I—

Introduction

On 22 February, 1997, the world's first transgenic sheep was created. It seems unusual to talk of a lamb not being born but rather being created, but this is because the lamb was like no other before it. It was created using DNA extracted from a sheep's mammary gland. To some, the creation of a genetically engineered animal opens up amazing new possibilities for the future of medical research, while to others, it raises questions regarding the ethical nature of cloning. The two extreme views have equally large armies of followers which have frequently clashed over questions relating to the use of genetic material for research, and the release of genetic material into the environment, either for testing new products or for marketing genetically engineered products.

The problem with the extreme views is that neither one is entirely accurate. Biotechnologies can cause harm through release if they are not tested and not correctly utilised. On the other hand it is not entirely correct or realistic to argue that because they may be dangerous if not tested before hand, biotechnologies should not be utilised at all. In fact, like technologies before them, biotechnologies have the potential to produce miracle drugs and cures and improve agricultural productivity many times over. However, it is equally true that we know very little about the effects of releasing genetically engineered organisms into the atmosphere without adequate safeguards. The emphasis, then, should surely be on encouraging the use of genetically altered material but in a responsible manner through controls and adequate testing. Throughout the short history of modern biotechnology this emphasis has been lacking. As this book points out, there are, however, reasons to believe that the realisation is slowly sinking in that this cautionary yet forward looking approach is the most sensible course of action open to all.

The aim of this book is to discuss the emergence and growth of modern biotechnologies in the very different research and development environments presented by industrialised and developing economies. The
book outlines the successes of biotechnology in these countries in fulfilling their social and development goals. It also discusses the considerable challenges that have been raised for scientists and policymakers in charting out a development path for biotechnology. The latter group has also had to contend with the difficulties of finding a balance between regulation and development, while also heeding calls to protect the world's biological resources.

1.1—
Biotechnology:
A Brief History

Biotechnology or bioengineering, as its name suggests, straddles a number of scientific disciplines, including molecular biology and chemistry. The discovery of the structure of deoxyribonucleic acid (DNA) by Watson and Crick at the Cavendish laboratory in Cambridge, England, in 1953, began a race to develop new products and processes based on this important discovery. In 1973, the insertion of a foreign gene between two ends of a strand of DNA produced recombinant DNA (rDNA) and the technique we call genetic engineering was born in a laboratory at Stanford University. This technique has formed much of the basis of modern biotechnology research since then.

The 1970s and 1980s were marked by attempts to utilise this scientific knowledge to produce marketable new products and technologies that would revolutionise modern medicine and a number of industrial and agricultural techniques. The first country to make its mark in this endeavour was the USA, where a number of small companies dedicated solely to genetic manipulation and modern biotechnologies were established in the 1970s and 1980s. The 1980s were characterised by heavy investment in biotechnology as a number of these companies built up cash reserves for their initial investments. This was achieved through a number of methods, beginning with short term investment capital provided by venture capitalists and then later through public offerings for a relatively smaller number of firms. In some cases the relative lack of channels through which to raise money for risky new technology ventures, such as those being undertaken by these firms, severely impeded their ability to grow. The fact that most of them to this day remain unprofitable and have yet to show any new commercial products emerging out of their research, demonstrates the difficulty of ensuring public investor confidence in this technology.

However, despite the relatively difficult beginnings, the public has shown a remarkable confidence in commercial biotechnology and ready money was available in the 1980s for those companies that dared to go public (see Chapter 2). The chronology of events given in Table 1.1 provides the reader...
with a quick and selective overview of the major developments in biotechnology during the last two decades.

As is evident, it has not been an easy process, slow at times, with a spurt of growth and a flurry of activities coming in the 1980s. This was largely due to the excitement generated by the first new biotechnology patent and the granting of the Cohen-Boyer process patent for their genetic engineering technique. These major landmarks not only gave a green light to biotechnology companies but also encouraged governments in industrialised and developing countries to establish policy guidelines and frameworks, both to encourage investment and research and development (R&D) in biotechnology, and also to regulate its development and potential negative effects on the environment or the economy.

Elsewhere, especially in Europe and Japan, the 1980s saw the beginnings of strong pressure from governments to encourage both basic and applied research, especially through public-private collaboration. In Europe, Germany quickly established itself as the strongest in biotechnology, while Japan appeared to be lagging only slightly behind. This is evident from patent statistics used to measure relative rates of innovation and discussed further in Chapter 3. Developing countries, with the exception of the newly industrialised countries in south east Asia, were less successful, struggling not only with the technology gap that had developed and appeared to be widening but also with a lack of capital markets and low levels of government funding. A severe shortage of skilled personnel to undertake biotechnology R&D has often exacerbated the situation in these countries. The experiences of some of these countries are the subject of Chapter 4.

By the late 1980s, however, recession, coupled with low levels of product development, led to fewer successes than could have been imagined during the period of high public confidence only a few years earlier. The stock market crash of 1987 also caused temporary alarm amongst investors. This was the period when small biotechnology startups increasingly started to form joint ventures or were taken over by large multinational firms who were starting to show an interest in this new technology. The simplest and most immediately rewarding way for them perhaps was to take over a relatively successful biotechnology firm. The first and largest of the biotechnology companies, established solely for biotechnology research, Genentech became one of the earlier examples of this trend in a much publicised merger with Hoffman LaRoche in 1990. Although this trend was seen then as dangerous because it would imply the end of the highly innovative biotechnology company, and was seen simply as an attempt by the large multinational to dominate the market, it soon became evident that there were benefits in this for the biotechnology firms as well. Thus the mergers and acquisitions were the result of both groups of companies realising and exploiting the others' complementary skills in biotechnology.
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1953</td>
<td>Watson and Crick discover the double helix structure of DNA</td>
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<td>1963</td>
<td>Nirenberg and Khorana decipher the genetic code</td>
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<td>1971</td>
<td>Founding of Cetus (biotechnology company)</td>
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<td>1972</td>
<td>General Electric apply for the Chakrabarty patent (see 1980 below)</td>
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<tr>
<td>1973</td>
<td>Cohen and Boyer demonstrate gene splicing technique</td>
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<td>1975</td>
<td>Kohler and Milstein produce monoclonal antibodies using hybridoma technology</td>
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<tr>
<td>1976</td>
<td>First firm to exploit rDNA technology, Genentech, formed in USA</td>
</tr>
<tr>
<td>1981</td>
<td>First monoclonal antibody (MABs) diagnostic kits approved in the US. MITI in Japan declares 1981 to be ‘The Year of Biotechnology’. Cetus goes public. Celltech established in the UK.</td>
</tr>
<tr>
<td>1982</td>
<td>First rDNA animal vaccine (for colibacillosis) approved in Europe. First rDNA pharmaceutical product (human insulin) approved in US and UK. Taiwan declares biotechnology one of eight priority areas.</td>
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<tr>
<td>1983</td>
<td>First plant gene to be inserted in a plant of a different species. Thailand establishes the National Centre for Genetic Engineering and Biotechnology within the Ministry of Science and Technology.</td>
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<td>1984</td>
<td>Genetic engineering bill passed in South Korea. Malaysian Government forms National Biotechnology Committee</td>
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<td>1985</td>
<td>Korea establishes the Genetic Engineering Centre</td>
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<td>1986</td>
<td>India forms Department of Biotechnology in the Department of Science and Technology. China launches biotechnology programme.</td>
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<tr>
<td>1990</td>
<td>US FDA approves first bioengineered food additive (rennin used to produce cheese). Federal Republic of Germany introduces Gene Law to regulate biotechnology. Hoffmann LaRoche declares its majority holding intent in Genentech.</td>
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<tr>
<td>1991</td>
<td>The Philippines establishes a programme on biotechnology. A Kenyan outline for a National Biotechnology programme is drafted. UPOV is altered, removing the ‘breeders exemption’ clause. Merck signs agreement with the Instituto Nacional de Biodiversidad (INBio) in Costa Rica (Chapter 7).</td>
</tr>
</tbody>
</table>
The period following the stock market crash of 1987 indicated slower activity in biotechnology. Companies struggled to continue as their sources of funding became scarcer than before. Governments also faced a period of...
extensive debate especially with respect to institutional and regulatory arrangement such as intellectual property rights and regulation of genetically engineered products and technologies. This was relatively uncharted territory and it was unclear what was the best course of action to take. In some countries, public debate on the potentially negative aspects of genetic engineering was particularly heated, while in others, notably the developing countries, there were no regulations on biotechnology at all.

The 1990s have seen a gradual improvement in the situation, as regulation becomes better established and the guidelines become clearer to firms. For companies the long period of product development in some cases is also drawing to a close and after the research and product development and clinical trials, several products have been approved by regulatory authorities and are appearing on the market. Several of the more successful biotechnology firms have started to make profits from their products, which can be reinvested in more innovative research. The 1990s appear to be an age of strategic alliances between big and small firms instead of takeovers, ensuring the complementary co-existence of both.

Thus, rather than the extreme swings characteristic of the 1980s when the industry was trying to find its feet, the 1990s appear to be a period of consolidation and a recognition by biotechnologists, governments and the public, of the very real problems and prospects associated with biotechnology.

1.2 —
The Characteristics of Technological Change

The development of biotechnology, as discussed above, has come in fits and starts and has had its fair share of defeats as well as successes. It has, moreover, been a difficult learning process for all the players involved. In this section we attempt to understand the main characteristics of new technologies, their requirements of infrastructure and of policies. This is by no means an attempt to provide a complete picture but tries instead to understand what are the key aspects of technologies, especially as they relate to biotechnology, and the process of technological change.

The Non-Appropriability of Technology

One of the first observations made about technology is its non-appropriability and public good nature. While a part of any innovation is tangible knowledge whose benefits can be appropriated by the modern inventor through the granting of a patent, or a blueprint as it is often referred
to in the literature, technology spillovers are a common part of any technological innovation. The spillovers are equally important in giving continuity to the process of technological change. They provide knowledge about the present state of technology and help the next generation of inventors with the next generation of technologies. Indeed the modern patent system was developed on the basis of both appropriable and non-appropriable aspects of technological change. Any new product or process that is granted a patent must also be accompanied by a disclosure of knowledge which does not reveal the technology protected by the patent, but nevertheless provides information or 'spillover of knowledge' to society and therefore to the next generation of inventors.

The non-appropriable nature of technological change also suggests that private and social returns from technological change are different, implying less than optimal investment by the private investor in the innovation process. Frequently, therefore, policy action is recommended as a conclusion, to bridge this gap and make investment in R&D or technological change optimal. In the case of biotechnology this has been reflected in Government policies to guide R&D in particular directions and to create learning and market environments conducive to the development and diffusion of biotechnology.

**Incremental and Radical Inventions**

It was Joseph Schumpeter who first talked about technological change in terms of a process of steps, from invention, to innovation, to diffusion (Schumpeter, 1934). Although these steps in themselves are not as distinguishable from each other as he implied, it is clear that technological change does not stop at invention but requires considerable skill and time before it diffuses throughout the economy. The product cycle of any new product or technology, as it is referred to in the literature, describes technological change in different stages of growth and decline depending on whether it is a new technology or whether it has matured over time and is being replaced by a modern new technology.

Moreover, technology does not develop in a vacuum but, as pointed out above, results from knowledge gained from previous generations of inventions, or knowledge spillovers. Technological change is therefore very much cumulative and based on previous knowledge or the current state of the art. The ability to convert this spillover into a new generation of inventions is also often incremental in nature as we learn through doing or using.

However, when does a series of incremental inventions reach a stage when they can collectively be called a new technological paradigm or a new technological age, such as the age of the railway or information technology?
Perez and Freeman have developed a taxonomy of innovations to guide us in this.

- **Incremental innovations** are those that occur almost continuously in all sectors. These occur at varying rates over time and are aimed mainly at improving production processes or the quality of a particular set of products. They, moreover, tend to cluster during the period after a radical innovation or breakthrough has occurred.

- **Radical innovations** as the name suggests, occur discontinuously and may reflect radical changes to old production methods. For example, the invention of the steam engine meant radical change in methods of transport.

- **New technology systems** are defined as far-reaching changes in technology, affecting several branches of the economy and potentially giving rise to completely new sectors.

- **Technological revolutions** or changes in the techno-economic paradigm reflect new technologies that have such pervasive effects in the economy that they shift the economy onto a whole new way of production and management.

Perez (1983), who initially coined the term, techno-economic paradigm, defined it as a new technology which develops within the structure of an older techno-economic paradigm but its effects become so pervasive that it results in economic and social ruptures which change the manner in which society functions. The best example here perhaps is that of the microcomputer which has not only changed the face of information technology, but has affected deeply the way in which all sectors of society function.

**The Role of Institutions**

When ruptures in a technology emerge and set the economy on the path to radical technological change, they create the need for new structures of management and develop new sectors in the economy. As Perez's comment above about technological revolutions indicates, the development of a new technology challenges and changes the previous structure of institutions and management. Institutional change has tended to trail behind new technological developments, reacting to rather than pre-empting the demands of a new technology. While the role of the innovator, as Schumpeter argued, will always remain central to innovation, our tendency
to linearise the innovative process will always downplay the impact that institutional structures and their ability to change can have on the process. In the case of biotechnology certainly, one sees the importance of the institutional structure in encouraging and supporting the innovator. As both surveys of industrialised (Chapter 3) and developing countries (Chapter 4) show, the demands of biotechnology have significantly changed the way in which governments look at issues relating to the nature and structure of the science base, its relationship to markets and management structures and regulation. Much of the focus during the next decade or so will have to be on the creation of new systems of management and of institutional development.

1.3—
The Structure of the Book

The book is divided into two broad parts, the first dealing with biotechnology and the second with biological diversity. Seemingly unrelated, the two nevertheless have an enormous potential to support or undermine each other as is discussed during the course of the book.

The first five chapters are devoted to biotechnology. Chapter 2 discusses some basic concepts relating to biotechnology, including its definition, which is often a crucial source of misunderstanding about the nature of the technology. Chapters 3 and 4 examine the way in which modern biotechnology, including second and third generation techniques, has developed in industrialised countries (Chapter 3) and in developing and industrialising countries (Chapter 4). The issues, as would be expected, are quite different in both groups of countries and there are also significant differences within each group. The problems faced by developing countries are also different from those of the industrialised countries as are the solutions which are sought and found.

The way in which biotechnology has manifested itself in terms of changing production processes and products is discussed in Chapter 5 which examines the trade effects of technological change. Here biotechnology has the greatest potential to be destructive towards older technologies and trade and production patterns as well as supportive of efforts to develop new technologies and products. Moreover, the chapter points out, the division between those negatively affected and those affected positively can no longer be made along the traditional lines of north vs south as is frequently argued. In fact, the greatest degree of adjustment and change will come within the developing world as a result of competition, primarily between the developing countries themselves. Much will therefore depend on how quickly countries are able to react to and adopt some of the rapid changes being ushered in by the new technology.
The second part of the book is devoted to biological diversity and consists of two chapters. Biotechnology and plant breeding, and modern medicine before it, have made extensive use of the world's biological resources. The characteristics of these resources and the knowledge contained in them continue to be utilised by biotechnologists as by other scientists before them. If anything, it is argued, the ability of modern biological techniques to screen and analyse vast numbers of organisms, has created greater interest in the potential of biotechnology, especially in uncharted areas of biological diversity. Heightened interest in exploiting the world's biological resources has also added to fears of conservationists that biotechnology, along with other human activities, will increase the rate at which biological resources are being depleted. However, as this section argues, the very same biotechnologies that are being blamed as the cause of exploitation and depletion, could also be utilised to conserve biological diversity.

The first of the two chapters, Chapter 6, first discusses the nature of biodiversity and how biotechnology and biodiversity are linked. Until now, the linkages between the two have been considered as negative, especially by conservationists, who argue that biotechnology and its use of biological material accelerates the pace of biodiversity loss. While acknowledging the often acrimonious nature of this debate, it is argued here that we cannot expect biotechnology or indeed any technical progress to stop. Technical progress has made a major contribution to economic and social progress in the world and for it to stop would not be feasible or even desirable. Instead, the efforts of the biotechnology industry and conservationists should be to concentrate on the sustainable use of biodiversity, which implies its use but also its conservation. The second chapter of this part, Chapter 7, looks precisely at the manner in which biotechnology can and is contributing to conserving and sustainably utilising biodiversity. The main argument made in both these chapters is that even though the issue of biodiversity conservation has become, unfortunately, rather confrontational between the biotechnology industry and conservationists, the most realistic long-term solution is for the biotechnology industry to acknowledge the role of conservationists, especially indigenous communities which are perhaps most knowledgeable about the value and characteristics of local flora and fauna, and for the conservationists to acknowledge the need for access by the biotechnology industry to that local flora and fauna. It is only by acknowledging the contribution that both have to make to economic and social progress that a long-term solution to this grave problem be found.
Notes

1. Indeed, barely had the scientists unveiled their new product when the President of the United States expressed his concerns about the ethical nature of such research in the USA. The EU has similarly expressed deep concerns about cloning research.

2. In fact, the Nobel prize for Chemistry in 1993 was awarded to two Chemists for their work on the genetic modification of DNA. K. Mullis developed the technique of Polymerase Chain Reaction (PCR) which has subsequently been used in gene sequencing and gene cloning research, while M. Smith's work on changing the structure of an amino acid is being used by biotechnologists working on human diseases, to insert altered genes into organisms (Economic Times, N. Delhi, 30 October 1993). Similarly, the work done by Watson and Crick in the early 1950s was carried out at the Department of Physics at Cambridge University.

3. Although fears were initially expressed about the disappearance of the small companies, it is evident, as discussed later in Chapter 3, that this trend towards joint ventures and mergers has not been as disadvantageous for the small company as earlier predicted.

4. For example, while the biotechnology firms excelled in innovative research, their product development and marketing networks were not as highly developed as those of the incumbent firms. This was one of the reasons why biotechnology firms also considered the trend in mergers and acquisitions beneficial for themselves. This issue is also discussed further in Chapter 3.


6. Although genetically engineered plant and animal varieties were not patentable according to the EPO's rules, in this case, the mice were granted a patent because 'the benefits to mankind outweighed the suffering of the mice' (van Wijk et al., 1994, 5).

7. In modern economic theory this aspect of technological change has been modelled by Kenneth Arrow (1962) and has since been used in the so-called 'New growth theory' by Romer (1987, 1990) and Grossman and Helpman (1991 for example) among a number of other studies.

8. See, for example, Posner (1961)

9. See, for example, Perez and Freeman (1988).

10. Dosi's use of the term technological paradigm (for example, 1982) reflects technological change that is perhaps less pervasive in terms of its impact on the economic structure.