The Biotechnology Industry in Germany and Japan

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Abstract

Biotechnology is considered as one of the key high-technology sectors in the future. It has been increasingly accepted that small, innovative businesses were the major stimulus for the development of this emerging industry. Many studies on new entrepreneurial entrants in biotechnology are mainly addressed to the situation in the United States and neglected developments in other countries. Therefore, the present paper concentrates on two latecomers into the industry of biotechnology, namely Japan and Germany, and addresses the question how different institutional frameworks may have an impact on its emergence. More specifically, we investigate the role of venture capital, governmental initiatives, large companies, and entrepreneurship on the development and current situation of the biotechnology industry. The comparison of the biotechnology industry between two countries against the background of their different institutional settings provides some important insights for management scholars as well as policy makers.

Introduction

The rapidly emerging biotechnology industry is regarded as one of the key industries in the future[1]. The application fields of biotechnology are as diverse as health care, chemistry, material science, agriculture, and environmental protection. Advances in biotechnology are leading to improvements of health conditions, food quality as well as environmental issues. Because of unmet medical needs (cancer, AIDS, Alzheimer) and the high growth of population along with the scarcity of resources, the biotechnology industry will play a major role in ensuring continued worldwide prosperity in this millennium.

The starting shot of the modern biotechnology industry can be traced back to the discovery of Stanley Cohen and Herbert Boyer in 1973 who have shown the manipulation of DNA sequences. Since this groundbreaking discovery, the biotechnology industry has grown rapidly. There exists nearly 1,300 biotechnology companies in the United States, providing employment to approximately 150,000 people.

Today, most of these biotechnology firms are still relatively small, with approximately two-thirds employing fewer than 150 people. It has been increasingly accepted that these small, innovative businesses were the most important key driver for the emergence and development of the biotechnology industry (Casper, 2001; Robbins-Roth, 2000, Saviotti, 1998).

[1] More precisely, biotechnology is not an industry *per se* it is rather a set of technologies. However, in this paper we define the boundary to other industries by the entirety of organizations who use mainly biotechnologies for doing R&D and developing products.

Particularly in the health care sector, where patents for more and more blockbusters - i.e. drugs with more than US$ 500 Mio. annual sales - expire, pharmaceutical companies ("Big Pharma") are increasingly turning to biotechnological products. In order to fill up their product pipeline, pharmaceutical companies entered into alliances with specialized small biotechnology companies (Forrest, 1992).

The awareness of importance of this rapidly upcoming industry has been increasingly recognized by the academic management literature in the last few years. Of particular interest are small, innovative bioventures which are breaking new technological ground in the most advanced branches of the life sciences. Many studies on new entrepreneurial entrants in biotechnology are mainly addressed to the situation in the United States. However, there is little research on the emergence of bioventures in countries with a different institutional setting (see as one of the few exceptions : Acharya, 1999).

Certain elements such as the role of technology transfer between universities and industry as well as the existence of venture capital play an important part in the formation and establishment of these small businesses. Thus, it seems to be fruitful to investigate in more detail the emergence of the biotechnology industry in different countries against the background of their national settings. The present paper concentrates on two latecomers into the business of biotechnology namely Japan and Germany which both are highly industrialized countries.

In this article, we pursue two purposes: First, we provide a comprehensive picture of the evolution and the current developments of biotechnology in Japan and Germany. Second, we compare the influence of certain environmental factors on the emergence of the biotechnology industry in Germany and Japan.

In doing so, we develop an institutional framework for the emergence of the biotechnology industry in which certain environmental factors are integrated (see figure 1). More specifically, we investigate the role of venture capital, governmental initiatives, large companies, and entrepreneurship on the emergence of the biotechnology industry. This framework allows us to structure the complex industrial environment and to compare the influence of each factor on the development of the German and Japanese biotech industry.

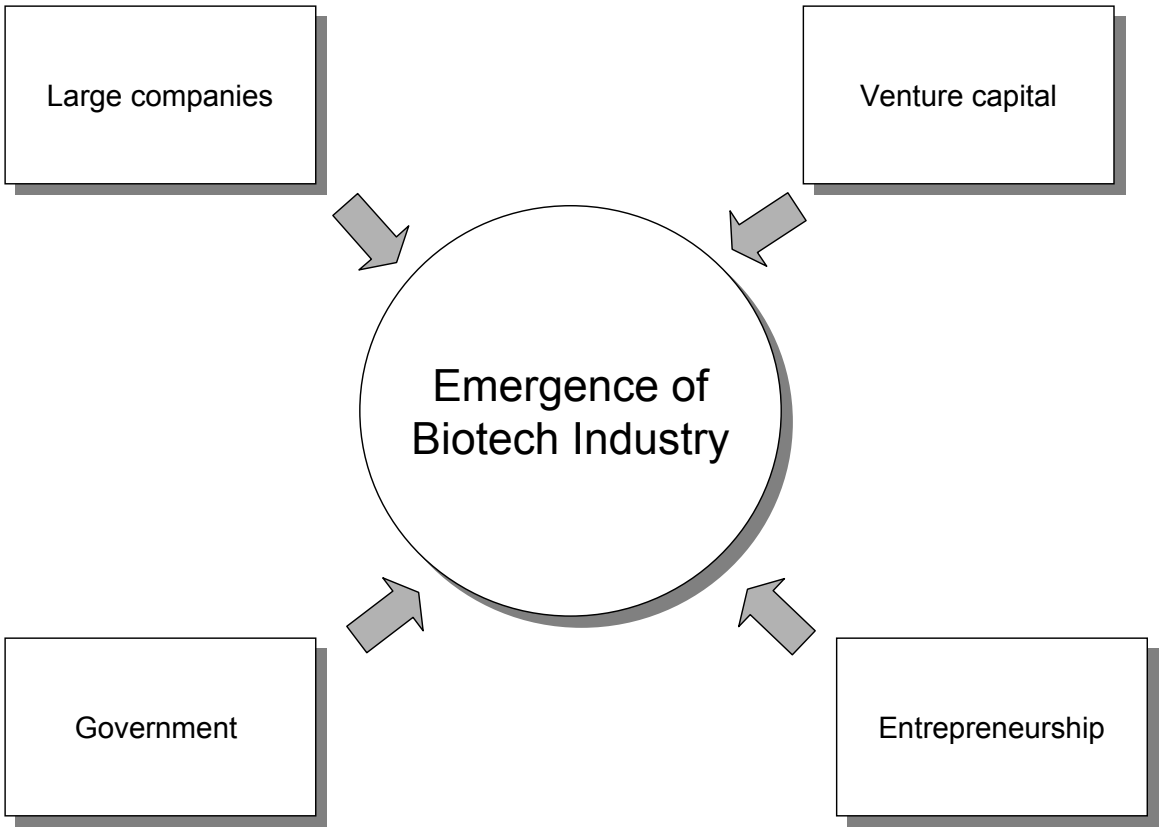

Figure 1: Institutional framework for the emergence of biotechnology.

To fully understand the impact of different institutional settings on the emergence of the biotechnology industry in Germany and Japan, it is necessary to begin with a brief overview of the historical developments as well as the current status of the biotechnology sector in both countries.

Overview of the evolution and development of biotechnology in Germany

According to the latest European Biotech report published by the consulting company Ernst & Young (Ernst & Young, 2001), Germany could take the lead in biotechnology in Europe in terms of number of companies. Using a very narrowly defined understanding of biotech companies[2], Germany has currently 333 biotech companies compared to 271 companies in the UK and 240 in France. Five years ago, there existed only a handful bioventures in Germany and there was no sign of change on the horizon at that time.

[2] Biotech companies "[...] are defined as companies that use modern biological techniques to develop products or services to serve the needs of human health-care, agricultural productivity, food processing, renewable resources or environmental affairs. Medical device, seed companies, and large pharmaceutical companies ("Big Pharma") are excluded [...]."

Basically, strong negative public attitude towards biotechnology and especially genetic engineering, which prompted politicians from the federal as well as the local governments to establish strict regulations for biotechnology-related research, characterized the situation in the early 90s.

The role of large companies

Because of this hostile environment large pharmaceutical companies like Bayer, Hoechst (now Aventis) and BASF set up research sites in the United States in order to obtain a „window on technology“ in biotechnology. Furthermore, they established cooperation with leading research institutions (e.g. Hoechst with Massachusetts General Hospital) and with dedicated biotechnology firms (e.g. Bayer with Genentech) in the United States. Although Germany has a world-class research base in the life sciences, e.g. the well-known Max-Planck-Institutes, there was a missing link between basic research mainly carried out at universities or at other research institutions and applied sciences in large pharmaceutical and chemical companies.

All in all, one can say that a biotechnology sector with small bioventures similar to the United States did not exist in Germany in the middle of the 90s. How could this bio-boom then arise within only a few years?

In short, key drivers for the evolution of the biotechnology industry in Germany were the introduction of several governmental support policies, emergence of venture capital, the launch of a stock market for high-technology companies, cultivation of an entrepreneurial spirit along with the situation at the labor market. In the following we discuss these key drivers in more detail.

Initiatives of German Government

After reunification in 1989, the German economy has run into a time of stagnation. One result has been the high unemployment rate in Germany, especially in the region of the former East Germany. In the middle of the 90s the German government recognized that in order to sustain the standard of living new entrepreneurial business models have to be introduced. Therefore, governmental support policies changed to foster entrepreneurial business models in high-technology sectors such as information technology and biotechnology.

One lesson learned from the successful development of biotechnology companies in the United States was the establishment of clusters, namely in Boston, North Carolina, San Diego and in the so-called Bay Area around San Francisco. These clusters consists of a network of venture capitalists, patent attorneys, specialized consultants, politicians, researchers from universities as well as from pharmaceutical companies (see figure 2).

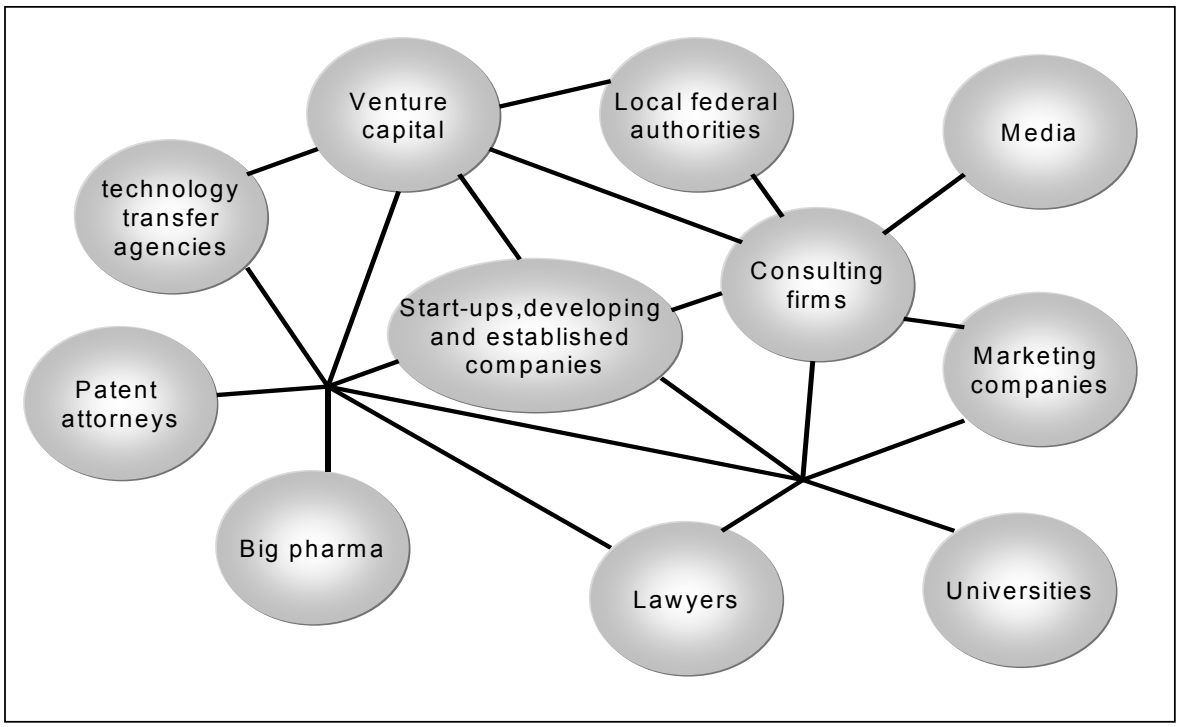

Figure 2: Clusters of innovation in biotechnology.

Knowing the importance of these networks, the German Federal Ministry for Education and Research (BMBF) launched the supra-regional BioRegio competition in 1995. The main objective of this competition between 17 regions in Germany has been the commercialization of biotechnological research from universities and other research institutes. Therefore, the different regions were encouraged to submit proposals in which integrated concepts for biotechnology research and implementing its results commercially were worked out. More specifically, the proposals pinpointed the strategic core competences of each region and how the network of research institutions, incumbent companies, public administration and service organizations fosters entrepreneurship. In doing so, young scientists and researchers at universities as well as other research institutions worked closely together with regular authorities, technology transfer agencies and executives from pharmaceutical and chemical companies. Each region established a coordination center which was (and still is) in charge of linking together all activities strategically.

Out of these 17 participating regions, three winners were selected by an international jury of experts in biotechnology. The decision was based on the following criteria (BMBF, 1995):

- Nature, number, profile and potential of biotechnology-orientated research institutes, colleges and technical colleges in the region.
- Quality, scope and extent of existing interdisciplinary interlinking of biological research.
- Existing industrial companies and available services (Patent offices, data networks, advice from a duly organized service on making application to authorities and banks).
- Making use of available scientific know-how and regional research resources in the field of modern biotechnology in order to develop and market new products, production processes and services (laboratories, patents etc.).
- Measures already taken to help settle or to start up new biotechnologically-orientated companies.
- Willingness of banks and private investors to finance regional biotechnology companies.
- Co-operation of research institutions and hospitals in the region.
- Practical approval for bioengineering plants and emission tests in the region.

The most convincing and matured concepts for commercializing biotechnological research were: BioRegio Munich, BioRegio Rhineland (with its center Cologne) and BioRegio Rhine-Neckar Triangle (with its center Heidelberg).

Since 1997 and for a period of 5 years, the selected model regions will receive an additional total of 150 Mio. DM out of the national biotechnology program. A special vote was given for the BioRegio Jena in East Germany which has been acknowledged for its specific core competence in bio-instruments. However, the other 13 defeated region pursued also their concepts by raising funds from state government and other sources. For instance, the losing region Berlin is now one of the hot spots for commercialized biotechnology in Germany. To put it in a word, just the concerted interaction among people from universities, industry and public administration induced by the competition led to a bio-boom in the regions (see figure 3).

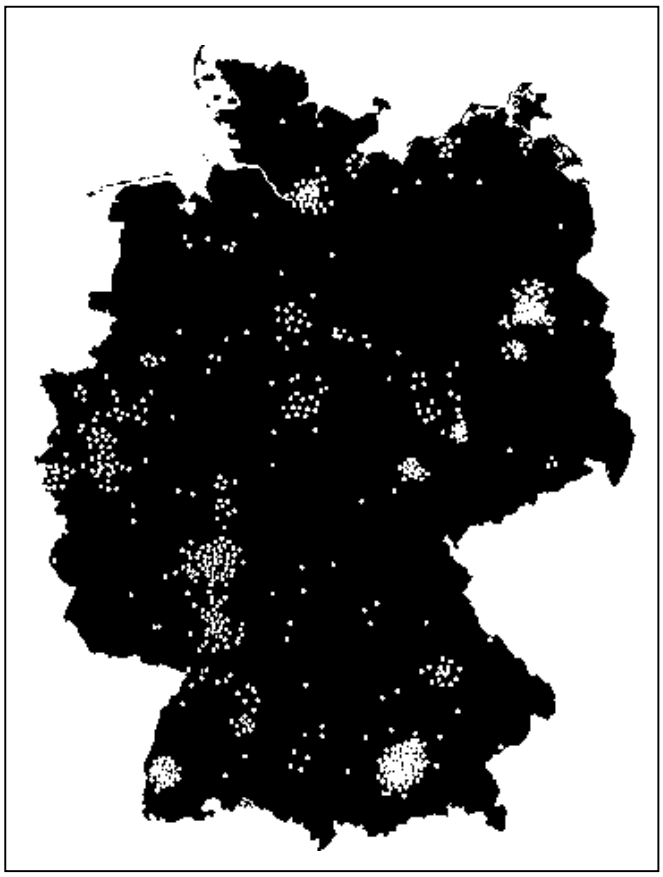

Figure 3: Distribution of biotechnology companies (one dot could represent one or more companies) according to Ernst & Young (Ernst & Young, 2000)

Besides the BioRegio competition, several other initiatives are sponsored mainly by the Federal Ministry for Education and Research in order to support young scientists ("BioFuture"), to fund pre-competitive research of young biotech companies ("BioChance") and to foster certain regions in specific fields of biotechnology, e.g. bioinformatics ("BioProfile").

Emergence of venture capital in Germany and the launch of the "Neuer Markt"

Biotechnology has a high level of complexity and uncertainty. According to the Tufts Center for the Study of Drug Development the process of developing a drug takes on average 15 years from basic research to market introduction (DiMasi, 1995). During this time, up to US$ 500 Mio. (Boston Consulting Group, 1999) have to be invested. Moreover, it can be statistically shown that 5 out of 5000 drug candidates go from the research to the clinical stage, and out of these 5 only one reaches market introduction (Pharmaceutical Research and Manufacturers of America, 2000).

These industry-specific figures make it clear that investments in biotechnology have a risky and rather long-term character. Therefore, the traditional German investment system - credit financing by house

banks – was inappropriate for bioventures. Fortunately, national as well as international venture capitalists became increasingly aware of the growth potential of the biotechnology industry.

Investments in high-technology sectors were facilitated through generous co-financing options available through the German government-owned banks "Technologie-beteiligungsgesellschaft" (TBG - subsidiary of "Deutsche Ausgleichsbank" who finances medium-sized companies) and the "Kreditanstalt für Wiederaufbau" (KfW). In 2000, the TBG invested about Euro 504,9 Mio. in high-technology start-ups and 24% thereof in biotechnology. There are certain requirements for receiving TBG funding, e.g. the company must not have more than 50 employees, must have less than Euro 5 million on its balance sheet and must have a large company ownership less than 25%.

In addition to loan funding, research grants are available from the Federal Ministry of Education and Research (BMBF) of up to 50% of the cost of a research project. Beyond that, some states ("Länder") provide additional loans and research grants so that financing models depend largely on the location of the company.

Because of these manifold variety of sources for "soft money", venture capitals were willing to invest in new businesses in high-technology sectors such as biotechnology and information technology. At present there exists more than 200 venture capital firms and approximately 60 of them invest partly or exclusively in biotechnology. According to Schitag, Ernst & Young more money was invested in European biotech companies by venture capitalists in 2000 than the previous 5 years put together (Ernst & Young, 2001). In addition, some pharmaceutical and chemical companies (Aventis, Bayer, Henkel) set up corporate venture capital providing exclusively financing options for bioventures. The largest single investments in German bioventure have been Metagen from Berlin (spin-out of the pharmaceutical company Schering AG) with Euro 55 Mio., Ingenium from Munich with Euro 46 Mio. and Morphochem from Munich with Euro 40 Mio. raised all in the year 2000.

However, venture capitalists need to have a clear exit strategy for their investments. The most attractive exit strategy is by far an Initial Public Offering (IPO) at the stock exchange. The launch of the stock market for young high-tech and high-risky companies "Neuer Markt" in 1997 was clearly a cornerstone in the development of the German biotechnology industry. After being accepted by the financial community "Neuer Markt" quickly became the dominant financing option for (venture-backed) Biotech companies. Similar to the NASDAQ stock market in New York it has implement stringent disclosure standards. "Neuer Markt" companies, for example, have always to file quarterly and publish annual reports. Moreover, the issue must place at least 20 percent of shareholders' equity. These conditions are designed to secure a minimum liquidity. By far the largest biotech IPO in 2000

was the going public of Lion Bioscience located in Heidelberg (BioRegio Rhine-Neckar Triangle) with Euro 228 Mio. and a valuation of Euro 774 Mio. at IPO.

To sum up, matching „soft money“ by governmental research grants and loans (public venture capital) with “smart money” by venture capitalists together with an exchange market for high-tech companies created an environment conducive for entrepreneurial activities. However, implementing a supportive infrastructure is just one prerequisite, existence of scientists willing to take the risk to set up a new venture is the other.

Cultivation of an entrepreneurial spirit

Starting from the scratch small high-tech companies and entrepreneurship became *en vogue* in Germany. Mainly, the high levels of unemployment have triggered a strong inducement for considering other job opportunities. Particularly, large pharmaceutical and chemical companies downsized staff so that graduated students of Chemistry or Biology had to look for other career options. Besides, the bureaucracy in large incorporations created some dissatisfaction among senior managers and researchers resulting in an increasing interest in alternative employment options at small bioventures.

One innovative approach to cultivate entrepreneurship has been the introduction of business plan competitions in Germany. In cooperation with some consulting (e.g. McKinsey and Ernst & Young) and venture capital companies (e.g. 3i) as well as large incorporations (e.g. Aventis) these competitions are intended to encourage young scientists for commercializing their ideas. For this reason workshops and seminars provide participants with the essential knowledge on how to develop a sound business plan. To further support the underlying idea, some universities established professorships for entrepreneurship[3].

All these developments flanked with increased Media coverage on entrepreneurship moved more and more young researchers as well as senior managers from pharmaceutical companies to set up their own business. Since they encountered a receptive environment for entrepreneurship, biotechnology companies mushroomed throughout Germany.

Current situation of the biotechnology sector in Germany

Although the swift increase of number of biotech companies in Germany is impressive, the German biotech industry is still in its infancy. This immaturity of the biotechnology sector in Germany

compared to the United States as well as to its European counterpart United Kingdom can be clearly exemplified by the following indicators:

- only approximately 5% of the biotech companies in Germany generate more than Euro 50 Mio. annual sales.
- In 2000, there were in total 6 drug candidates in the pipeline (preclinical to clinical phase III) from publicly-traded German biotech companies compared to 128 of British companies.
- 17 German biotech companies were listed on the "Neuer Markt" in 2000 compared to over 400 at the NASDAQ.

Basically, this backlog can be explained by the youth of the German biotechnology industry. However, globalization, skyrocketing costs of research and development, fragmented and demanding markets, accelerating technological advancements and high competitiveness do not allow time for a little by little company growth.

Therefore, bioventures have to develop quickly a critical mass. Some German biotech companies have recognized that integration of activities along the value chain is crucial for sustainable growth. As more and more pharmaceutical companies outsource certain parts of their research and development efforts, specialized (biotech) companies have to offer a set of integrated platform technologies (one-stop-shopping). Responding to these challenges, German companies acquired other European (Evotec`s (located in Hamburg) acquisition of Oxford Asymmetry International, UK) and in particular US-American biotech companies (e.g. GPC Biotech (Munich) acquired Mitotix, USA; Lion Bioscience (Heidelberg) acquired Trega Bioscience and Medigene (Munich) acquired NeuroVir Therapeutics).

In contrast to the situation in the US and the UK, platform technology-based companies are the prevailing business models in the German biotechnology industry. These business models have compared to product-based ones the advantage of being less risky since the so-called enabling technologies can be used for a wide range of applications. However, technological advances can make one company`s enabling technology obsolete. Thus, platform technology-based companies have to invest huge amount of money into research in order to be on the cutting edge of technology.

Although investments in product-based companies are more risky, they promise higher returns in the long run. Thus, an increasing number of investors prefer these business models in the hope to have an equity stake in a company with potential blockbusters in its R&D pipeline. Therefore, some German biotech companies will be under pressure to change their business models in the future.

[3] As of July 2001, at 25 German universities chairs for entrepreneurship have been established or will be

Recently, company growth is hampered in Germany by the lack of specialists in bioinformatics as well as experienced senior managers for business development assignments. Some universities push bioinformatics in their curriculums and sponsor chairs for bioinformatics, however, because of the rather long-term character it does not avoid the shortage of skilled employees in the short-term.

Although public opinion changed favorably towards biotechnology in the health care sector, it is still ambivalent as one can see in the highly controversial debate about research on embryonic stem cells. Furthermore, any application of biotechnology and precisely genetic engineering in agriculture is dismissed categorically.

To sum up, the German biotechnology industry has prospered well in the last few years but now in the next phase of its life cycle it faces some severe challenges. Only the future can tell us whether this model of the emerging German biotechnology industry, induced and subsidized by the German as well as local governments, will be a success story in the long run.

Overview of the evolution and development of biotechnology in Japan

The commercialization of biotechnology in Japan has undertaken a roller-coaster ride within its short history. In the early 1980s, many Japanese companies recognized the potential of modern biotechnology. In contrast to the developments in the United States, these companies were already established companies or part of an industrial group (Keiretsu). Interestingly, not only traditional pharmaceutical, chemical and food processing companies stepped into the modern biotechnology but also many companies with totally unrelated core businesses such as steel manufacturers and even construction companies. Because of the oil crisis and diminishing profits in their core businesses, these companies conceived biotechnology as an opportunity to diversify their business.

In the 1990s, however, the biotechnology upswing ended. Several Japanese large corporations stopped or reduced their research efforts in biotechnology, since they doubted on the commercial possibilities of modern biotechnology. Therefore, only food and beverage enterprises, pharmaceutical and chemical companies invested significantly in the modern biotechnology in Japan during the 90s.

Since biotechnology has so far its greatest impact on the health-care industry, we investigate in more detail the activities of the Japanese pharmaceutical industry in the following.

The role of large companies

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established in the near future.

Although Japan is the second largest market for pharmaceuticals in the world as a single country (see also figure 4), there are no Japanese pharmaceutical companies under the top ten worldwide in terms of sales. The largest pharmaceutical company from Japan, Takeda Chemical Industries, ranks only 14th globally.

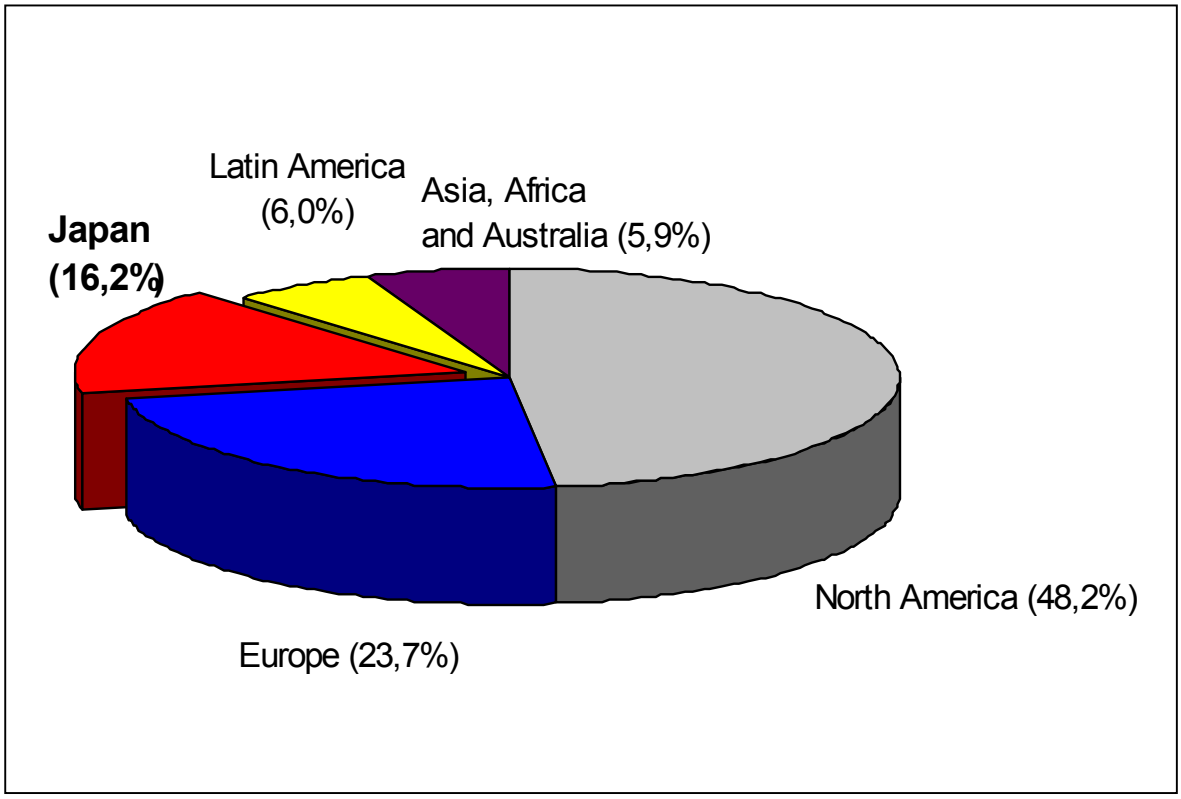

Figure 4: Breakdown of the global pharmaceutical market in 2000 according to IMS-Health.

Clearly, one reason is the lack of basic research conducted in Japanese pharmaceutical companies, this is particularly evident in the field of biotechnology. Most pharmaceutical companies have previously neglected the importance of biotechnology for research and development on drugs. Their strategy was mainly focused on me-too products such as generics for which efficient low-cost manufacturing was put in place.

Some major pharmaceutical companies have started to reorganize their efforts in biotechnology and have put greater emphasis on research activities because of the shrinking markets for generics which benefit innovative drugs. Thus, in order to obtain a window on innovative technologies, which will eventually result in new products, large pharmaceutical companies looked overseas for new opportunities.

Recently, many Japanese pharmaceutical companies entered into different types of cooperation such as research contracts, joint ventures or licensing agreements with leading American universities or

specialized small-and-medium-sized biotech companies. As shown in figure 5, all leading Japanese pharmaceutical companies have established several cooperation with foreign universities or biotech companies in early R&D stages. In addition, research centers and subsidiaries were established abroad to monitor recent developments in leading biotechnology clusters as well as to facilitate collaborations with researchers.

Company	Partner	Date	Type of cooperation
Takeda Co.	Celera Genomics (USA)	2000	licensing
	Affymetrix (USA)	1999	licensing
	Interneuron (USA)	1999	licensing
	Human Genome Sciences (USA)	1995	licensing
Eisai	Incyte Genomics (USA)	2001	licensing
	Neurogenetics (USA)	2001	research agreement
Fujisawa	University of Edinburgh (UK)	2001	R&D-cooperation
	CV Therapeutics (USA)	2000	R&D-cooperation
	Arena Pharmaceuticals (USA)	2000	R&D-cooperation
	Discovery Therapeutics (USA)	1999	licensing
	Gene Logic (USA)	1999	licensing
	Protein Design Labs (USA)	1999	R&D-cooperation
Chugai Pharmaceuticals	Immusol	2001	R&D-cooperation
	Protein Design Labs (USA)	2000	licensing
Sankyo Pharmaceutical	Gene Logic (USA)	2001	licensing
	Genetic Institutes (USA)	1999	R&D-cooperation
	Affymetrix (USA)	1999	licensing
	Metabasis Therapeutics (USA)	1997	R&D-cooperation
	ArQule (USA)	1997	R&D-cooperation

Figure 5: Selection of recent cooperative activities of major Japanese pharmaceutical companies.

Furthermore, this trend for internationalization has been facilitated by the loosing of the highly protected domestic market e.g. due to the harmonization of regulation standards of clinic tests for drugs in accordance to the International Converence on Harmonization (ICH). This in turn resulted in increased competition on the domestic market for drugs, which was enforced by declining drug prices, so that Japanese pharmaceutical manufacturers had to look overseas for new markets for their products. However, as Jungmittag et al. (1999) has shown, the degree of internationalization of Japanese pharmaceutical companies is compared to their US-American and particularly European counterparts still low.

While several large pharmaceutical companies entered into licensing agreements with US-American biotechnology companies, some other large Japanese companies spin off their biotechnology activities.

In 1999, Hitachi has set up a Life Sciences Group devoted to promote commercialization of biotechnology. Hitachi`s center for genome analysis is located in Kawagoe, Saitama prefecture, and is

well-equipped with analyzer and information systems. In addition, companies such as the brewery Takara Shuzo Co. and precision instrument manufacturer Shimadzu Corp. are investing in this area.

These spin-off activities are not solely limited to large companies since medium-sized enterprises are also interested in new business opportunities based on biotechnology. As an example, in 1997 NIDEK Corp., a medical device company with 1241 employees and an annual sales of 42.3 Billion Yen, in cooperation with the ceramics company INAX Co., the chemical company Toyama Chemical, Co., and the Tokai Bank Group established the biotechnology company J-TEC. This new company, which is located in Gamagori (Aichi prefecture), focuses on tissue engineering and received 8.91 Mio. US$ from the Japanese Government for the next 5 years plus further project-based research grants totalling 17 Mio. US$.

Initiatives of Japanese Government

After the burst of the so-called "bubble economy" in Japan it was eventually clear that this old system has to be changed in order to sustain competitive in the global and ever-changing economy. Similar to Germany, Japanese government has acknowledged the dynamism of small entrepreneurial businesses in high-technology sectors.

It is hoped that the promotion of these small business will be the basis for technological innovation which finally ends in increased employment. Small businesses can react more quickly and flexible to changes in their environment. They adopt their business models to changing customer needs or technological advances which is especially important in biotechnology.

There exists several supporting programs for entrepreneurial activities providing no-interest loans and grants for individuals who want to start their own businesses. Besides, starting a new business is facilitated by loosing governmental approval. It is hoped that these initiatives promote new business development and thus revitalize the economy sustainable.

Particularly, the Japanese government considers biotechnology as one of the fifteen key sectors for future industrial development under its Action Plan for Economic Structural Reform. However, the biotechnology industry in Japan lags several years behind other countries such as the United States and the UK so that much of the innovative technology has been imported from abroad. One reason for this is the low level of basic research in biotechnology in Japan. Therefore, government has recently promoted basic research carried out in public laboratories. As seen in figure 6, total funding on Life Sciences has increased steadily in the last few years.

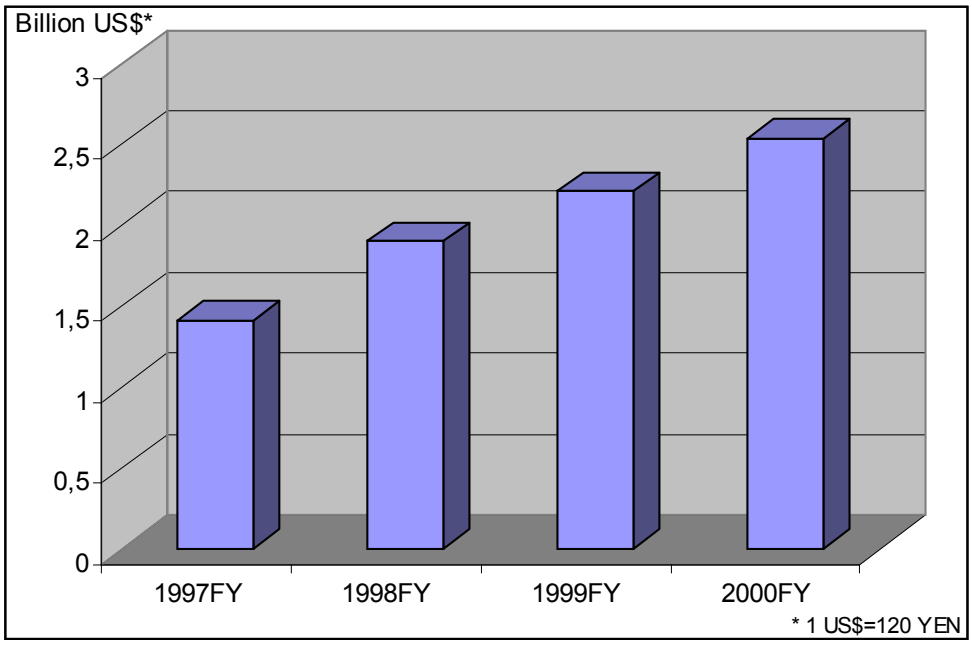

Figure 6 : Japan`s Government Life Science Budget (Source: Japan Bioindustry Association).

One important Government project in biotechnology is the so-called "Millennium Project" which was introduced in December 1999 . The total budget in the fiscal year 2001 is intended to be approximately 93.3 billion yen compared to 64.1 billion yen in 2000 (+49% growth) as shown in figure 7.

project name	**2000 FY (in billion yen)**	**2001 FY (in billion yen)**
Analysis on Human Genome - Post-Genome-sequence - Analysis on Genome Sequence	33.8	60.6 (28.1) (32.3)
Tissue Engineering	10.8	13.1
Analysis on Rice Genome	5.6	7.3
Assurance of safety in biotechnology	0.4	0.6
others	13.5	13.7
total	**64.1**	**95.3**

Figure 7: Japan`s "Millennium Project" Budget for promoting biotechnology.

However, the success of Japan's biotechnology sector will strongly depend on the degree to which basic research can be transferred to the private sector for commercial development. The Japanese Government has, therefore, promoted the technology transfer from research institutions and universities to the industry.

In August, 1998, Technology Licensing Organizations (TLO) were established by the Ministry of Education, Science, Sport and Culture (MEXT, formerly Monbusho and STA) to encourage the

patenting of university research and to facilitate technology and knowledge transfer between universities and the industry. Particularly, Government research and development funds are also now being channeled to small businesses by these organizations.

Technology Licensing Organizations play a bridging function between academia and industry in order to promote the development of small and medium-sized high-tech enterprises (see figure 8).

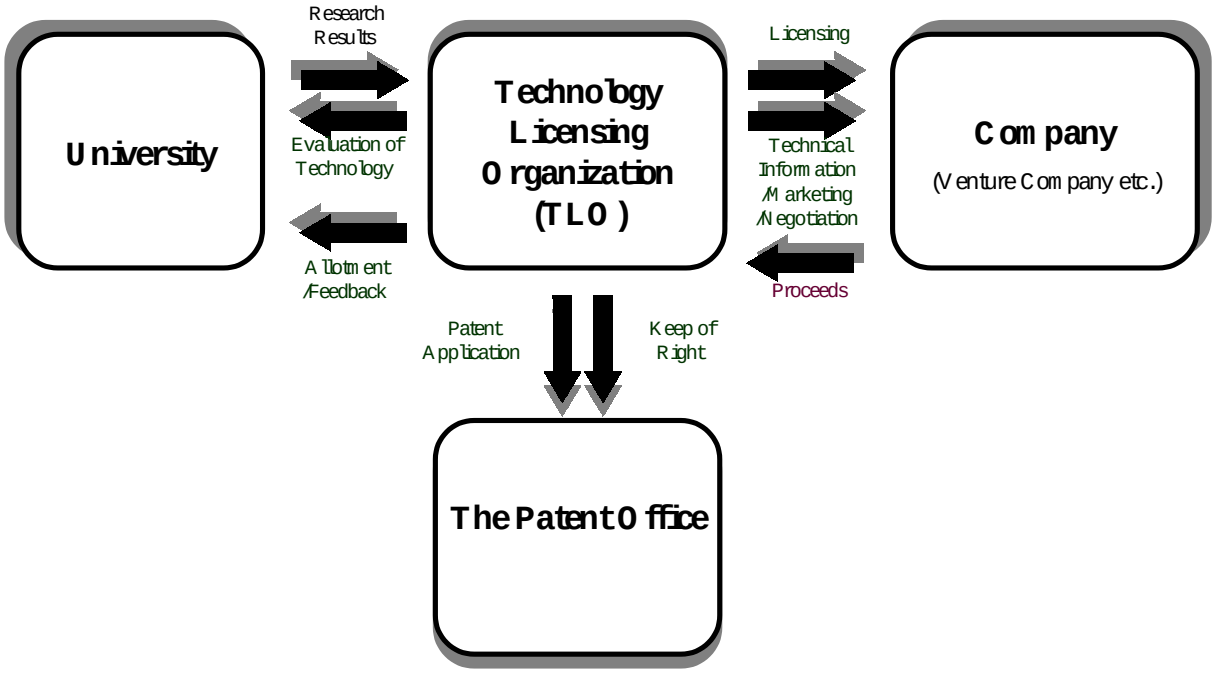

Figure 8: Technology Licensing Organizations in Japan extracted from "Industry-University Collaborative Research Now", The Ministry of Education, Science, Sports, and Culture.

Basically, Technology Licensing Organizations, which have to be authorized by the Ministry of Economy Trade and Industry (METI) (formerly known as MITI) based on the law of promoting technology transfer from universities to industry, offer the following support:

- Offering consulting services and dispatching consultants to small and medium sized enterprises.
- Supporting technology transfer through patent attorneys.
- Hosting educational seminars by experts of high-tech fields to enhance technical capabilities and to promote developments in new fields.
- Support information exchange and networking to promote joint research and development projects by government, business, and academic institutions.
- Presenting information via the Internet.
- Supporting study groups and meetings for technical experts.

● Providing office and lab space as well as parking spaces.

Depending on the size and age of each TLO, all or some part of these activities are offered to match research carried out by universities and research institutes with the technical needs of business. Until August 2001, 21 Technology Licensing Organizations were authorized by METI (see figure 9). Many of these organizations have their main focus in biotechnology. In the first three years 740 patent applications were filed in Japan and 93 were filed abroad which is a first success since the number of filed patents was about 100 per year before 1998.

University	Technology Licensing Organization (TLO)	established
National:		
Hokkaido Univ. etc	Hokkaido Technology Licensing Organization, Co., Ltd.	12/99
Tohoku Univ. etc	Tohoku Techno Arch Co., Ltd.	11/98
Univ. Tsukuba	Institute of Tsukuba Liaison Co., Ltd.	04/99
Univ. Tokyo	Center for Advanced Science and Technology Incubation, Ltd. (CASTI)	08/98
Tokyo Inst. Tech	The Circle for Promotion of Science and Engineering	09/99
Yamanashi Univ. etc.	Yamanashi Technology Licensing Organization, Co., Ltd.	08/00
Nagoya Univ. etc.	Nagoya Industrial Science Research Institute (CHUBU)	04/00
Kobe Univ. etc	New Industry Research Organization (NIRO)	03/00
Yamaguchi Univ.	Yamaguchi Technology Licensing Organization, Ltd.	11/99
Kyushu Univ.	University and Industrial Partnership (UIP)	01/00
University of Tokushima etc.	Techno Network Shikoku	02/01
Yokohama National University etc.	Yokohama TLO	12/00
Kyushu Inst. Tech.	Kitakyushu Techno Center Co., Ltd.	04/00
Private:		
Keio Univ.	Keio Intellectual Property Center	11/98
Tokyo Denki Univ.	Center for Research Collaboration	04/00
Nihon Univ.	Nihon University Business Incubation Center (NUBIC)	11/98
Kokugakuin University etc.	TAMA-TLO (Technology Advanced Metropolitan Area)	07/00
Meiji University	Meiji University Intellectual Property Center	10/00
Waseda Univ.	Waseda Univ. Technology Licensing Organization	04/00
Other:		
Universities in Kansai	Kansai Technology Licensing Organization Co., Ltd.	12/98
National Institute of Advanced Industrial and Technology	AIST Innovations	04/01

Figure 9: Technology Licensing Organizations in Japan authorized by METI.

As an example, Chubu Technology Licensing Office in Nagoya were established in April 2000 and has currently 6 directors plus several part-time employees. In this organization, 17 universities and research institutions in the surrounding area of Nagoya joined forces in order to promote technology transfer to the industry. Currently, 29 large companies and 21 small-and medium-sized enterprises are members of this TLO which have to pay admission fees between 1 Mio. Yen (large companies) and 25,000 Yen (SMEs) per year. It ranks 3rd of all technology licensing organizations in Japan in terms of

number of faculty members from medical schools. All directors have long-year experiences in the industry (Nippon Steel, Toyota Automotive, Denso), as attorneys or professors. Besides the admission fees of its members, the organization receives Government support of 9 Mio. Yen over the next 5 years to cover the operating costs. The three main activities of the Chubu TLO are to foster technology transfer in cooperation with specialized patent attorneys (particularly in the field of biotechnology), consulting services as well as information providing. So far, further activities such as equity investments in start-ups or support for the developing of business plans are not offered directly by this TLO.

The role of venture capital and the stock market for biotechnology companies

Since doing business in biotechnology has a risky and rather long-term character, venture capital is basically the main financing source for young bioventures. Until recently, venture capital was nearly absent in Japan. However, more and more venture capital funds has been raised in the last few years and some of them invest solely in biotechnology companies (see figure 10).

Besides, there are few analysts in these venture capital companies who possess the skills to evaluate the potential of a biotech start-up during the due diligence process. Therefore, the main part of venture capital has been invested into other sectors such as information and telecommunication technologies.

name	establishment	size of fund	focus
Soft Bank Life Science Ventures I,L.P.	decided	14 Billion Yen	Worldwide
Biotech Healthcare Venture Fund	01/2001	3 Billion Yen	Japan
JAIC Bio No. 1 Investment Fund	11/2000	2 Billion Yen	Japan
Bio Frontier Global Venture Fund	03/2000	5.5 Billion Yen	Japan/Overseas
Life Science Venture Fund	02/2000	3.5 Billion Yen	Overseas
CSK-VC Bio incubation Venture Fund	06/1999	2 Billion Yen	Overseas

Figure 10: Japanese investment funds devoted to Life Sciences companies (according to Ministry of Economy, Trade and Industry).

Basically, emergence of venture capital for high-technology companies is strongly connected with the existence of a stock market which serve as an attractive exit strategy for these risky investments.

In cooperation with the software company Softbank the National Association of Securities Dealers (NASD) of the United States formed in 2000 NASDAQ Japan as a stock market for young high-growth companies similar to NASDAQ in the US and the “Neuer Markt” in Germany. This 50-50 joint venture allows young companies without a proven track record on profitability to raise capital for their development and expansion plans. Set up half a year before NASDAQ Japan, Tokyo Stock Exchange established its counterpart for this market segment called Mothers. Providing venture capitalists an attractive exit strategy through an IPO, these stock markets are intended to foster

entrepreneurial activity in the high-technology sector. Furthermore, they should facilitate foreign investment companies to invest directly into Japanese companies. As of July 2001, in total 52 companies are listed on NASDAQ Japan compared to 33 traded at Tokyo Stock Exchange's Mothers market. However, NASDAQ Japan also has not yet met its expectations due to internal (teething) problems as well as the worldwide downturn at capital markets. Only two biotech companies have made their IPOs until August 2001. Intec Web & Genome Informatics Corp., Tokyo, develops systems for analyzing human genes, became the first bio-related startup firm to list on the Tokyo Stock Exchange`s market segment Mothers in December 2000. The second company related to biotechnology is Precision System Science Corp. (PSS), Tokyo, which specializes in DNA extraction devices.

The role of entrepreneurship

The educational system in Japan prepared mainly for a lifetime employment at larger corporations which offer secured jobs and provide prestige for the workers. Thus, working for a larger company until retirement is the first choice for the brightest graduates. This is one reason for the lack of entrepreneurship in Japan.

Furthermore, any entrepreneurship at public universities and research institutions were stifled by strict regulations for active participation of professors in private companies. This system discouraged university professors to support the creation of new ventures. However, several of these formal barriers have been removed by the Japanese government.

Current situation of the biotechnology sector in Japan

Recently, we can witness the establishment of several new biotechnology companies in Japan. According to the Japan Bioindustry Association (JBA), there exists currently 247 companies in biotechnology[4] and main of these were founded in the last two years as shown in figure 11.

[4] Note that the definition of biotechnology related companies differ significantly with the Ernst & Young term of Entrepreneurial Life-Sciences Companies. The Japan Bioindustry Association defines biotechnology companies as companies which conduct research in biotechnology (modern as well as old biotechnology) and which were established after 1980.

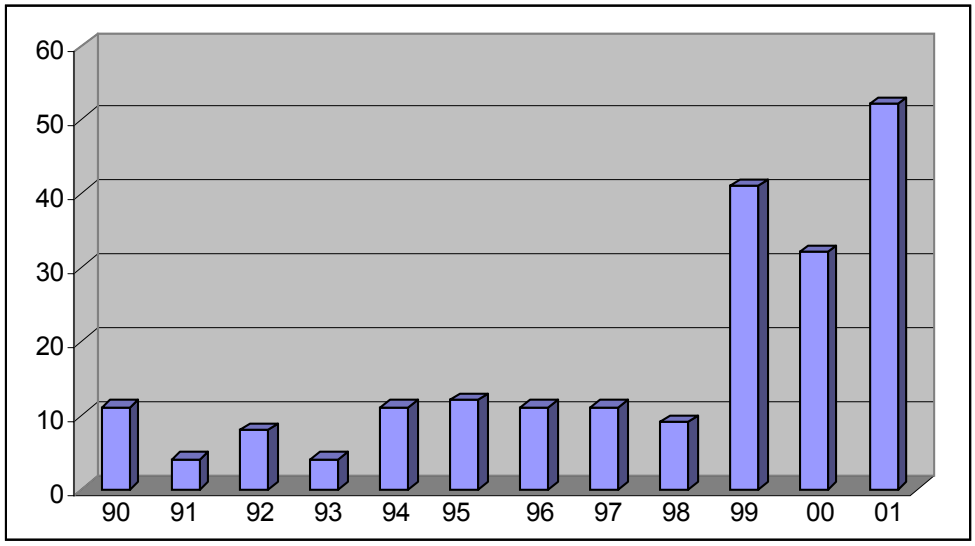

Figure 11: *Number of New Start-up companies in Japan from 1990 to 2001 according to Japan Bioindustry Association.*

One third of the biotechnology companies was approximately established by university researchers, one third represents spin-offs of large and medium-sized enterprises and the remaining were established by others (Japan Bioindustry Association).

These companies focus on different fields of biotechnology (figure 12). Two promising fields of biotechnology are bioinformatics and biochips in which 20 (e.g. Yokogawa Analytical Inc.) and 10 (e.g. PharmaDesign) Japanese bioventures are involved.

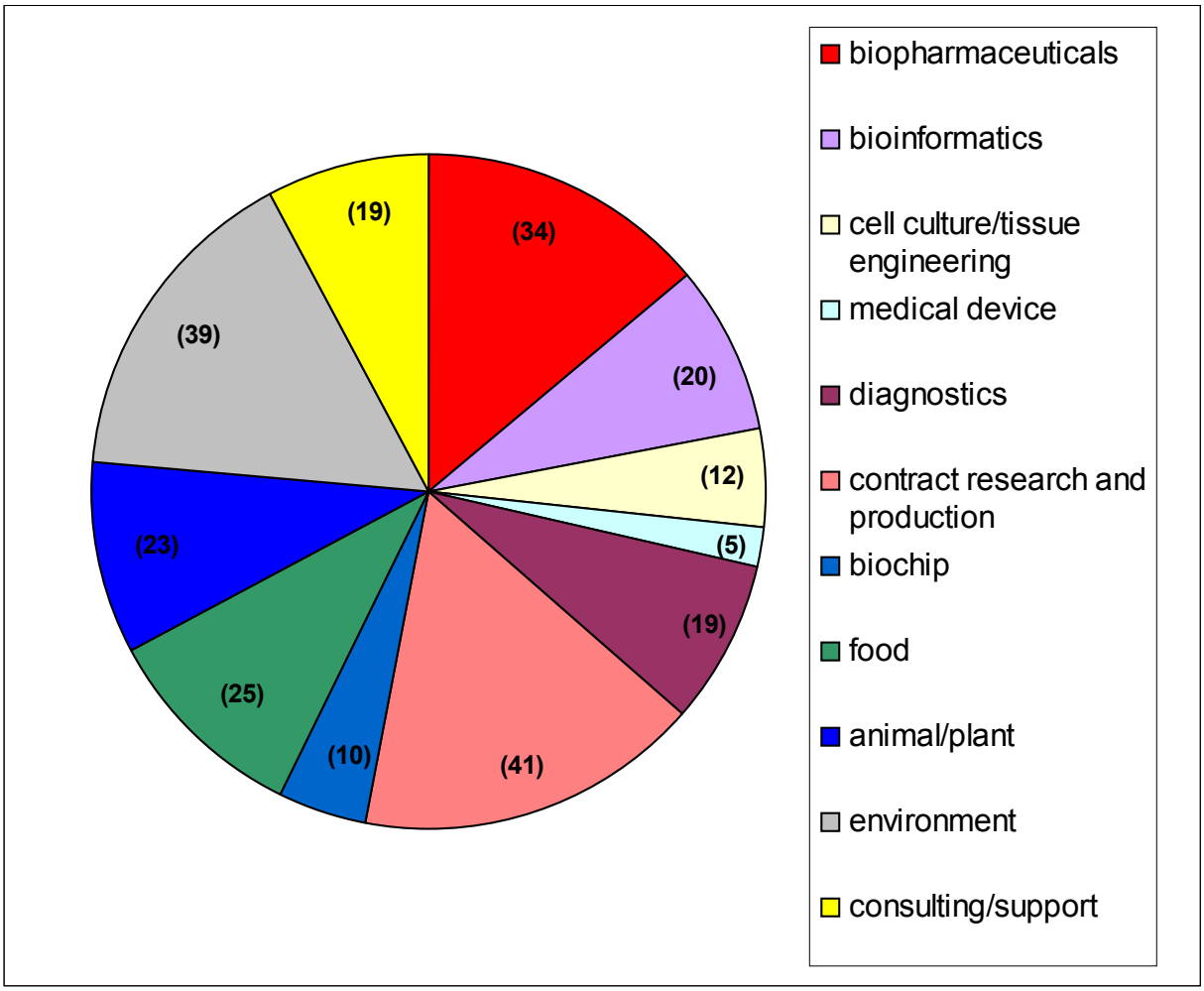

Figure 12: Focus of Japanese biotechnology companies according to Japan Bioindustry Association (number of companies in parenthesis)

Japan considered its strength in manufacturing. This can be seen in some applications of biotechnology where productions skills matter, for instance, Japan possesses a strong competitive position in the production of amino acids.

In the post-genome era, it is hoped that the Japanese biotechnology industry can make use of these production skills in the long run. For instance, if the biochip technology shows its potential impact on diagnostics, mass production will be the result. The biochip technology opens up many applications in different fields, e.g. it allows to automate analysis work in medical laboratories, which is previously done manually, and it can be used for patient stratification in order to develop customized drugs with less side-effects. However, in many applications of biotechnology competitive advantages are solely based on product innovation instead of process innovation at present.

Conclusions

In this last section we draw some conclusions how the Japanese institutional framework differs from that found in Germany. In the preceding sections we have described the role of large companies, government, venture capital, and entrepreneurship.

In contrast to Germany, large companies play an active role for the formation of biotechnology companies. As already mentioned, one third of all new biotech companies is based on spin-off activities of incumbent companies and in addition, these companies are also involved as research sponsors, investors or co-founders in many other start-ups, which were established by university researchers.

The initiatives of the German government, in particular the BioRegio-competition, were clearly one cornerstone for the development of the biotechnology sector. Since then, this strong initial influence is gradually diminished due to the maturing of the whole sector. In Japan, government plays a pacemaker role and has brought into effect many projects and laws for promoting entrepreneurship and technology transfer in high-technology sectors. Particularly, the budget for Life Sciences has increased steadily in the last few years.

Factor	Germany	Japan
Large companies	-	++
Government	++/+	++
venture capital	++	-
entrepreneurship	++	-

Figure 13: Impact of certain institutional factors on the development of the biotechnology industry in Germany and Japan (-: weak influence; + minor influence; ++: strong influence).

The emergence of venture capital in Germany has significantly contributed to the biotech-boom in Germany. National as well as international venture capitalists became increasingly aware of the growth potential of the biotechnology industry in Germany. In contrast, venture capital has been nearly absent in Japan until recently. However, more and more venture capital funds has been raised in the last few years and some of them invest solely in biotechnology companies.

In the last few years, entrepreneurship has been increased steadily in Germany so that many researchers as well as senior managers have been taken the risk to set up their own companies. In Japan the situation is quite different compared to Germany. Until now, there exists no culture for entrepreneurship yet and life-long working for one large company is still the career ideal for many Japanese.

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