Understanding technology adoption in the German pharmaceutical industry

Iciar Dominguez Lacasa

Fraunhofer Institute for Systems and Innovation Research (ISI),

Breslauer Str. 48, 76139 Karlsruhe, Germany

idl@isi.fraunhofer.de

Paper presented at the DRUID Academy Winter 2003 Ph.D. Conference
Aalborg, Denmark
January 16-18

Abstract

At the beginning of the20th century classical biotechnology and chemical synthesis were for many purposes alternative technologies. Spite of the importance of classical bio-technology (which mainly drew on the application of enzymatic processes and microbiology for the production of good and services) at that time specially in Germany, the German drug producers made use of the organic chemical synthesis in the drug development and production processes. This technological decision was a conscious choice. Since the 1970s bio-technology plays a key role in the pharmaceutical sectoral system of innovation. The revolutionary advances in molecular biology of the early 1970s had open a new era in the drug discovery process. The advent of modern biotechnology has forced German incumbents to learn the advances in the technology they ignored 100 years before. The aim of this paper is to review historical contributions to the history of technology and the pharmaceutical industry to identify some of the factors that may have influenced the technology adoption decisions of the actors in the German pharmaceutical industry. The findings disclose that the research traditions, the organizational structures, and the firm capabilities in terms of human capital strongly influenced the selection criteria of the pharmaceutical corporations for the production of raw materials and pharmaceuticals. The analysis of the technological trajectories of the chemical synthesis and biotechnology reveals that unexpected technological breakthroughs in other technological fields radically influenced their development paths. Finally, examples of policy action disclose how that policy measures can influence technology trajectories and adoption by actors.

1. Introduction

In simple words the pharmaceutical industry is the business of discovering, developing, producing and commercialising medicaments. One interesting aspect of the pharmaceutical industry is that drugs can be obtained from many sources and by applying different technologies. By sources is meant the raw materials used and by technologies the procedures and practices with the function of finding and developing drugs. For instance, many inorganic materials, such as metals, have therapeutic properties. On the other side hormones, vaccines and antibiotics come from living organisms. Further, drugs can be synthetic or semisynthetic, which means that they can be developed by putting together molecules that lead to substances with therapeutic properties. Alternatively biological process can lead to the production of these substances.

The German corporations were be very successful with their technological decisions in the origins of the modern pharmaceutical industry. They had a strong innovative performance until the 1940s. However, after World War II German companies have not been able to introduce innovations the way the used to earlier in the 20th century. Furthermore, the slow development of biotechnology in Germany compared to the advances in this field in other countries and the concern about the innovative competitiveness of the German pharmaceutical sector has provoked an enormous political excitement since the 1980s for the support of the biotechnology science base and its application for industrial purposes, specially in the medical field. For this reason, it might be interesting to take a look back in history to understand the landscape of institutions involved in drug development and the logic behind the processes of technology adoption. These may explain to a large extent, the performance of the pharmaceutical corporations today and disclose some of the key factors for sustainable innovative competitiveness.

Scholars have chosen alternative levels of analysis to try to understand (i) the process leading to new drugs, (ii) the landscape of institutions and technologies involved, its dynamics and (iii) the impact of endogenous and exogenous changes on both, the process and the landscape[1].

The aim of this paper is to review the historical contributions to the history of technology and the pharmaceutical industry to identify some of the factors that may have influenced the technology adoption of the actors in the German pharmaceutical industry. Technology adoption involves a decision, and by our own experiences in decision making we may be aware of the complexity of this process, which in some cases might be more determined by our past experiences; in other the environment, or even external factors intending to guide us in the decision making process, may be more important for the result.

This contribution is a preliminary result of the search for factors that have influenced the adoption of technologies in the modern German pharmaceutical industry. The paper is divided in three sections. The first section presents a short review of the history of the pharmaceutical industry taking into consideration the organisational and institutional changes of the industry has gone through in the 20th century. The second section focuses on the development of two major technologies applied for drug discovery and production: biotechnology and the chemical synthesis and their application in pharmaceuticals and in other in other production processes that shaped

---

1 This paper skips a literature review on the contributions to economic and innovation studies focusing on pharmaceuticals.

their development path. The third section sketches the role of the policy actions in shaping the development of technologies and the technology adoption process. Finally, a short summary of the preliminary findings and further points for the research agenda are presented.

2. The development of the modern pharmaceutical industry in Germany

The German pharmaceutical industry arose in last quarter of the 19th century from two sources: the traditional pharmacy and the coal-tar dyestuff industry (Drews 1998).

The traditional pharmacy: pharmaceuticals from plants

Before the formation of the modern pharmaceutical industry in the last decades of the 19th century the process of drug discovery and development was carried out by the small traditional pharmacists. The responsibilities of doctors and pharmacists were clearly defined. The state guaranteed the pharmacists the responsibility of producing and commercialising the medicaments prescribed by the doctors. Already in the first half of the 19th century the analytical chemistry[2] became the toll to isolate from plants those compounds with therapeutic character. The successful isolation of this compounds raised the questions of how to disseminate the drugs to as many persons as possible and how to make sure that the medicines had homogenous standards. Some of the traditional pharmacies (which developed in companies like Shering AG, Boehringer Ingelheim, Boehringer Mannheim, and Merck) recognised the need for large scale production and standardisation measures. From the technical point of view there were no major constraints for the large scale production of the known compounds, however the lack of infrastructure for transportation limited the regional scope the pharmacists could supply with medicaments (Wimmer 1991).

The German dyestuff industry: dyestuffs as pharmaceuticals

The second half of the 19th century saw the advent of organic chemistry[3] and scientific advances to understand the chemical structure of organic compounds[4]. This process was parallel to the emergence of the dyestuff sector in Germany which developed from the large scale production of illuminating gas. This production process produced a major by-product, the "coal tar". This black mass seemed at first to have no significant industrial use, however it turned out to contain dyes of great interest for the textile industry. Instead of being extracted from animal or vegetable sources dyes could be made chemically from the coal tar. This was the solution to satisfy the demand for dyes in the rapid growing textile industry. The interest for the coal tar as raw material increased as it became clear that the organic compounds it contained could be used as raw materials to produce disinfectants, explosives, plastics and, most importantly, pharmaceuticals. The largest German coal-tar dyestuff producers were established between 1863 and 1872[5]. They started their activities by copying the dyes of French and British manufactures. However, already in 1877 half of the dyestuff world production had German origin and the producers diversified into pharmaceuticals applying the same technology: the chemical synthesis (Murmann et al. 1998).

---

2 Analytical chemistry. is a collection of techniques that allows exact laboratory determination of the composition of a given sample of material.

3 Branch of chemistry dealing with the compounds of carbon.

4 In chemistry, almost any material is considered organic if its molecules contain carbon atoms. Aspirin is organic, as are all the other over-the-counter analgesics, as well as gasoline and most plastics.

5 Farbehandlung Bayer (in the city of Wuppertal, 1863); Farbwerke Meister, Lucius, und Bruening (in Hoechst, 1863), Aktiengesellschaft fuer Anilin-Fabrikation -Agfa- (in Berlin, 1873).

The German dyestuff industry and the industrial scientific laboratory

The innovation flow in terms of products maintained by the German coal-tar dyestuff companies occurred parallel to the introduction of what has been called the major organisational innovation so far: the establishment of the industrial scientific laboratory and the industrial application of scientific principles.

The research and development (R&D) activities that used to be carried out in laboratories at a small scale were then preformed at large industry scale. This transition from laboratory to industrial scale R&D activities was possible through the institutionalization of science in the industry. Science was now able to convince the businessman of its usefulness (Beer 1959, p. 71). The innovative strength of the German dyestuff sector since the last quarter of the 19th century and until the first world war draw on the ability to learn the industrial applications of the organic chemistry. That is, to learn how to apply the chemical synthesis[6]. This learning process was supported by (i) a large supply of well university trained chemists that were hired by the dyestuff companies (ii) the strong collaboration patterns between industry actors, research institutes and universities and (iii) large amounts of R&D expenditures.[7]

With the new R&D practices the inventor, which up to that point had been playing a decisive role in the research and discovery process, was not able any more to undertake the large investments required for successful R&D activities. Under these conditions large firms took the major role in the innovation process. It was the rise of the industrial research laboratory[8]. The companies' recruitment strategies adapted to this organizational innovation by recruiting workers with experience in scientific research. Meyer-Thurow (1982, p. 376) gives evidence for the academic profiles of the research scientists at the company Bayer. Already in 1897 all research chemist in the main laboratory held Ph.D. in chemistry and the majority had research working experience at the university[9]. Further, patent and trade-marks protection laws appeared as the appropriate instrument to incentive R&D investments in dyes and pharmaceuticals. The year 1877 saw the first harmonised German patent law and the establishment of the intellectual property rights office. This law had a strong impact on the chemical sector by supporting company-sponsored research and the university-industry interaction. German dye-stuff manufactures were successful in shaping their external environment according to their needs. On the one side by influencing the patent policy and, on the other, by shaping academic curricula and sponsoring reforms at universities and polytechnic institutes (Meyer-Thrurow, 1982 p. 376).

The meeting of two research traditions: the industrial pharmacy and the coal-tar dye stuff industry

---

6 In chemistry, synthesis refers to putting together new molecules.

7 Beer (1959, pp. 70-94) and Meyer-Thrurow (1982) present excellent contributions to the study of the process of institutionalization of science and research and development activities in the German dye stuff industry in the last decades of the 19th century and until the first world war.

8 Libenau (1988, p. 118) points out that there is little evidence that the decisions taken by German corporations leading to the creation of the industrial laboratories were the result of a systematic analysis or long-term planning that went into the decisions to grow. According to him the good performance allowed them to afford slightly speculative investments.

9 Beer (1959, pp. 57-69) gives a general overview of the influence of the German university and the polytechnic institutes on the corporate R&D activities of the dye-stuff industry.

The diversification process of the dyestuff producers into the production of pharmaceuticals faced a traditional structured shaping the process of drug discovery and commercialisation. Pharmacists, that had been traditionally the responsible for the discovery, development and production of drugs and their classification according to pharmacologist principles, had to accept the role of the new comers, the dyestuff producers, as providers of raw materials and drugs. The dye-stuff producers, in turn, accepted that medicaments were to be sold by pharmacists (Wimmer 1991). However, there were still strong differences among the large corporations providing raw materials and producing drugs. The R&D and production practices of the industrial pharmacists very much differed from the practices of the dyestuff producers.

According to Marschall (2000) until the 1950's both sub-sectors of the pharmaceutical industry (the more traditional pharmaceutical companies and the pharmaceutical companies from the coal-tar sector) were very different in what concerned their historical development, their product lines, and most importantly in the skills of the employees and in their research and innovation strategies. Table 1 summarises these aspects.

Coal-tar dyestuff companies	Traditional pharmaceutical companies
• Large diversified companies from the dye sector; • Science base strategies (the structural theory and the stereochemistry[10] guided their research activities); • Continuous innovation flow; • Chemists in charge of the drug discovery activities.	• Small and medium enterprises arising from traditional pharmacies; • Empirical "try-and-error" methods for the discovery and production of drugs and chemical compounds with therapeutic properties; • Pharmacists responsible for the drug discovery activities.

Table 1 Characteristics of the industrial actors in the German pharmaceutical industry at the beginning of the 20th century.

These differences become more clear if we consider their ability to apply biotechnology in the first half of the 20th century. On the one side companies of the more traditional pharmaceutical industry applied biotechnological methods with great success in the production of basic chemicals (like butyric acid, acetic acid or lactic acid) while companies of the coal tar sector were less interested in developing and applying biotechnology methods. The leading players in the sector (Bayer, BASF and Hoechst) reacted very cautious and sceptic (even with prejudice) to the possibilities offered by biotechnology. Even though the were strongly oriented towards the application of innovative technologies they did not recognised the applications of biotechnology for the pharmaceutical industry (Marschall 2000).[11]

The sector leaders had accumulated knowledge and capabilities on the application of the chemical synthesis. Biotechnology methods offered an alternative to the chemical

10 The structural theory is used to develop an understanding of the physical properties and chemical reactivity of organic compounds.

11 To illustrate this attitude towards biotechnolgy and other „non-science driven" practices Marschall studies the research and production practices of the German pharmaceutical companies in the 1930s and 1940s, the era of the antibiotics. For instance, after the properties of penicillin to treat bacterial infections had already been discovered in the late 1930s and its production by fermentation processes optimised, American and Swiss drug companies started to establish departments of microbiology and fermentation units. In Germany chemical engineers kept trying to synthesized antibiotics chemically.

synthesis in many industrial fields and also to produce drugs. However, the leader companies in the sector did not engage in the development of this technology and kept implementing their skills and using their knowledge to try to chemically synthesis compounds with therapeutic properties. The companies excluded from the beginning the biotechnology alternative given that it not always led to predictable results. Its scientific base was weak.

Marschall (2000) points out that the reluctance of the coal-tar dyestuff companies was not an unconscious disregard in their innovation strategy. It was a conscious decision. The process of institutionalisation of science in the industrial corporation during the establishment of the industrial laboratories had influenced the self perception of the chemist working for the industry. The focus on structural chemistry and on the chemical synthesis as the tool-kits to search for new compounds with therapeutic properties had rationalised their conception of research and the industrial application of science shaping hence their understanding of the research processes and their evaluation criteria in the assessment of new technologies. The fact that the German corporations were the strongest innovators in pharmaceuticals until the second world war probably reaffirmed the trust of German chemists in the chemical synthesis.[12] Further more, the initiatives to apply biotechnological process for the production of raw materials, which was successfully carried out by some of the actors died out (Marschall 2000).

The advent of modern biotechnology and the biotechnology industry

German pharmaceutical corporations did not change their research and development strategy until the early 1980s. The revolutionary discoveries of recombinant DNA and monoclonal antibodies radically changed both, the drug discovery and development process and the structure of the pharmaceutical industry.

The contribution of the revolutionary advances to the process of drug discovery lied in the new potential to understand diseases and to determined the optimal molecular target for drug intervention. In these sense what we could called „modern biotechnology" opened up a new era in the pharmaceutical sector. Pisano (1991) or Freeman (1995) have already referred to the emergence of modern biotechnology as a competence destroying technological advance in the sense of Tushman and Anderson, a new technological trajectory in Nelson and Winter's sense or a new Paradigm in Dosi's sense.

Biotechnology has gradually gained importance as instrument for the drug discovery and development process. Patent indicators help us to analyse the extent to which biotechnology is shaping the R&D process in drug discovery and development. The empirical evidence speaks for the strong increasing influence of biotechnology in pharmaceuticals in Germany specially since the 1980s. Figure 1 presents the empirical results[13].

Regarding the structure of the pharmaceutical industry after the biotechnology revolution scholars[14] describe the development of a new form of industrial organization presenting (i) a high number of knowledge/science-intensive small and medium-sized

---

[12] Achiladelis et al. (2001) present data on innovation counts in the pharmicaeutical industry since the 19th century. According to their data German corporations were until the 2nd world war the major introducers of innovations in the pharmaceutical sector.

[13] For a discussion about the influences on the process of drug discovery and development see Reiss et al. (2000).

[14] See for example Saviotti (1998)

enterprises dedicated to the development and commercialisation of biotechnology[15], and (ii) constantly growing inter-institutional collaboration agreements between the new entrants and the large pharmaceutical corporations.

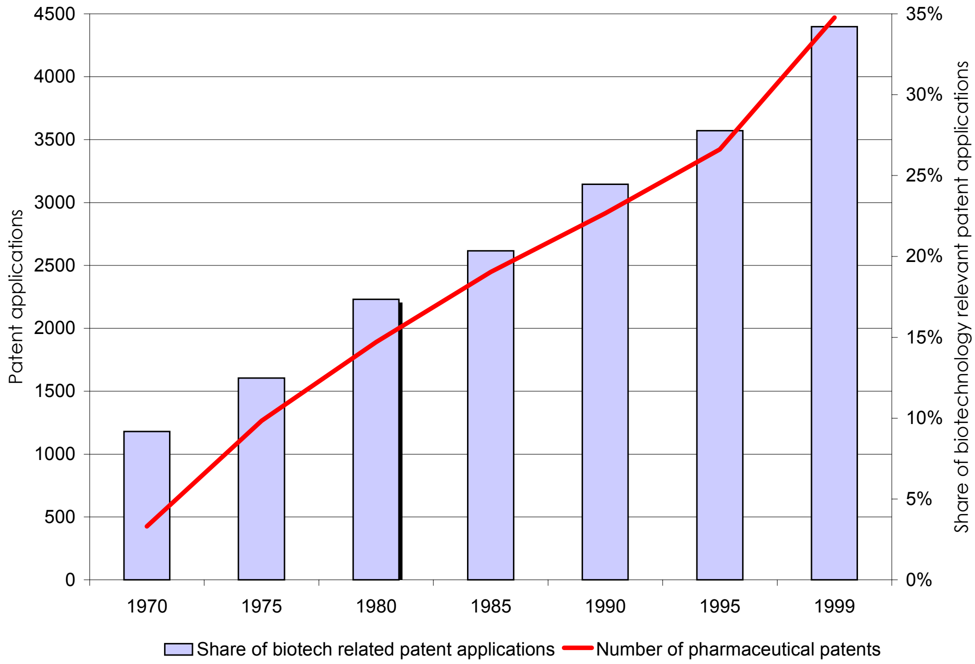

Figure 1 Patent applications in pharmaceuticals and the share of biotechnology related patents[16]. German patent applications filed at the GPO and EPO with Germany as designation country. Source: PATDPA.

Collaboration occurs at R&D level, in the production processes and even at the marketing level. At the present development stage of the biotechnology industry, mostly developed in the US, vertical and horizontal collaboration patterns among small firms, large firms and public sector research organisations continue. However, this industrial organisation presents regional asymmetries in both the organisational structure and in the time frames of development. Germany's performance in the development of biotechnology after the biotechnology revolution has been very disappointing if compared with the developments in the US. The indicators for the lag in the development

[15] These firms build up the so called biotechnology industry, which has mostly developed in the US.

[16] The continuous line represents the number of pharmaceutical patents, the columns are the share of biotechnology related patens in the pharmaceutical patents counted each year.

3. Biotechnology and the chemical synthesis: two competing technologies

In the next paragraphs the analysis focuses on the technologies applied for drug discovery and production: biotechnology and the chemical synthesis and their application in pharmaceuticals and in other production processes that shaped their development path.

There is no general agreement about what biotechnology really is. Among the several definitions of biotechnology the one proposed by the OECD has been influential in both academic and government circles:

> Biotechnology is the application of scientific and engineering principles to the processing of materials by biological agents[17] to provide goods and services (Bull et al. 1982).

To trace the roots of biotechnology we need to go back thousands of years to the first applications of the fermentation processes to process foods, beverages and other substances (Mckelvey 1996). The scientific fundaments of fermentation remained unknown until 1830s when J. v. Liebig and in the 1850s Pasteur concentrated on it and developed two alternative theories to explain the transformation of sugar in alcohol in the presence of yeast. At the end of the 19th century Pasteur`s biological approach was broadly accepted.[18] It was the first impulse in the scientific development of microbiology which represents the methodological and experimental basis of biotechnology production practices. At the beginning of the 20th century microbiological applications and a large number of biotechnological processes had already been introduced. Waste water treatment, distillery, brewery, vinegar production, wine production, creamery, tannery, fertilizers, sugar production and production of organic acids were some of the fields and production processes were biotechnology was first applied.

After the scientific advances in molecular biology and genetics along the 20th century and specially, since the revolutionary discoveries of recombinant DNA and monoclonal antibodies in the mid 1970s nobody doubts about the importance of biotechnology at different stages of the drug development process and in other industrial sectors.[19] However, the possibility of using of biological agents in the drug discovery and development processes was already present in the first years of the modern pharmaceutical industry.

Like already put forward above, the more traditional representatives of the industry applied biotechnological methods with great success already at the beginning of the 20th century. The company Schering produced in the early 1900s organic acids with the application of micro-organisms, Luitpold was active in 1931 in the biotechnological production of enzymes and Knoll in the production of Ephedrin since 1930. Roehm and Boehriger Ingelheim are other examples of early adopters of biotechnology. After the 2nd World War Boehringer Ingelheim, was a leader the in the microbial transformation

---

17 Biological agents are micro-organisms like virus, bacteria, algae, fungi, or protozoa.

18 His explaining model of the fermentation of alcohol, the lactic and the butanoic acids focused on the action of micro-organisms.

19 Sharp (1995) presents a short but clear overview of the applications of biotechnology. Her contribution focuses on the biotechnology applications after the revolutionary discoveries of the 1970s.

technology[20]. All these companies had grown from traditional pharmacies in late 19th century. According to Marschall (2000) the years between 1900 and the first World War were of most prosperity for the industrial biotechnology in Germany. Between 1881 and 1912 a broad range of discoveries contributed to major advances of the fermentation processes. Biotechnology was applied in different industrial activities from the biological production of fertilizers up to the production of rubber, fuel, lactic acids and in waste water treatment.

On the other side, the chemical synthesis, guided first by the scientific developments in organic chemistry, started to be applied by the dye-stuff industry in the late 19th century. Along the 20th century the importance of the chemical synthesis reached most sub-sectors of the chemical industry in Germany like the production of nylon and polyester fibers, the production of plastics, pharmaceuticals and the production of even artificial sweeteners.

In the pharmaceutical industry biotechnology and the chemical synthesis competed first in the large scale production of organic basic chemicals (alcohols) like milk acid, butanoic acid and ethanol. Biotechnology, in this case fermentation process, had the advantage of being an inexpensive production method that relied in the availability of carbohydrate-based raw materials.

An unexpected technological breakthrough in engineering, the development and application of the Haber-Bosch process for the production of ammonia[21], influenced dramatically the development of the technological trajectories (Hughes 1975). By shaping the technological capabilities of the German chemical companies it partly determined the technological orientation of the industry towards the application of the chemical synthesis. With the high pressure synthesis of the Haber-Bosch process, the chemical industry intensified its strategy of chemically synthesizing natural materials or replacing them by chemical supplements. The starting raw material was coal and Germany had enough coal reserves at that time. For instance, the IG Farben[22] decided to specialised on the coal based product. This was similar to the decision of adopting the high pressure synthesis as main production technology. This technological choice was crucial for the development of the chemical path (Marschall 2000).

To sum up, the historical material the beginning of the 20th century faced two possible technological trajectories for the pharmaceutical industry in Germany. Until the first world war fermentation and microbiological processes were widely applied in the German industry. Among other factors, the development of the Haber-Bosch process supported the success of the chemical synthesis in the chemical sector. Its wide range of applications determined the formation of a technological path that repressed the application of biotechnology and its further development in the German innovation system. Accordingly substances and materials like methanol, ethanol, acetic acids, and rubber were synthesised and produced with high pressure technologies. German chemical corporations did not invest in biotechnology research and development until

---

20 Technology to transform hormones.

21 Ammonia (the synthesis of nitrogen and hydrogen) is an important intermediate product for the production of fertilizers and nitric acid. The Haber-Bosch process operates at high pressure allowing for the synthesis of ammonia in the presence of a catalyst.

22 Corporation funded in 1925 with the merger the 8 largest chemical companies in Germany.

the 1980s. These historical stylised facts matched remarkably well with historical patent indicators made available through online databases.[23]

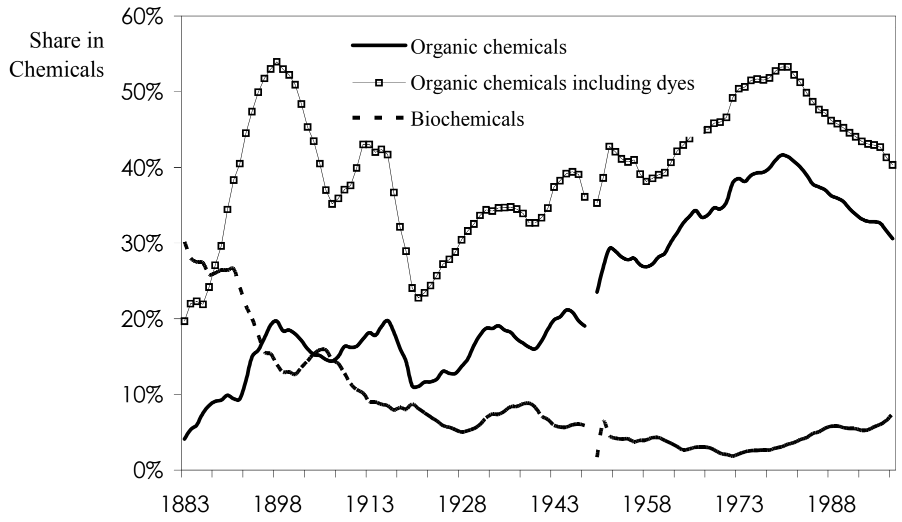

Figure 2 Organic chemicals and bio-chemicals in Germany. German patent applications filed at the GPO and EPO with Germany as designation country.
5-year moving average; Sources: EDOC and PATDPA.

In figure 2 bio-chemicals, which represent the patent documents related to biotechnology through out the period (1879-1999), held 30% of the inventions in the chemical sector at the beginning of the period. Their importance decreased along the whole century until the 1970s where the trend changes.

Figure 3 presents a comparison of bio-chemicals in 1900 and in 1998. The definition is constant along the entire period 1879-1998; that is, in both years (1900 and 1998) the technology definition includes the same patent classes allowing for a historically consistent comparison. But as we see the distribution of the patent classes is remarkably different: In 1900 bio-chemicals were mainly applied in development and production processes of food and beverage products.

23 For the a methodological discussion on the retrieval of historical time series of patent indicators from the German patent office with historically consistent technology definitions see (Grupp et al. 2000). The same source discusses the definition of the technology fields presented in the figure and the presentation of bio-chemicals are representatives of biotechnology in the time frame considered.

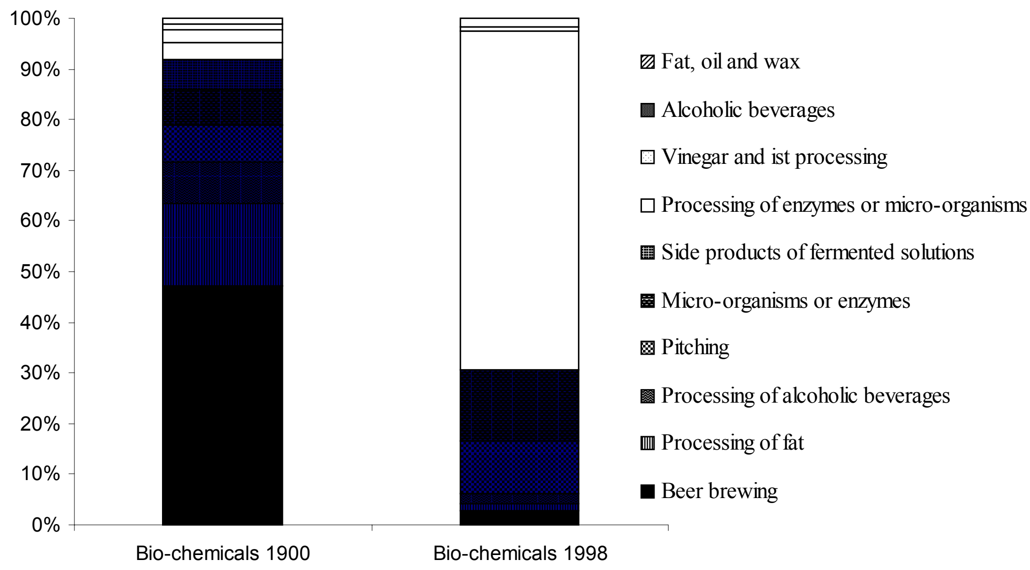

Figure 3 Bio-chemicals in Germany. Distribution of the patent classes defining bio-chemicals in 1900 and 1998.
Sources: EDOC and PATDPA**.**

4. Policy influence in technology adoption

If we consider the historical contributions focusing on the patterns of development of the chemical/pharmaceutical industry in Germany we can identify two major policy actions that have influenced the technology trajectories and the technology adoption in the German pharmaceutical industry.

The autarkic policy of the German National Socialist government (1933-1945)

The national socialist government attempt to build a self-sufficient economy with the aim of being totally independent from foreign raw materials. To reach this goal the government largely supported financially the chemical industry in the development and application of the Haber-Bosch process and the use of the chemical synthesis. Public support for the high pressure synthesis reinforced the choice for this technology in the long term by influencing the capabilities of the chemical / pharmaceutical companies. Accordingly, the chemicall/ pharmaceutical corporations applied the Haber-Bosch process in the production of raw materials even though the chemical synthesis of the coal-base products was not rentable. The world economic crisis push the prices for natural raw materials down and made other production technologies like biotechnology more rentable. Since the political aim was to reach self-sufficiency the German government financed the expensive synthetic production of coal-based products (Marshall, 2001). Even though this option meant an enormous effort in terms of infrastructure and energy resources, until 1945 the chemical synthesis of raw materials and products remained the dominant technological choice of the chemical industry. The explicit support of one technology may have hampered the development of alternative technologies or driven them to niche applications.

The government support of biotechnology in the last quarter of the 20th century

The major conscious policy contribution to the development of biotechnology in Germany was probably the introduction of the Genetic Engineering Act in 1989 to set the legal framework for the activities involving genetic engineering. Still today the German legislation, also the one related to IPR for biotechnology inventions, is going through gradual modifications in tune with the European directives. However, the government concern for biotechnology in Germany began in the 1970s in terms of public funding for research and development in biotechnology.

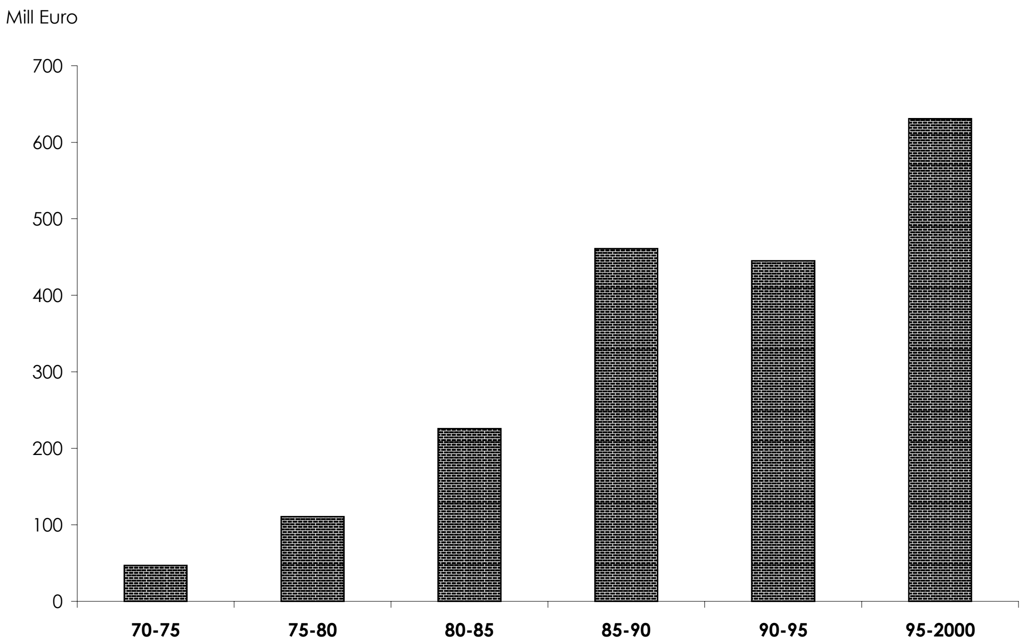

Figure 4 Direct project funding for for biotechnology related research in Germany[24]. 1970-2000.
Source: Public Promotion Catalogue of the BMBF

Figure 4 presents the public direct project funding in biotechnology since 1970. The figures give evidence for the increasing policy concern for biotechnology in Germany. Research and technology policy have explicitly target the development of the biotechnology science base and the improvement of the commercialisation of biotechnology in terms of patent applications and firm creation. Industrial actors have been an important target of the policy measures until the mid 1980s (see figure 5). Since then, public finding has concentrated mainly on large public research institutes. According to the budget allocation among actors, now a days companies and public research institutes receive more than 75% of the direct project funding for biotechnology.

---

24 Figures include only the federal investments clasified as biotechnology activities by the German Federal Ministry of Research and Education and does not consider expenditures in medical, health and enviromentl research that may directly support biotechnology but not appear in the ministry's biotechnology statistics. Institutional funding is also not included.

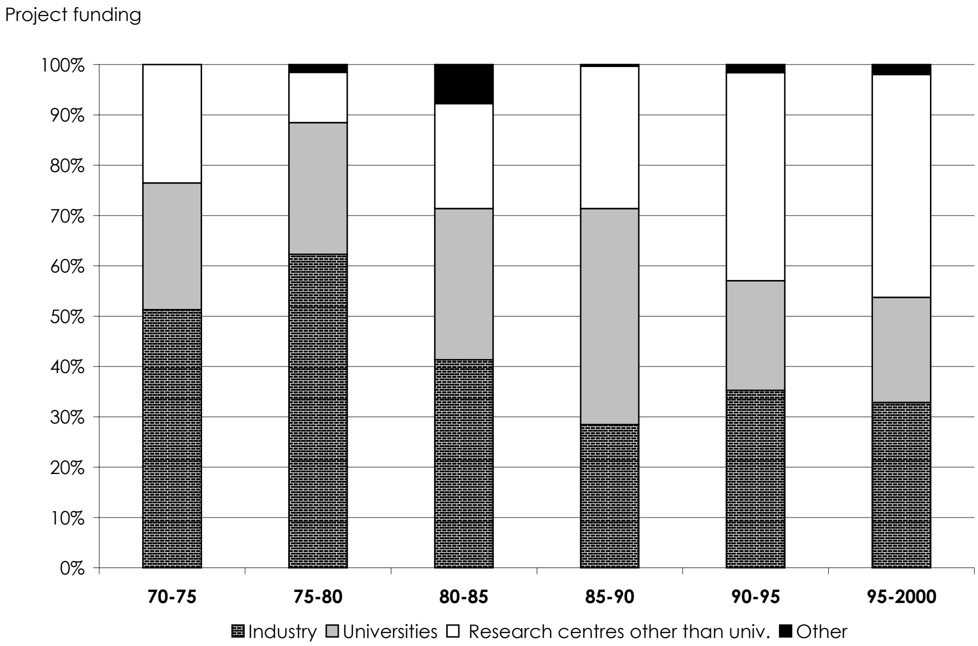

Figure 5 Direct project funding for biotechnology research for biotechnology related research in Germany[25]. 1970-2000.
Source: Public Promotion Catalogue of the BMBF

Regarding the policy goals, the public funding system has put special emphasis on collaborative research[26] and on the commercial application of scientific research results[27]. In the 1990s policy targeted the formation of scientific networks[28] and the establishment of regional innovation cluster.

Recent industry and policy reports identify Germany as the country with a strong growth rate in terms of patent and publication intensity in biotechnology related fields and the largest European biotechnology industry in terms of companies (Hinze et al. 2002). We do not know the extent to which the policy goals have been reached and the policy instruments have been effective. However, we can say that the government has played a major role in setting the adequate legal framework for the development of biotechnology, in supporting both, the rise of the German biotechnology industry and

---

25 This figure includes only the investments clasified as biotechnology activities by the German Federal Ministry of Research and Education and does not consider expenditures in medical, health and enviromentl research that may directly support biotechnology but not appear in the ministry's biotechnology statistics.

26 To allocate the funding the ministry supported only those public and industry research units organising their research projects as "linked" and "lead" projects (Verbund- und Leitprojekte). These projects had to be carried out by research consortia that included an industrial partner and, most importantly, expected research results of industrial interest. This instrument was explicitly directed to stimulate collaboration between industry and academia in biotechnology research.

27 Those research projects with a direct commercial application had funding priority.

28 In 1995 the German Human Genome Project was launched. This was a key initiative for the support of basic research on the human genome. In 2000 the initiative entered its second phase. Most of the funded projects have been allocated to national research centres (Helmholtz-Centres) and Max Planck Institutes in the form of "linked" projects. A resource centre was established to gather and co-ordinate the information and the scientific results of all the projects.

the scientific developments in the German biotechnology knowledge base in the last years of the 20th century.

4. Conclusions

As already put forward in the introduction the aim of the contribution is to identify some of the factors that ha had strong influence in the technology adoption of the actors in the German pharmaceutical industry.

The findings of historical overview of the industry and the study of the major industrial actors signals that the research traditions, the organizational structures, and the firm capabilities in terms of human capital strongly influenced the selection criteria of the pharmaceutical corporations for the production of raw materials. The influence of the leaders in shaping the innovation system tailored it according to the necessities of their innovation strategies determining the future developments.

The analysis of the technological trajectories reveals that while the leaders of the pharmaceutical sector were ignoring the application of biotechnology, the technology was being successfully used by more traditional pharmaceutical companies in the development and production processes of raw materials and in other sectors like, for instance in the production of food and beverages. Unexpected technological breakthroughs in other technological fields (the Haber-Bosch process) determined the development path of biotechnology.

Finally, the examples of policy action to attain self-sufficiency before the second World War and the support of biotechnology in the last decades of the 20th century disclose the fact that policy measures can very much influence technology trajectories and adoption. However, the unconditional and exclusive support of one technology to attain a policy goal that might appear advantageous at a certain point in time can undermine the development of alternative technologies in the future.

At this point, new research questions appear. On the one side it remains unclear the extent to which the innovation networks of the German dye-stuff manufactures were tailored to the application of the chemical synthesis with too “strong ties” to allow for the adoption of alternative technologies. Similarly, at the level of the innovation system, we can not make any assessment on the capability of the German institutional landscape (universities, financial institutions, innovation culture, etc.) to support the development of the scientific disciplines and technologies that, even though were not so attractive for the coal tar dyestuff industry, were crucial for the technological breakthroughs that occurred in history latter on.

The next steps of research shall focus on the collaboration patterns of the major pharmaceutical companies and their research activities with institutions conducting medical and non-medical research (universities, hospitals and other relevant research institutions).

5. References

Achilladelis, B. and Antonakis, N. 2001. "The dynamics of technological innovation: the case of the pharmaceutical industry." *Research Policy*, 30, pp. 535-88.

Arora, A., Landau, R., and Rosenberg, N. eds. 1998. *Chemicals and Long Term Economic Growth - Insights from the chemical industry*. New York: John Wiley and Sons.

Beer, J. J. 1959. *The emergence of the German Dye Industry*. Urbana: The University of Illinois Press.

Bull, A. T., Holt, G., and Lilly, M. 1982. "Biotechnology: International Trends and Perspectives." Organization for economic cooperation and development (OECD): Paris.

Drews, J. 1998. Die verspielte Zukunft - Wohin geht die Arzneimittelforschung? Basel, Boston, Berlin: Birkhaeuser Verlag.

Freeman, C. 1995. "Technological Revolutions: Historical Analogies," in *The Biotechnology Revolution?* M. Fransman, G. Junne and A. Roobeek eds. Oxford, Cambridge: Blackwell Publishers, pp. 7-24.

Grupp, H., Dominguez-Lacasa, I., and Friedrich-Nischio, M. 2002. *Das deutsche Innovationssystem seit der Reichsgruendung. Indikatoren einer nationalen Wissenschafts- und Technickgesichte in unterschiedlichen Regierungs- und Gebietstrukturen*. Heidelberg: Physica-Verlag.

Hinze, S., Reiss, T., Dominguez-Lacasa, I., and Stefan, W. 2001. "Einfluss der Biotechnologie auf das Innovationssystem der pharmazeutischen Industrie." Bericht an das Bundesministerium für Bildung und Forschung
Referat Z25.

Liebenau, J. 1988. "Ethical business: The formation of the pharmaceutical industry in Britain, Germany, and the United States before 1914." *Business history*, 30, pp. 115-30.

Marschall, L. 2000. *Im Schatten der chemischen Synthese - Industrielle Biotechnologie in Deutschlandd (1900-1970)*. Frankfurt/New York: Campus.

Mckelvey, M. 1996. *Evolutionary Innovations - The Business of Biotechnology*. Oxford: Oxford University Press.

Meyer-Thurow, G. 1982. "The industrialization of Invention:A case study from the German chemical industry." *ISIS*, 73:268, pp. 363-81.

Murmann, J. P. and Landau, R. 1998. "On the Making of Competitive Advantage: The Development of the Chemical Industries in Britain and Germany Since 1859," in *Chemicals and Long Term Economic Growth - Insights from the chemical industry*. A Arora, Ralph Landau and Nathan Rosenberg eds. New York: John Wiley and Sons, pp. 27-70.

Pisano, G. P. 1991. "The Governance of innovation: Vertical integration and collaborative arrangements in the biotechnology industry." *Research Policy*, 20.

Reiss, T. and Hinze, S. 2000. "Innovation Process and Techno-scientific Dynamics," in *Changing Innovation in the Pharmaceutical Industry*. Andre Jungmittag, Guido Reger and Thomas Reiss eds. Heidelberg, Berlin: Springer, pp. 53-69.

Saviotti, P. 1998. "Industrial structure and the dynamics of knowledge generation in Biotechnolgy," in *Biotechnology and Competitive Advantage*. Jacky Senker ed. Cheltenham, UK: Edward Elgar, pp. 19-43.

Sharp, M. 1995. "Applications of Biotechnology: an Overview," in *The Biotechnology Revolution?* M. Fransman, G. Junne and A. Roobeek eds. Oxford, Cambridge: Blackwell Publishers, pp. 7-24.

Wimmer, W. 1991. "Tradition und Transformation: Die Pharmazeutische Industrie in einem ständisch geprägten Markt." *Zeitschrift für Unternehmensgeschichte*, 36:3, pp. 179-203.