Economic Aspects of Biotechnology

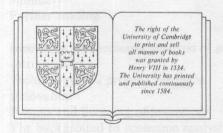
Andrew J. Hacking

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Economic aspects of biotechnology

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Preface

The aim of this book is to relate the expanding subject of biotechnology to economic principles and general theories on industrial and technological development. It is also intended to inform academic scientists of the complexities of industrial markets, patenting, profitability and cash flow problems. A lack of knowledge of these areas was referred to in the Spinks Report on British biotechnology (p. 23) and was true of my position when I started in industrial research. Some sections of the book stem from my first experiences of costing and project appraisal. I learned that fermentation is in essence an expensive technology and many of the expenses only became apparent after a somewhat lengthy learning process. The comment made by J. B. S. Haldane in 1926: 'Why trouble to make compounds yourself when a bug will do it for you?' may be answered in part 'because it's cheaper that way'. Many biotechnological processes are not attractive when compared to the alternatives under the prevailing conditions. The problems of industrial secrecy (sometimes excessive) obscure much economic reasoning, but there are in fact sufficient data, even if most of them arise from projected costs, to permit many generalizations and conclusions. This information is however scattered and sometimes in obscure locations. To a great extent this book is a collection of facts from widely differing sources.

The book is intended for those who have a training in biotechnology and are interested in its commercial development for career purposes, to make money, or just out of curiosity. I have assumed a knowledge of biotechnology (microbiology, biochemistry, genetics) to probably at least final year undergraduate level, but have aimed to explain economics and accounting from first principles.

I have drawn the scope of biotechnology as wide as possible to encompass fermentation, enzyme technology, genetic engineering, bulk chemicals, expensive pharmaceuticals, energy and waste treatment. This may only be a passing phase. For example the General Secretary of the Society of Chemical Industry, Peter King, believes that biotechnology will split into large scale processes and expensive small volume (mostly health-care) products with little or no middle ground. By the turn of the century, with further fissions such as plant strain improvement, the term 'biotechnology' will have become obsolete. This may be so, but at

present I think that there is sufficient common ground in terms of concepts, processes, raw materials and costs to link them all together.

In economic terms the intention is to discuss biotechnology both on a world and national (macroeconomic) level and in microeconomic terms of costs, investments and markets. There is more coverage of the latter and there is a bias towards bulk products as a consequence of available information. Economic analysis is strongest on existing products and processes. The newer developments are inevitably speculative and may well not develop as envisaged at present. As far as possible the approach taken is of positive rather than normative economics, that is how things are, not what they ought to be. In general I have avoided discussing future policy. In some cases values or opinions on what may be beneficial do appear, but this has been kept to a minimum.

To some extent commercial and economic terms are used which will be unfamiliar to a reader with a biotechnological background. Some are defined in the text, but explanations of others can be found in the *Penguin Dictionary of Economics*, which is very useful. Unfortunately it is not as easy to find definitions of biotechnological terminology. The *Chambers Dictionary of Science and Technology* is sometimes helpful, while various more up-to-date medical dictionaries can be used; otherwise textbooks must be consulted.

I am indebted to many people at Tate and Lyle Research and elsewhere for contributions of all kinds. I would like to mention specifically Dr Chris Bucke for much information on enzyme technology and corn wet milling, for reading the manuscript and supplying many helpful comments; Dr Peter Cheetham for data on immobilized enzymes, corn wet milling and some broad ranging ideas on biotechnology and innovation; Dr Derek Fewkes for assistance on patents; Dr Brian Hollingsworth for information on Bacillus thuringiensis and other microbial pesticides; Dr Chris Lawson for contributions on microbial polysaccharides in general and xanthan in particular; Brian Manston for help on the economics of anaerobic digestion; Dr George Nowacki of Miles Enzymes for interesting facts on aspects of marketing enzymes; Stuart Slocombe for sharing his extensive knowledge of capital investment; and Dr Gordon Walker for supplying data on downstream processing and immobilized enzyme processes. I would also like to thank Jane Cox and Frances De Banks for typing the manuscript, and Andrew Elliston and Jane Marsden for expert and patient information gathering.

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1 The interrelationships between biotechnology and economics

The two disciplines compared

In the widest context biotechnology may be understood as referring to the commercialization of all biological processes. More precisely it has been defined as the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services (Bull, Holt and Lilly, 1982). The scientific and engineering principles are chiefly microbiology, biochemistry, genetics and biochemical and chemical engineering. It is customary not to include agriculture in this definition, although there is inevitably much overlap with agriculture, both as a supplier of raw materials and in genetic improvement of crop plants. As biology is being considered as a manufacturing technology, there must now be some analysis of costs and benefits; it must enter the sphere of economics.

Economics is most often defined as the study of the allocation of scarce resources among competing uses. Its fundamental tenets are that because productive resources are scarce, choices must be made about their use and that these choices be analysed to enable every society to make decisions on what to produce, how to produce it and for whom. In this framework biotechnological processes must be analysed both against one another and against competing technologies to determine the most beneficial route to a given commodity. Unfortunately there are aspects of both the present state of economic theory and of biotechnology which make straightforward analysis difficult. To enlarge upon this point it is necessary to outline the areas of the two disciplines which present the complications.

Biotechnology is not an industry defined by products or services such as automobiles, textiles or television. It refers to the use of microbial, animal or plant cells and enzymes to synthesize, break-down or transform materials. It is a *means of production*. Its products and services span a range of applications from food to fuel, from waste disposal to pharmaceuticals. Similarly genetic engineering is a technique to alter cells to perform functions more beneficially, that is to produce more or better products or to do so more efficiently. Genetic engineering itself cannot be subjected to economic analysis, only the processes or the improvements that it makes possible.

Biotechnology presents another obstacle to economic analysis in that the majority of its benefits lie in the future. It is speculative, research orientated and dependent upon a high rate of innovation at this point in time. Economists have had much more success in dealing with the consequences of technological change than with its determinants (Rosenberg, 1982). Economic theory too has tended to concentrate on issues involved in managing national demand rather than on problems of production. In particular the problems of invention and innovation and their transition into new industry are poorly understood. Similarly much biotechnological development has been undertaken with scant regard to economic issues. Technology push rather than market pull has tended to be the order of the day. A great deal of even applied research has been directed at problems which either do not justify the effort in terms of total market potential or have competing forms of technology which can do the job more efficiently. In common with some other areas such as aerospace or railways, biotechnology has engendered a fervour which has often transcended economic analysis. While having attracted funding and very favourable publicity, this phase must inevitably give way to more pragmatic considerations. Perhaps the greatest danger to advancement of the subject in the near future is a hostile overreaction to perceived failures or what in reality may be slower progress.

In common with electricity a century ago biotechnology is today a technology in search of applications. Many economic and social problems have had a biotechnological solution proposed, from precious metal extraction to a population fed by giant yeast fermentation plants. Electricity was similarly endowed with claims as diverse as sugar refining and the improvement of sexual vigour. When the early exponents of electricity such as Faraday were questioned on the utility of their discoveries they could not have been expected to predict radio, television or the laser. Similarly, with biotechnology today it is not possible to predict or even hazard a guess at all the developments that might take place. All that can be achieved is a step-wise exploration starting with the strengths and weaknesses of the technology at present.

Currently it can be stated in theory that biotechnology could have an impact across a great range of chemical substances. The list includes virtually all organic chemicals, solvents, polymers, pharmaceuticals, flavour and aroma compounds and so on. The specific products can only be identified on a case by case basis. For each chemical the relative merits of competing means of production will determine where the economic threshold for a biotechnological route will lie. Within biotechnology there will be further competition between different methods, for example immobilized cells or fermentation, batch or continuous culture.

Modern economic theory is divided into two main branches. *Microeconomics* is concerned with individual behaviour. It is the theory of small consumers, producers and markets. *Macroeconomics* is concerned with mass or aggregate behaviour. It is the theory of large scale consumer expenditure, investments and government policy. It is essential to consider biotechnology in both branches. In microeconomic terms this means looking at individual processes and plants, cost structures and management investment decisions. At a macroeconomic level it involves looking at the impact of biotechnology on national and global economics, on balance of payments questions, and issues such as energy and raw material supply.

Another complication is the uncertainty in many areas of economic theory, even at a basic level. In macroeconomic terms the workings of the modern economy are incompletely understood. There is conflict on the role of the state, arguments over monetarist and Keynesian theories and uncertainty over the best action to be taken (Godley & Cripps, 1983). This uncertainty extends to policies on biotechnology. There are conflicts of opinion on whether for example programmes to produce fuel from indigenous biomass are of net benefit, whether new industrial developments should receive government aid, whether government should be involved in industry at all. As a consequence there is a wide range of different national policies and attitudes to biotechnology.

Similarly much knowledge of industrial organization is empirical. Some of the empirical findings can be said to confirm predictions from economic theory, but the theory has rarely offered hypotheses of the accuracy with which other branches of science are used to working. Thus only limited comparisons can be drawn between biotechnology and other industrial sectors. It is not possible to say whether the same pressures that affected the computer industry will affect biotechnology or if the outcome will be the same. The development of modern businesss organization in most Western (OECD) nations has raised many controversial issues which seem to extend beyond economic theory and beyond the control of individual nations. Biotechnology then enters an arena of uncertainty where only an exploratory approach can be adopted. The decisions and their outcomes are nonetheless crucial; economic utility will ultimately shape the industry.

Limitations of cost-benefit analysis

One of the most intractable problems in the economic analysis of an industry such as biotechnology concerns how to define both the costs and benefits of the activity to society. There are several levels at which this may be examined and a number of economic models. There are also macro- and microeconomic considerations.

Firstly, economics is only one measure of the utility of an activity; while it does not necessarily apply to many areas of social activity, it is the measure industry must use. It is argued that it is the role of government to support uneconomic research when there are other reasons for doing the work. In fundamental terms industry must convert raw materials and manpower into products which meet the needs of society. In doing so it must add value and create wealth. The value of the output of the majority of industries must be greater than the resources consumed, to provide finance for such functions as social services, administration or defence, and to provide for research, development and the construction of new manufacturing plant. These tenets, it is argued, must hold – whatever political system is adopted. They are clear enough in a mature production industry such as automobile manufacture and have been used in a comprehensive text on the social and economic aspects of the chemical industry (Bradbury & Dutton, 1972). They are however less clear in new industries, particularly in the short term. Many forms of modern technology are viewed as having long lead times, but great benefits in the long term. Firms or nations which are not in at the beginning are unable to enter the race. Thus many firms which in the past have eschewed long term and unprofitable research have been prepared to make an exception of biotechnology, even to the extent of constructing large manufacturing plant which can only operate uneconomically at present, just to gain expertise. The reasons for this policy will become evident later, but it can only be a transient phase. Biotechnology will ultimately have to produce more than it consumes, but the question of measurement of costs versus benefits still remains.

The most commonly used method of analysis is that of cost minimization and profit maximization. It assumes that profits are the only relevant goal of a firm or manufacturing activity. Other possible goals such as social welfare or prestige are regarded as unimportant. This is the easiest way of viewing the activities of firms in the capitalist West. In terms of investment decisions it means that a firm looks for a return which exceeds that which it can obtain by other methods, either by direct investment at the prevailing rate of interest or in other manufacturing or service industries. Other factors such as risk enter into this decision, but in general it is a model which will determine a firm's behaviour and attitude towards biotechnology projects as well as elsewhere. Government may choose to make this investment favourable by selective taxation policies or import tariffs, with macroeconomic considerations in mind, but the individual manufacturer still operates within this model.

Profit is only one measure of the benefit of an activity. Other welfare factors can be cited, for example employment, lack of pollution, use of

renewable resources, appropriate technology and many more. Such factors assume more importance in developing nations and in decisions on government policy. The approach used in this book in the main is on cost minimization and competition with other technologies aimed at profit maximization, with reference to other factors where appropriate. Some processes, notably in waste treatment, are not solely treated in this way, but this is made clear. The main reason for this approach is simply on the basis of available information. It is not possible to examine the policies or reasoning of Eastern Bloc nations towards biotechnology because the data are not obtainable. Similarly the policies of many developing nations, or the actual costs and benefits, are not quantifiable.

An historical outline of biotechnology

The history of a technology can prove to be an important source of information for its economic analysis. It can provide a starting point for understanding its strengths and weaknesses and its present size and importance.

The roots of modern biotechnology lie in the fermentation of foods and drinks, industries spanning almost every society and evolved over centuries by empiricism combined with adherence to tradition. Alcohol fermentations date back at least to ancient Egypt or the Biblical flood (Genesis i, 8) depending on individual beliefs. Even today the output of these industries in volume and value far exceeds new fermentation processes for the production of drugs, amino acids and industrial ethanol (Table 2.1). The essential selling points of the products, with the exception of the intoxicating effect of ethanol, are still incompletely understood. The flavour profiles and organoleptic properties of beer, wine, cheese and other products still cannot be explained in molecular terms. As a consequence the processes retain strong elements of craft and tradition, although some rationalization based on the carefully controlled conditions of the chemical fermentation industry have had notable success, for example in the American wine industry.

In economic terms, however, the craft industries and chemical fermentation are poles apart despite similarities of process and organism. A comparison of the costs of beer production and industrial alcohol illustrate this very well (Tables 5.5, 5.6 and 5.7). Excluding taxes, ethanol is sold for between \$10 and \$20 per litre in an impure form in dilute solution in beverages in the Western world (supermarket prices). Industrial ethanol producers must expect a price of only \$0.45–1.0 per litre for 95% or absolute ethanol, which may cause many to think that they are in the wrong business. Despite their age and reliance upon traditional methods the craft fermentation industries have all shown growth which has paralleled or exceeded overall economic

growth even in the most affluent societies. Because of flavour and toxicological restraints they do not have competition from other processes.

In contrast the production of bulk chemicals, such as ethanol, by fermentation has been dictated by cost, particularly in relation to the petrochemical industry. The industry developed as an outgrowth of traditional fermentation in the late nineteenth and early twentieth century to supply certain compounds to the emerging chemical and armaments industries. Early products were ethanol, glycerol, acetone and butanol, followed in the inter-war years by organic acids, notably citric, lactic, fumaric and gluconic acids. With the exception of gluconate these fermentations benefited from and ultimately were dependent upon the availability of molasses, traded increasingly on a world-wide basis as a by-product of the expanding sugar-refining industry. The technology, mostly based on stirred tank fermenters, never received sufficient impetus to develop in the way that, for example, chemistry did and the industry stagnated somewhat. It fell into a quite severe decline in the face of a greatly expanded and efficient petrochemical industry in the post-World War II years. Some processes (for example citric acid production) have survived where the product has food uses, but the industrial markets have nearly all been taken over by chemical synthesis, unless regulated by government.

The discovery of penicillin, which has now virtually passed into folklore, and the subsequent development of the antibiotic industry, has been one of the major milestones of the twentieth century and arguably one of the most beneficial discoveries of all time. Its impact on biotechnology and the public perception of biotechnology should not be underestimated. Today the antibiotic industry has sales in excess of \$5 billion which ranks it alongside some of the larger products of the chemical industry. It can be said to have given biotechnology a showing in the major industrial league tables. Along with new antibiotic discoveries and commercial success there have been tremendous improvements in process development and productivity. Penicillin is now manufactured in 100000 litre fermenters at concentrations of 50 g l⁻¹ and it costs less than 1% of its cost in 1945. A less well known factor in its development has considerable significance in the economic development of biotechnology today. During the Second World War the US Government imposed an excess profits tax of 85% as one measure to pay for the war effort. As many pharmaceutical companies were liable for this tax, additional research cost them effectively only 15% of its total cost, 'the 15¢ dollar'. Several of the early large antibiotic screens and the process development of penicillin were funded on this basis.

Even in the aftermath of the success of antibiotics biotechnological