# INFORMATION SOURCES IN BIOTECHNOLOGY

Second Edition

A. Crafts-Lighty

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## Introduction

The purpose of this book is to describe the information sources which are available in the field of biotechnology. Biotechnology is a multi-disciplinary applied science and an exciting new field of endeavour. It has captured the imagination of both business and the general public and as a result, has received substantial attention in the press over the last ten years. The governments of most developed countries have allocated large sums of money to support research and industrial development in biotechnology and over 500 specialist biotechnology companies have been formed world-wide, many of whom have made very successful public share offerings. As a result of all this, the proliferation of articles, books, journals, patents and newsletters about biotechnology has been nothing short of staggering. Most people have, probably, heard of biotechnology by now, but few seem to know how to find out more about it. As the manager of information services for Celltech, the UK's major specialist biotechnology company from 1981-1985, I receive many letters and telephone calls from students, teachers, researchers, business executives and librarians asking for advice and assistance in finding information about biotechnology and clearly finding it hard to know where to start. This book is for all those people and all the others who have been struggling valiantly alone or contacting my colleagues around the world.

In mid 1983, when the first edition of this book was written, biotechnology was definitely an 'in' subject; a buzzword even, increasingly used to create a high technology image by companies and universities in the hope of attracting attention and money. By early 1986, the glamour has worn off only a little and though the vogue among publishers for anything biotechnological has diminished some what, the flood of new information is still considerable.

One aspect of biotechnology, genetic engineering, is still a topic of considerable public interest and debate because of the long-term possibilities it offers to alter and improve the genetic heritage of agricultural plants, farm animals and even human beings. This potential raises a number of important moral, ethical and ecological questions as well as posing a formidable scientific challenge but there is much more to biotechnology than genetic engineering and much genetic engineering is only concerned with the manipulation of bacteria and yeasts, not

higher organisms. Biotechnology can, with some difficulty, be defined and treated as a single subject area, albeit one with very fuzzy edges! At least ten different definitions have been published in the last two years, each differing slightly in scope but all encompassing a wide range of industrial processes using biological systems and methods.

In this book, those information sources which are clearly concerned with modern biotechnology (as defined in Chapter 1) will be covered in the most detail. However, in many sections it has also been possible to mention some peripheral material which relate to specific applications for biotechnology and to more traditional biotechnological processes as well as some guides to particular types of information sources. The choice of which of these sources to include was often difficult, since no work on biotechnology in its broadest sense can be totally comprehensive and remain a readable, managable size. Three further constraints were also placed on the coverage of this book. Only English language publications have been included, no works announced after March 1986 are reviewed and with the exception of a few special review issues mentioned in Appendix 201, individual journal articles are not listed.

Chapter 1 briefly describes the science and business of biotechnology. This is intended as a first introduction to the subject for those who have little or no knowledge of it. Chapter 2 is an overview outlining the types of information sources available in biotechnology. Chapters 3 to 12 discuss particular categories of sources in detail and review the most important ones in some depth. Chapter 13 discusses library management of biotechnology material and the provision of information services in biotechnology. In each chapter, the aim is to provide brief critical reviews of the most important information sources, together with bibliographic details of many others. A final appendix contains a complete list of the addresses of all the publishers mentioned in this book. Additional appendices at the end of some chapters give lists of publications for further reading and other information. For the readers' ease, the tables have been placed at the end of each chapter just before the appendices.

It is inevitable that a few information sources will have been omitted and, as time goes on, of course, many new works will appear. In the appendices of this second edition, new or substantially altered entries are indicated with an asterisk so that new material may be spotted easily. It is hoped that a third edition of this book may be produced and, therefore, the author would be grateful to be notified of any omissions which readers may detect. All views expressed in this work are these personal opinions of the author and do not constitute any endorsement or otherwise of any cited source by the author's previous employers, Celltech Ltd or the author's company BioCommerce Data Ltd and no liability is accepted for any errors or omissions.

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# Chapter 1
# WHAT IS BIOTECHNOLOGY?
# THE SCIENCE AND THE BUSINESS

The purpose of this chapter is to explain briefly what comprises biotechnology. Both scientific and industrial aspects are considered but the treatment here is intended only as a very basic outline giving the flavour of the business. It is mainly to help those readers who do not have an extensive scientific educational background. A list of introductory books, reviews and pamphlets is given in Appendix 1-1 for further reading and additional more technical general books and conference proceedings are listed in Appendices 3-1 and 4-1 respectively. Included among those in Appendix 1-1 are several considering the social and safety aspects of biotechnology, the history of biotechnology, and the financial and economic aspects of the technology.

## Defining Biotechnology

Explaining exactly what is meant by biotechnology is certainly not easy. At least ten different definitions of biotechnology have been published during the last five years in various government reports. The differences are sometimes significant and attest to the problems in defining the boundaries of such a multi-disciplinary applied science. Most people agree that certain processes which utilize biological organisms definitely are biotechnology, what is less certain is which processes are not biotechnology.

The word biotechnology, a contraction of biological technology, came into general use in the mid 1970s, gradually superseding the more ambiguous bioengineering. This was (and still is) used to describe both biomedical engineering (which refers to the design and manufacture of such products as heart valves, artificial hips and body scanners) and biochemical engineering (which refers to chemical engineering processes using biological substances or living organisms such as fermenter operation and control, product recovery and biosensors). Such linguistic changes and developments, however confusing, are natural and unavoidable; it is instructive to note that the word biology was only introduced around 1800 as a substitute for physiology or zoology.

One of the most widely quoted definitions of biotechnology is as follows: "the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services" (1). The wording is carefully chosen. Agents includes a wide range of biological substances, such as enzymes, as well as whole cells or multicellular organisms and mentioning services as well as goods covers processes such as waste and water treatment. Another frequently quoted definition is: "The application of biological organisms, systems or processes to manufacturing and service industry" (2). Both these definitions are rather vague about the nature of the organisms or agents involved and therefore do not settle such questions as whether agriculture itself is biotechnology. It can be argued that systematic farming of plants and animals for food and fuel falls within both these definitions but, in practice, most people do not include conventional agriculture or animal breeding within biotechnology. To clarify this aspect, some other definitions have restricted biotechnology to the use of microorganisms, cultured cells and the parts thereof. Even then there are problems because food processes, such as baking, brewing and cheesemaking, are clearly still included within this definition of biotechnology. These methods have been in use for millenia and were developed long before man had any knowledge of the existence of the microorganisms involved. For convenience today, many people exclude these traditional processes from what they feel comprises biotechnology, which is feasible because these technologies, are such well-developed industries in their own right. In the main, this book will follow this slightly illogical convention but it must always be remembered that aspects of modern biotechnology may have significant affects on these traditional processes. Possibilities include genetic manipulation to improve brewing and baking yeasts or to introduce new characteristics in crops and animals, biological control of plant pests, and new methods of diagnosing and preventing plant and animal disease.

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[1] Biotechnology. International Trends and Perspectives, A.T. Bull, G. Holt and M.D. Lilly (Organization for Economic Co-Operation and Development, 1982).

[2] Biotechnology. Report of a Joint Working Party, Advisory Council for Applied Research and Development, Advisory Board for the Research Council, The Royal Society (HMSO, 1980).

**Basic Biological Principles**

Before discussing specific aspects of biotechnology, and to help clarify the definitions just presented, it is useful to review a few fundamental biological principles. The most significant is that the basic unit component of all life is the cell. A cell is a physical compartment in which the complex biochemical reactions of living organisms occur. Viruses may be considered an exception as they usually contain just genetic material and some proteins. Viruses can exist independently, but must find a living cell in which to replicate.

Each cell contains a polymeric chemical substance, deoxyribonucleic acid (DNA) which specifies the genetic heritage of that cell. The DNA is akin to a computer program and carries a set of instructions which effectively defines all the components of the cell and how they are to be made. DNA is a very long molecule made up of four different types of very similar organic compounds called nucleotides. These components are made up of four 'bases' called adenine, thymine, cytosine and guanine, and abbreviated to A, T, C and G respectively. Each base is attached to a sugar molecule (deoxyribose) and a phosphate group to form deoxyribonucleotides. The sugar phosphate groups of the nucleotides can link chemically to form a chain carrying the bases somewhat like beads on a string. When a strand of nucleotides (called an oligonucleotide or polynucloetide) is brought very close to another, the bases can interact chemically forming hydrogen bonds. These interactions are very precise and result in the formation of specific pairs of bases. A always pairs with T and C with G. Thus, if two strands of DNA have complementary sequences, say AAACCC and TTTGGG, they will stick together forming a ladder-shaped molecule where the base-pairs form the rungs and the sugar-phosphate backbone the uprights. This form of DNA is described as double-stranded and is the normal configuration of cellular DNA. Double-stranded DNA usually spontaneously adopts a twisted shape like a corkscrew, the so-called double helix described by Watson and Crick in 1953.

In order to pass on genetic information and replicate themselves, cells divide. During this process, the DNA must also divide. The twisted helix unwinds at one or more points and the specific hydrogen bonds are disrupted allowing a copy to be made of each complementary DNA strand. This process of DNA replication results in two identical double-stranded molecules, one strand of each having been newly synthesized. These can then be used in two separate 'daughter' cells.

DNA, however, does more than just replicate itself. The sequence of bases has a meaning and by a complex biochemical process, allows DNA to synthesize other very different biological substances. The first of these is ribonucleic acid (RNA). This is a chain of nucleotides with a structure very similar to DNA, except that the nucleotide components of RNA all have an extra oxygen atom on their sugar (ribose) part making them ribonucleotides and the base thymine is replaced by a base called uracil (abbreviated U). RNA polymers are made using DNA as a template. The double-stranded DNA separates over a short portion of its length, while a single-stranded

RNA chain of complementary base sequence is synthesized using it as a template, in a process called transcription. This 'messenger' RNA (mRNA) is then used by the cell to direct other syntheses. Each group of three RNA bases (a codon) is specifically recognized by another type of RNA, known as 'transfer RNA' (tRNA), which allows the cell to translate the RNA and produce protein molecules. Proteins are another type of biological polymer but they are built up out of amino-acids, of which there are about twenty different common naturally-occuring kinds. Proteins are very important to cells because they provide most of the structural components and many can catalyze chemical reactions. Proteins with such catalytic functions are called enzymes. Enzymes perform many tasks in the metabolism of cells: they break down unnecessary proteins, synthesize other structural materials, such as lipids, metabolize small molecules, act as receptors mediating external interactions and assist in DNA replication and RNA synthesis.

The basic process by which DNA makes RNA and then protein (gene expression) was mainly elucidated during the late 1960s. The existence of inherited genes for specific traits was demonstrated in the nineteenth century but the nature of the genetic material was then unknown. We now know that genes comprise stretches of DNA which code for protein molecules but our understanding of gene expression at a molecular level is only just beginning. Of course, as research proceeds, new complexities are revealed, for example the existence of viruses containing only RNA. These viruses cannot replicate themselves independently, but they can infect cells, convert their RNA into DNA and fuse with the cellular DNA. There are also DNA viruses with similar properties and there is increasing evidence that such viruses may be involved in carcinogenesis (the process of stimulating a cancer to develop). However, the discovery of viruses and parts of DNA which do not code for proteins but instead interact with various proteins to regulate gene expression has also helped to facilitate genetic manipulation. It has been found that many of the viruses that infect bacteria exist as (usually circular) pieces of double-stranded DNA called plasmids. Plasmids can be transferred between bacteria by the process of conjugation (bacterial mating) or transformation (a nonspecific uptake of foreign nucleic acids). Plasmids are important in nature, carrying many genes that enable bacteria to live in particular habitats. For example, the genes for the enzymes that are responsible for the synthesis of (and for the resistance to) certain antibiotics are often on plasmids. Plasmids have also become a vital part of the genetic engineer's tool-kit, although bacterial viruses (bacteriophages), plant and animal viruses are also used in gene manipulation and foreign DNA can be introduced into cells by various physical methods such as injection and electric shock.

**Genetic Engineering**

Despite its possible inaccuracy and unfortunate connotations, the phrase genetic engineering seems likely to remain in our vocabulary for many years. A better phrase is probably genetic manipulation, but in deference to its popularity genetic engineering has been used throughout this book. Genetic engineering may be described as the extracellular creation of new forms or arrangements of heritable material in such a way as to allow the incorporation or continued propagation of the new genetic form in nature. This definition actually includes the random mutation (changing) of isolated DNA with chemicals or ultraviolet light but would exclude the mutation of intact cells and any forms of selective breeding. Although it is possible to synthesize an entire gene chemically (using a so-called gene machine to produce synthetic oligonucleotides), as yet, genetic engineering has mainly comprised the transfer of natural genes from one organism into another, sometimes via complementary DNA (cDNA) produced from messenger RNA for various reasons of convenience.

At this point, it is necessary to emphasize that biological organisms come in two types: prokaryotes and eukaryotes. Prokaryotes are simpler and are characterized by the fact that their DNA floats about freely inside their cells and is mostly in one long chromosome. In eukaryotes, the DNA is packaged within the nucleus, a subcellular compartment or organelle, bounded by a membrane composed of lipids and proteins. In eukaryotes, protein synthesis occurs outside the nucleus, in the cytoplasm, after messenger RNA is made in the nucleus. Some eukaryotic organisms, such as yeast, are unicellular (single-celled) but all higher (multicellular) organisms from sponges to man also have eukaryotic cells. Prokaryotes are much better understood at a biochemical level, particularly the coliform bacillus, Escherichia coli.

E. coli, having well-defined genetics and the ability to reproduce itself once every twenty minutes, being easy to grow in the laboratory and having many non-pathogenic strains, was a natural choice for early experiments in molecular genetics and genetic engineering. The first objective of this work was to insert DNA from one E. coli strain into another E. coli strain. The second hurdle was to get this 'cloned' DNA to produce a functional protein. The next step then was to repeat the process using eukaryotic DNA. Since the mechanisms of gene expression in prokaryotes and eukaryotes differ very considerably and a cell may not necessarily tolerate or express a foreign protein, it is by no means obvious that both these objectives can be met for every gene.

The actual process of gene cloning however, is comparatively straightforward. In E. coli, a plasmid is usually used as the vector whereby the foreign DNA is introduced. The DNA being cloned is first cut up into small pieces using enzymes which break the DNA only at specific base sequences. These are called 'restriction' enzymes. If the circular plasmid is also cut with the same enzyme at one site, its