CHAPTER 1 INTRODUCTION

1.1. Introduction

Global economic competition becomes increasingly driven by technology and innovation. New technologies can transform industry by creating new products and services, improving manufacturing processes, and accelerating the pace of R&D. Of these, biotechnology is believed to have the most potential to contribute to economic growth. Biotechnology at the dawn of the 21st century aids the world's progress in treating and curing diseases; in providing more food for a growing world population; in reducing reliance on non-renewable energy sources; in sustaining escalating industrial production without harming the environment; in cleaning up existing pollution; and in saving endangered species. Although the manipulation of biological architecture is both ancient (fermentation and brewing) and modern (recombining genes, and using computers to analyze nucleotide sequences and protein structures to pinpoint drug targets), the full economic and social impacts of new developments in biotechnology have yet to be realized.

Less than 30 years ago, the new biotechnology industry began with a handful of U.S. start-ups using genetic engineering to manufacture human protein drugs. Today, most states are committed to promoting biotechnology industry in their countries, irrespective of the level of economic development. Each place competes to build up so-called bio-clusters in the local area. However, though biomedical research takes place throughout the world, more than three-fourths of all biotechnology pharmaceutical patents have their origin in a handful of regional clusters in the U.S.

So the dissertation addresses the following questions. What can we learn from experiences of the U.S. biotechnology industry? What are the critical factors for success in the development of a biotechnology industry, or even for research-based industries in the knowledge-based economy? What are the underlying relationships between academia, biotech firms and the other industrial sectors? And what are the policy implications for the developing countries?

Based on the discussions for these questions, this dissertation aims to examine how national and firm-level features function together as a system to shape country-specific patterns in the development of the biotechnology industry in Taiwan, as an example of developing countries. This dissertation is organized as follows. Chapter 1 briefly illustrates the definition, scope and characteristics of the biotechnology industry. Chapter 2 explores how the biotechnology industry emerged, and in particular, how it relates to the universities and to the traditional sectors in the U.S. With a better understanding of the underlying innovation model in the U.S., chapter 3 summarizes the theoretical underpinnings of the concept of ***National Innovation Systems***, to characterize the emerging research-based industries. Chapter 4 describes the national institutional context and the development of the biotechnology industry in Taiwan. Chapter 5 applies the framework of ***National Innovation Systems*** to an analysis of Taiwan's biotechnology industry by employing a large-scale survey, and thus examines Taiwan's innovation systems and performances. Finally, chapter 6 concludes by proposing the science and technology (S&T) policies for the developing countries.

In short, the dissertation tries to identify the institutional factors affecting the development of research-based industries by analyzing the developments of the biotechnology industry in Taiwan, in light of the experience of the U.S., the leading country in the field, based on the framework of ***National Innovation Systems***.

1.2. Definition of Biotechnology

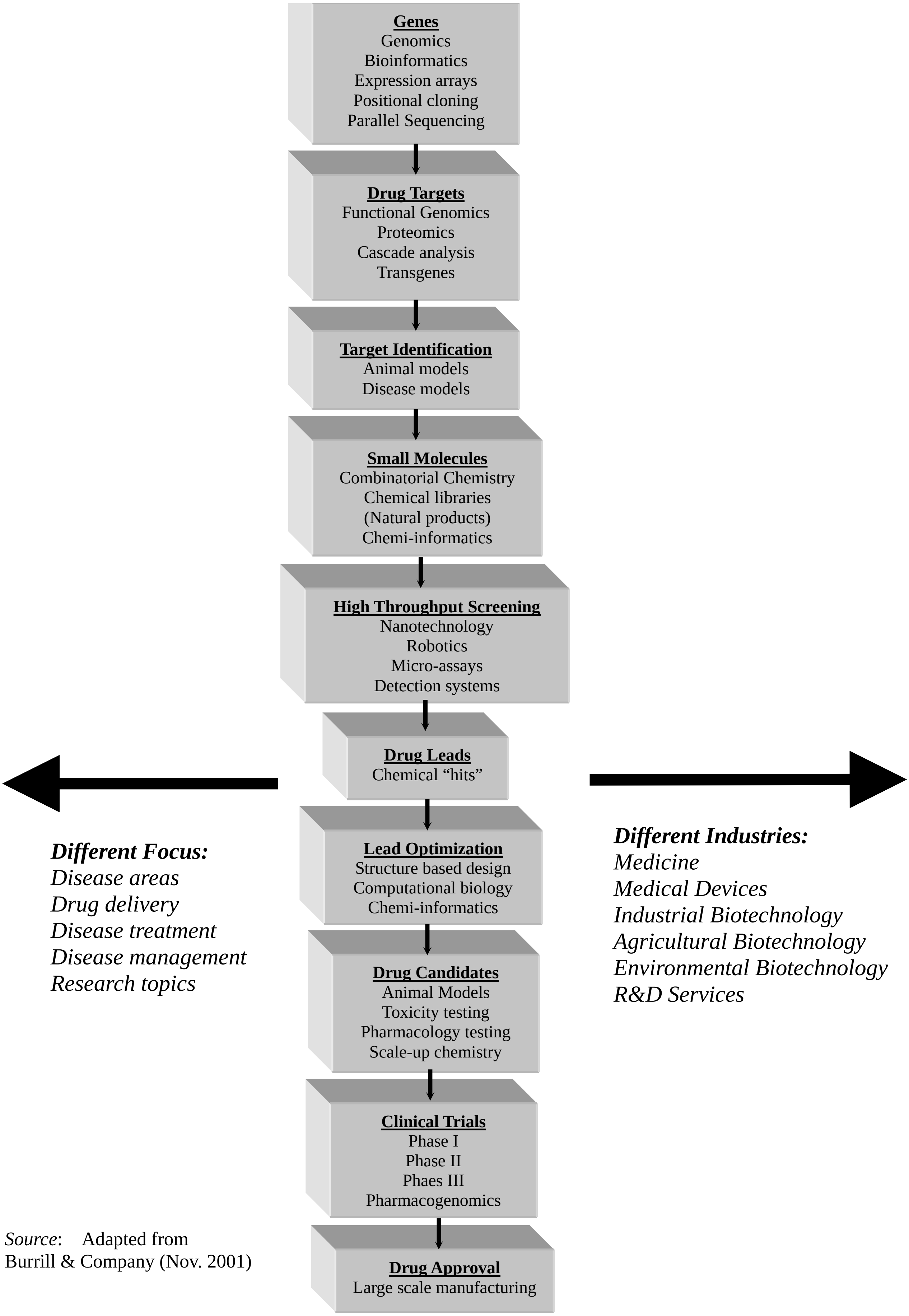
The definition of biotechnology, developed by the OECD, focuses on the techniques that either modify existing living organisms/part of them, or transform material, of living origin or not, by the use of processes involving living organisms, for the purpose of producing new knowledge or developing new products or new processes.

Broadly defined, biotechnology is about the manipulation of living organism or parts for the production of goods and services, including old practices like selective breeding, cross-fertilization, and using micro-organisms in the making of bread, wine and beer. Today, based on the developments in molecular biology, it is specifically about altering the genetic structure of living organisms, such as genetic engineering (recombinant DNA) and cell fusion (hybridoma technology). In addition, there are so-called "platform technologies" for drug discovery and development, for example combinatorial chemistry, high-throughput screening, and bioinformatics…in this area. These technologies are essentially research tools, and their developers do not aim to become producers but rather providers of services to big pharmaceutical companies, and thus being able to sell customized services to a wider range of potential buyers. In short, biotechnology is a set of key enabling technologies, which can be applied in academia and industrial sectors related to life sciences (Figure 1.1).

1.3. The Scope of the Biotechnology Industry

The scope of biotechnology industry involves the techniques mentioned above, and besides, the development of tools, instruments, and devices that apply directly and prevalently to bio-related products, as well as the products and services generated by the technique or tool mentioned above. Therefore, the applications of biotechnology span a number of industrial sectors, namely, pharmaceuticals, chemicals, medical devices and supplies, environment management, food processing, agriculture, and research-based services…and so on. So the biotechnology industry, as defined by Biotechnology Industry Organization (BIO), is about the application of biological knowledge and techniques to develop products and services. It is not only an industry defined by products or services in the traditional sense, but also by *the means of production* or by *the way to do innovation* for other bio-related industries. The categories and contents of the biotechnology industry are as follow (Table 1.1).

Figure 1.1: Biotechnology: Life Science Based Technology Scope
Vertical vs. Horizontal Division in a Two-Dimension Space



Source: Adapted from Burrill & Company (Nov. 2001)

Table 1.1: The Contents of Biotechnology Applications

Category	Examples
Medicine	Biopharmaceuticals Therapeutics Diagnostics Drug design and delivery Drug discovery Cell and tissue engineering Gene therapy Regenerative medicine Alternative medicine Traditional Chinese Medicine (TCM), botanical drugs, herbal medicine Vaccines Antibiotics
Medical Devices	Bio-chips (e.g. Protein-chips) Bio-sensors Gene probes Reagents, kits, assays Biologicals Medical devices Medical instrumentation Medical supplies Homecare (e.g. Diabetes monitoring)
Industrial Biotechnology	Specialty chemicals (e.g. Amino acids) Bio-processing (e.g. Bacteria culture) Bio-based lubricants and functional fluids Renewable alternative fiber papers and packaging Plant-based plastics, polymers and films Wood-based composite materials Fermentation Enzymes Catalysts Flavors or fragrances Cosmetics (e.g. Collagen) Phytochemicals Neutraceuticals Medical food Functional foods Supplements or vitamins Food processing
Agricultural Biotechnology	Bio-fertilizers Bio-herbicides Tissue culture Seeds and plant breeding Genetically modified products Transgenic plants Livestock Transgenic animals Veterinary products Animal vaccines Aquaculture
Environmental Biotechnology	Bio-based energy (e.g. Microbiologically enhanced petroleum) Bio-based waste treatment Bio-based pollution prevention

	Natural resource recovery (e.g. Mineral recovery) Bio-processing Bioremediation Phytoremediation Bio-pulping Bio-bleaching Bio-filtration Biodesulphurization Biomaterials Biomass conversion Enzymes Marine microbial Terrestrial microbial
Enabling Technologies and R&D Services	DNA, peptides, or proteins sequencing DNA, peptides, or proteins synthesis DNA markers Polymerase Chain Reaction (PCR) amplification Bio-informatics Single-Nucleotide Polymorphisms (SNPs) Genomics Proteomics Cellomics / Cell receptors or signaling Pharmacogenomics High throughput screening Combinatorial chemistry 3-D molecular modeling Cloning / Culturing of cells, tissues, embryos Stem cells Extractions, purifications, separations Clinical tests Clinical trial management Contracted research (CRO) Contracted manufacturing (CMO)

Sources: 1. U.S. Department of Commerce (2003), ***A Survey of the Use of Biotechnology in U.S. Industry***.

2. Burrill & Company (2003), ***Biotech 2003***.

3. Industrial Development Bureau, Ministry of Economic Affairs (2002), ***White Paper for Biotechnology Industry in Taiwan 2003***.

4. Taiwan Institute of Economic Research (2003), ***The Scope and Classification of the Biotechnology Industry***.

1.4. The Drivers of the Biotechnology Industry

According to ***A Survey of the Use of Biotechnology in U.S. Industry*** (U.S. Department of Commerce, 2003), patent data demonstrate the dynamic and rapidly evolving nature of biotechnology. In 2002 alone, the survey respondents indicated that they had pending U.S. patent applications for 33,131 new biotech-related products or processes, compared to 23,992 current U.S. biotech-related patents in their portfolios[1]. The other survey data also underscore the point that recent discovery, development, and application of biotechnologies are not only creating new products and services, but that biotech processes and products are now applied in all types manufacturing, agriculture, aquaculture, and even at the microbial and nano-scales.

One of the drivers of the biotechnology industry is basic research. It can be demonstrated by the Science Linkage (SL) of the biotechnology patents. SL is the average number of scientific journal papers cited on the front pages of a set of patents in a technology area. SL reflects the dependence of a given technology on contemporary scientific research. So Table 1.2 shows the biotechnology is more heavily built on basic research than the other technology areas[2]. On average, 16.76 scientific journal papers were cited on the front pages of a set of the utility patents granted in the U.S. in the biotechnology, much more than average 1.59 papers in all technology areas.

[1] This shows the growth potential of the biotechnology. The USPTO data show that, *85,979*, *61,167*, *16,826*, and *14,438* patents were granted to those in *ICT*, *Medicine* (including *Biotechnology*), *Semiconductor*, and *LCD* sectors respectively in the U.S. during the period from 1998 to 2002 (TIER, 2003).

[2] Meyer (2000), however, argued that SL does not necessarily indicate a direct science link of technology, but illustrates the multifaceted interplay between science and technology.

Table 1.2: Science-Linkage of 1994-1998 U.S. Utility patents

Technology Area	Taiwan	UK	US	World
Biotechnology	10.52	10.68	20.62	16.76
Pharmaceuticals	3.88	6.97	13.52	10.17
Chemicals	1.80	2.33	5.68	3.81
Medical Electronics	0.44	2.00	3.39	2.82
Agriculture	0.10	2.72	3.06	2.55
Semiconductors & Electronics	0.43	1.78	1.92	1.39
Computers & Peripherals	0.34	1.39	1.73	1.24
Medical Equipment	0.08	0.86	1.35	1.14
Food & Tobacco	0.04	0.61	1.34	1.05
Plastics, Polymers & Rubber	0.48	0.79	1.66	1.04
Primary Metals	0.00	0.43	1.77	1.02
Telecommunications	0.25	1.11	1.29	0.98
Measurement & Control Equipment	0.18	0.86	1.19	0.90
Glass, Clay & Cement	0.67	0.64	1.22	0.86
Oil & Gas, Mining	0.12	0.26	0.96	0.77
Fabricated Metals	0.23	0.36	0.99	0.67
Industrial Process Equipment	0.18	0.33	0.89	0.63
Power Generation & Distribution	0.45	0.38	0.71	0.59
Office Equipment & Cameras	0.12	0.68	0.70	0.41
Electrical Appliances & Components	0.08	0.38	0.49	0.38
Aerospace & Parts	0.00	0.12	0.45	0.35
Wood & Paper	0.01	0.13	0.27	0.25
Textiles & Apparel	0.01	0.67	0.23	0.18
Heating, Ventilation, Refrigeration	0.00	0.40	0.23	0.18
Industrial Machinery & Tools	0.01	0.07	0.21	0.14
Motor Vehicles & Parts	0.00	0.06	0.12	0.08
All Patents	**0.22**	**1.62**	**2.20**	**1.59**

Sources: CHI Research Inc. (2000)

Besides basic research, the more important driver encouraging development of a biotechnology industry is turning scientific breakthroughs and technological achievements into commercialization. The progress of the biotechnology industry involves a complex sequence of interactions between economic, technological, and scientific factors. The milestones of the biotechnology industry are described as follow (Table 1.3).

Table 1.3: Milestones of Biotechnology Industry

1953	"Double-helix" structure of DNA is first described by Watson and Crick in the U.K.
1966	The genetic code is cracked, demonstrating that a sequence of three nucleotide bases determines each of 20 amino acids.
1973	Cohen and Boyer develop genetic engineering techniques to "cut and paste" DNA and reproduce the new DNA in bacteria.
1975	Milstein and Kohler develop the first monoclonal antibodies.
1976	The first working synthetic gene is developed.
	The first biotech company, Genentech, is founded by Swanson and Boyer.
1980	Cohen and Boyer receive the first U.S. patent for gene cloning.
	Biotech's first IPO, Genentech, goes public.
1983	Polymerase Chain Reaction (PCR) is conceived.
1985	The first recombinant biotech drug, Protropin for growth hormone deficiency in children, is manufactured and marketed by Genentech.
1989	Epogen, developed by AMGEN, is approved for the treatment of renal disease anemia. It is the first biotech product, which become a blockbuster.
1990	An international effort to map all of the genes in the human body, Human Genome Project (HGP), is launched.
1997	Dolly, the first cloned from a mammary cell of a six-year-old sheep, is created by the Roslin Institute and PPL Therapeutics[3].
2000	The first draft of the human genome sequence is completed by the HGP and Celera Genomics.
2003	The human genome sequence mapping is finished by the HGP.

Source: News reports.

[3] Fransman (2001) explored that the causal relationships between economic, scientific and technological forces let to the cloning of Dolly, the sheep, and that the institutions within which the economic, scientific and technological processes were embedded. He found that economic factors played a crucial role in the birth of Dolly, previously acknowledged as a major scientific breakthrough. The advent of Dolly was not the result, intended or unintended, of purely scientific research but was rather the result of conscious design, i.e. developing transgenic animals for commercial purposes. Expected economic payoffs motivated the research program undertaken at Edinburgh University, the Roslin Institute, a government-funded research institute, and PPL Therapeutics, a private for-profit firm. Economic processes interacted intimately with scientific and technological processes in the designing of Dolly.

1.5. Innovation of the Biotechnology Industry

What follows is characteristics of innovation of the biotechnology industry, which mainly based on the findings of European Commission (2002)[4].

(1) The biotechnology industry has to be understood as a system. Its innovation and commercialization activities involve a large variety of actors: research-based firms, established companies, universities, public research institutes, venture capitals, regulatory authorities, health care systems… and so on. The competitiveness of the biotechnology industry cannot be assessed by studying only individual firms. We must also consider the broader set of infrastructures and policies that influence the actions of firms, and more importantly, the dynamic interactions between different actors and levels.

(2) Biotechnology depends heavily on basic research at universities and thus is highly science-based. So the key to develop biotechnology is the availability of leading-edge scientific capabilities. In addition, biotechnology includes a mixture of diverse disciplines and fuses separate streams of science and technology. Without a strong and diversified scientific research base, technological progress in biotechnology is impossible.

(3) There is a close relationship between academia and industry in the development of biotechnology. The demand for more efficient technological innovation, pulled by the industry, and the supply of scientific research for innovation associated with molecular biology, pushed by the academia, have promoted the emergence of a market for enabling technologies in the biotechnology industry, for example, genomics, proteomics, combinatorial chemistry, high-throughput screening, and bioinformatics… and so on[5].

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[4] Allansdottir, A., Bonaccorsi, A., Gambardella, A., Mariani, M., Orsenigo, L., Pammolli, F., and Riccaboni, M. (2002), "Innovation and competitiveness in European biotechnology", ***Enterprise Papers***, No.7, Enterprise Directorate-General, European Commission.

[5] Please see Chapter 2 for detailed illustration.

(4) The biotechnology industry is characterized by a new breed of small specialized (research-based) firms, which are dedicated to exploit the new technologies of life sciences for different industrial purposes, such as pharmaceuticals and agriculture. Therefore, dedicated biotech firms play an important role in transferring knowledge from universities to the industries. They are widely considered to be the most efficient available organizational solution for the development of innovative activities in biotechnology[6].

(5) Biotechnology requires trans-disciplinary, where disciplines merge in search of solutions to practical problems related to life science or industrial sectors. Therefore, firms must have capabilities, which are the abilities to exploit knowledge across different scientific disciplines and industrial sectors, and to reach out collaboration among different types of firms and research institutes.

(6) Moreover, the research collaborations in biotechnology tend to be internationalized, with its knowledge base being developed on a global basis. The ability of firms to make use of markets for technology and to access networks of collaborative relations in the relevant area has become a crucial source of competitiveness under globalization.

(7) There is high level of uncertainty and controversy around the commercialization of genetic engineering research. Regulations, regarding things like patenting of life forms, clinical trials of new biopharmaceutical products, and producing genetically modified product… and so on, influence the speed with which new scientific discoveries make it to the market.

(8) The biotechnology industry in the world has been growing and its development

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[6] Orsenigo, Pammolli, and Riccaboni (2001) found that that two different logics of exploration and technological advance have been coexisting and complementing each other in the process of biotech evolution. The first path has been following a trajectory of increasing specification of biological hypothesis. The second has been progressing towards the development of transversal techniques to generate and screen compounds and molecules. These result in the growth of specialized technology producers, new biotech firms.

seems to be far from any equilibrium configuration at this moment[7]. The impact of the rapid entry on the long-term evolution of the industry is not known, but it could preface a period of stabilization, consolidation, and selection, with mergers and acquisitions, and exit offsetting new company formation in the near future[8].

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[7] Lemarie, De Looze and Mangematin (2000) used the data from the Genetic Engineering catalogue to analyzed 228 European biotech firms, and found that the rapid technological progress in the biotechnology cannot be derived from a rapid evolution of technology base of the established firms, and should instead be explained by the entry of a lot of new firms. It is because most of the biotech firms are so small that they are frequently associated with their original technology and cannot afford to adopt a lot of new technologies at a time. Therefore, the evolution of the technology base at the industrial level is primarily due to increasing number of new firms, not due to the growth of innovative capacity of existing firms. That is, the innovative base in the biotechnology is continuously enlarged by the entry of new firms for the moment.

[8] Orsenigo, Pammolli, and Riccaboni (2001) found that in the drug business, early entrants have enjoyed significant first mover advantages, while new entrants have tended to remain specialists. Large established companies, generalists, have been able to absorb increasingly specific knowledge by interacting with the universities and new biotech firms. While new biotech firms, specialists, could master at best only fragments of the technological knowledge, and found it much harder to move into more integrated phase.