country considered is fully integrated across all types of research in all the fields in which it exhibits positive specialisation.[8] On this basis, the US is positively specialised in medical chemistry and pharmacology and pharmacy in all typologies of research and positively specialised in a total of eight fields. Its indicator of integration is $2/8 = 0.25$. France, Italy and Germany are less dispersed, that is, more integrated, than the US. France scores $3/6 = 0.5$ (where the fields of full integration are crystallography, physical chemistry and inorganic chemistry out of a total of six fields of positive specialisation). Italy and Germany are integrated in two fields (medical chemistry and organic chemistry versus crystallography and inorganic chemistry) out of a total of seven fields of positive specialisation, giving an integration coefficient of $2/7 = 0.29$. Japan and the UK are not integrated at all and do not exhibit any overlap across the different typologies of research.

3.1.3. A taxonomy of knowledge specialisation

By combining the results on persistence and integration, it is possible to map the science and engineering bases of different countries in a two-dimensional space that summarises the results sketched above. We have mapped the indicator of integration on the horizontal axis and the indicator of persistence on the vertical axis. For persistence, we have used the results of the regressions for *all fields*, first and last year, country by country. We have also used the coefficients for Italy and the EU although, as stated earlier, they are not significant. As all coefficients except those for Germany (whose β equals 1) are $0 < \beta < 1$ (β-despecialisation), we set 0.5 as the threshold. For integration, we have used the simple indicator sketched above. The threshold between high and low integration is given by the arithmetic average of the indicator (0.22). Fig. 2 reports the result of such a combination.

It is fairly apparent that the US and Germany combine high levels of both integration and persistence. France, despite a high level of integration, exhibits

[8] The formula actually used to calculate the indicator is reported in Appendix A.

low persistence over time. Neither Japan nor the UK shows any integration, but the pattern of specialisation in the UK is more stable. Italy and the EU are somewhere in between. The EU as a whole is characterised by both average integration and low persistence (this latter coefficient was not significant in the regression). Italy appears to be relatively integrated, but exhibits low persistence (Italy's coefficient for persistence is not significant).

It is worth combining the results of this taxonomy with the analysis of the specific fields of specialisation listed in Table 2. Despite the high persistence and integration exhibited by both the US and Germany, their specialisation profiles appear to be very different. In particular, Germany's specialisation revolves around traditional chemistry fields, such as crystallography (C4) and inorganic chemistry (C5). The US is specialised in those fields more directly related to pharmaceuticals: medical chemistry (C6) and pharmacology and pharmacy (C10). The other EU countries studied also are more specialised in 'chemistry for chemicals', rather than pharmaceuticals. Furthermore, it is evident from the regressions we ran by type of research that the EU countries' specialisation in medical chemistry and pharmacology decreases as we move away from development type research towards applied and then basic research.

Such results are consistent with other studies of specialisation that rely on traditional methodologies. So, for Germany, specialisation in 'traditional' chemistry (i.e. inorganic and organic) is confirmed by Sternberg (2000, p. 98) who also highlights the German disadvantage in medical sciences. OST (1998) confirms both the integration of the German pattern of specialisation and its focus on chemistry. Furthermore, the UK seems to be more specialised in medical research than France or Germany. OST (1998) also confirms the strong EU specialisation in chemistry and its relative disadvantage (in terms of publications) in biology (basic research).

These different specialisation profiles hint at a possible explanation for the PACE questionnaire results. The PACE survey revealed that public research carried out in North America was valued and used extensively (even more than public research carried out in other European countries) by the largest EU R&D firms in the pharmaceutical sector. The PACE questionnaire does not allow speculation about why this happens, though. We argue that the reliance of EU firms on the North American knowledge base is consistent with the fact that the US exhibits a persistent as well as an integrated specialisation pattern in medical chemistry and pharmacy and pharmacology. The results for the chemical industry confirm this. EU chemical firms do not use US-generated research to the same extent as pharmaceutical firms. Their home country knowledge base is relatively more specialised, in a persistent and integrated manner, in those fields that are particularly relevant to the innovative efforts of the chemical industry. Thus, they rely heavily on the public research of their own country or other European countries.

Particular attention should be devoted to specialisation by type of research in EU countries. It was noted above that they are positively specialised in either medical chemistry or pharmacology at the level of applied and development research. However, those two fields do not show up as areas of positive specialisation in basic research (Table 2). Also, the results of the regression by type of research clearly show that only the US and Japan are increasing their specialisation in basic research. No clear pattern is discernible for EU countries except for the UK, which is β-despecialising. Therefore, these data do not allow us to talk about a 'European paradox', according to which EU firms would not be capable of exploiting an efficient basic research system because of lack of 'development' capabilities. Our interpretative framework and data seem to point to the fact that these types of capabilities do exist. What is missing is the basic research bit, with the result that EU pharmaceutical firms have to source research results from the US. The pattern of sourcing is consistently different when chemical firms are considered, as their home country knowledge bases seem more capable of providing basic research capabilities.Despite the limitations of the data and the simplicity of this analysis, the location of different countries along the grid defined by the measures of persistence and integration both matches with a few things we know about the institutional structure of each country, and also raises some interesting questions. For instance, the results concerning the 15 countries of the EU as a whole are hardly surprising. An EU-wide system of innovation is still in the process of formation. National industry and science and technology (S&T) policies still heavily influence country-level specialisation patterns, preventing them from converging toward a homogeneous whole.

4. Conclusions

The evolution of country-level sectoral specialisation has been conceptualised by the discussion on knowledge persistence and knowledge integration. Persistence is related to the evolution of specialisation over time. It hints at the cumulative, path-dependent nature of the learning processes. Integration is related to the evolution of specialisation across different typologies of research. It suggests the complex, non-linear interdependencies that link the scientific and technological domains. The interaction of the concepts of knowledge persistence and knowledge integration provide a head start for the development of a robust conceptual framework in which to compare countries' sectoral knowledge bases. It is quite significant that the conceptualisation proposed in terms of persistence is consistent with the results of micro-studies of technical change that pinpoint learning processes as cumulative and path-dependent (David, 1985). Also, innovation studies hint at the key role played by distributed (rather than narrowly-focused) capabilities in enabling technical change (Granstrand et al., 1997). This is captured by the concept of knowledge integration.

This paper provided an example of how to operationalise the framework on the basis of a statistical analysis of a large, original and custom-built data set that describes the scientific and engineering knowledge base in chemistry and pharmacology in the four largest European countries, the EU as a whole, the US and Japan during the period 1989–1996. Analysis of the relationships between core positive and negative specialisation, and of the typology of research (applied technology and engineering, applied research and basic research) has shown that the countries considered have different degrees of knowledge integration and knowledge persistence. Specifically, the US and Germany exhibit the highest coefficients of persistence and integration. However, the US is more heavily specialised in fields related to pharmaceuticals (that is, medical chemistry and pharmacology and pharmacy) than Germany and the other EU countries, which appear to be more specialised around traditional chemistry. These results are consistent with the views expressed by the EU R&D managers that responded to the PACE questionnaire. They stressed that public research developed in North America was particularly useful for their innovative efforts in pharmaceuticals. In contrast, domestic and EU localisation effects prevail in the case of the chemical industry.

As for the policy implications, the empirical results presented (although preliminary) allow us to make two main observations. First, our data set does not identify any 'European paradox' in pharmacology. EU countries exhibit capabilities in terms of applied and engineering research, but not in basic research. Instead, the US increases its β-specialisation in basic research in pharmacology and medical chemistry. No clear pattern is discernible for EU countries, with the exception of the UK, which is β-despecialising. Such lack of basic research capabilities may well explain the frequency with which EU R&D managers in the pharmaceutical industry approach the US knowledge base. For chemicals, the pattern of sourcing is different. As their home country knowledge bases seem more capable of providing a more integrated pattern of research capabilities, EU chemical firms rely chiefly on their home country knowledge base and then approach that of the EU. At least for pharmacology and medical chemistry we found no evidence of paradoxes.

Second, our approach hints at the possibility that government can actually influence the rate of technical change by fostering the development of an 'integrated' specialisation profile. Empirically, one can identify the NSI that firms consider to be more helpful to their innovative activities (for example, the US for pharmaceuticals), analyse it in terms of integration and then target the type of research that is lacking in the home country. We may call this the 'policy for integration' option. In fact, despite the enormous resources devoted by policy makers to the exploration of emerging technologies, 'picking a winner' remains a rather hazardous activity. The greatest successes of recent years are the unintended consequences of policies aimed at fostering other paths of research, for example, biotechnology being the unintended offspring of US cancer research programmes and the beneficiary of military research for the bio-war (Martin et al., 1990). Which specific scientific field will be responsible for the next revolution continues to be difficult to predict. We argue that our approach would not allow governments to pick the winners, but would allow them to support the development of an integrated knowledge base once a new path has emerged.

The limitations of this work open up a number of challenging questions for future research. First, publications are a very good way to trace the scientific knowledge base of a country, but are less successful as far as engineering research is concerned. Merging traditional data sets of patent activities with our data set of publications would provide a better picture of the interaction between scientific and engineering specialisation. Second, the concepts of knowledge integration and persistence can also be applied to the study of firms' knowledge bases to further confirm the consistency between micro- and macro-level dynamics.[9] It is important to expand such analysis to test the existence of a correlation or causation between knowledge integration and knowledge persistence in certain fields on the one side, and technological and economic performances of firms and countries, on the other. The qualitative indications provided by the PACE questionnaire are but a first step. Third, this analysis should be extended to a sample of 'small countries'. These may be much less integrated and persistent than large countries as they may find it more convenient (or just more feasible) to exploit the advantages of flexibility by specialising narrowly in terms of fields and/or types of research and then switching when new research trajectories emerge. Finally, on a more theoretical note, PACE reveals that firms can source knowledge not available in their home country by looking abroad. However, there are costs attached to such a choice. Traditionally, costs are related to the geographic distance between source and user. This paper hints at the possibility that there might be costs attached also to the relative position in the 'knowledge spectrum', so that the farther from a typology of research the more expensive it will be to develop knowledge exchange.

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Appendix A. Methodology

The symmetric relative specialisation index (RSI) is given by the ratio between the share of the given scientific field in the publication of the given country and the share of the given scientific field in the world total of publications (activity index, AI) minus one, divided by AI plus one. It may take values in the range [−1, 1]. It indicates whether a country has a higher-than-average activity in a scientific field (RSI $>$ 1) or a lower-than-average activity (RSI $<$ 1).

$$\mathrm{AI} = \frac{\frac{p_{ij}}{\sum_i p_{ij}}}{\frac{\sum_j p_{ij}}{\sum_i \sum_j p_{ij}}} \tag{A.1}$$

where p is the number of publications, $i = 1, \ldots, n$ number of scientific fields and it is equal to 11, and $j = 1, \ldots, m$ number of countries and it is equal to 7.

$$\mathrm{RSI} = \frac{\mathrm{AI} - 1}{\mathrm{AI} + 1} \tag{A.2}$$

As the denominator of AI is the share of the given scientific field in the world total of publications, the number and choice of the countries in the comparative analysis does not influence the robustness of this indicator.

[9] For a first example of a micro analysis focusing on the world largest pharmaceuticals groups see Brusoni, Criscuolo and Geuna (2004).

The indicator of integration was calculated as follows:

$$x = \begin{cases} 1 & \text{if } \mathrm{RSI}_{i,k} > 0 \quad \forall k = 1, 2, 3 \\ 0 & \text{otherwise} \end{cases}$$

$$y = \begin{cases} 1 & \text{if } \mathrm{RSI}_{i} > 0 \\ 0 & \text{otherwise} \end{cases}$$

$$\mathrm{INT}_j = \frac{\sum_i x_i}{\sum_i y_i}$$

where $i = 1, \ldots, 11$ number of fields, $j = 1, \ldots, 7$ number of countries, $k = 1, 2, 3$ number of research typologies.

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