A CONCISE HISTORY OF BIOTECHNOLOGY – SOME KEY DETERMINANTS

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Summary

In the beginning biotechnology was an artisanal skill rather than a science and involved the production of beers, wines, cheeses and breads etc. where the processes were well worked out and were reproducible. The role of microorganisms in all of these processes was not recognized until the microscopic observations by Anton van Leeuwenhook and the later experiments by Pasteur (see also *Fundamentals in Biotechnology*). Industries developed around non-sterile production of various organic acids together with the rapid development of waste water and solid waste treatment processes that were to lead to major improvements in the health of populations especially in cities. In the 1940s there was rapid development of aseptic fermentation processes (the bioreactor) which lead to the production of antibiotics (penicillin), amino acids, enzymes, steroids, polysaccharides and monoclonal antibodies creating a new range of biotechnology industries. Applied genetics and recombinant DNA technology were to improve important industrial microorganisms and to create new aspects in plant and animal agriculture. Recombinant drug production is now a largely important industrial aspect of biotechnology. Biotechnology is a complex, multifunctional but often maligned activity. Biotechnology will undoubtedly present major opportunities to human development in nutrition, medicine and industry but it cannot be denied that some aspects are creating social-ethical apprehensions.

Notwithstanding, biotechnology will undoubtedly be the major technology of the 21st Century and should be so recognized by the lay public.

1. Introduction

1.1. Biotechnology – What's in a Name?

In recent times there has been a growing concern about the misuse of the word 'biotechnology' as an overall term to cover several different categories. As stated by Anton Lavoisier – 'scientists must be precise in their speaking and writing as in their scientific determinations and measurements' while Lord Kelvin stated – 'that, when a person can define precisely and measure accurately that of which he/she writes or speaks their propositions have credibility, if not they must be regarded as suspect.'

In many circles ' biotechnology' is used as a blanket term to cover a wealth of activities such as brewing, wine production, cheese making, organic acids, antibiotics, monoclonal antibodies as well as genetic modification, whether within- or trans-species and whether by selective breeding or by way of modern molecular biology techniques. Biotechnology has been defined in many ways.

A collective noun for the application of biological organisms, systems or processes to manufacturing and service industries. The integrated use of biochemistry, microbiology and engineering sciences in order to achieve technological (industrial) application capabilities of microorganisms, cultured tissue cells and parts thereof. A technology using biological phenomena for copying and manufacturing various kinds of useful substances. The application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services. The science of the production processes based on the action of microorganisms and their active components and of production processes involving the use of cells and tissues from higher organisms. Medical technology, agriculture and traditional crop breeding are not generally regarded as biotechnology. Really no more than a name given to a set of techniques and processes. The use of living organisms and their components in agriculture, food and other industrial processes. The deciphering and use of biological knowledge. The application of our knowledge and understanding of biology to meet practical needs.

Table 1. Some Selected Definitions of Biotechnology
Source: Smith (2009) *Biotechnology*. 5th Edition. Cambridge University Press

The European Federation of Biotechnology (EFB) considers biotechnology as 'the integration of natural science and organisms, cells, parts thereof and molecular analogues for products and services. The aims of the Federation seek:

- To advance biotechnology for the public benefit;
- To promote awareness, communication and collaboration in all fields of biotechnology;
- To provide governmental and supranational bodies with information and informed opinions on biotechnology;
- To promote public understanding of biotechnology.

For the non-scientist the Concise Oxford English Dictionary states 'biotechnology is the exploitation of biological processes for industrial and other purposes especially the genetic manipulation of microorganisms for the production of antibiotics, hormones, etc.'

In older literature the word biotechnology has arisen in different contexts. Karl Ereky, a Hungarian agricultural economist published in 1919 a paper entitled 'Biotechnology of meat, fat and milk production in large-scale agricultural enterprises'. The word biotechnology was used to cover the interaction of biology with technology, connotating all productions by means of biological transformations.

In 1947 under the heading 'Biotechnology: a new fundamental in the training of engineers biotechnology was considered as a branch of technology concerned with the development and exploitation of machines in relation to various needs of human.

In 1962 the *Journal of Microbiological Technology and Engineering* edited by Elmer L. Gaden changed to *Biotechnology and Bioengineering* and undoubtedly was a major factor "involved in disseminating the word biotechnology to a wider readership, especially in engineering". Biotechnology was viewed as all aspects of the exploitation and control of biological systems.

The word biotechnology has evolved through different forms of usage. What may be called 'traditional' or 'old' biotechnology refers to conventional techniques that have been applied for centuries to produce beers, wines, cheeses and associated other foods using microorganisms and in recent times with the production of antibiotics and solvents of many types. 'New' biotechnology involves all methods of genetic modification by recombinant DNA and cell fusion techniques, together with the further developments of 'old' biotechnology processes.

Unfortunately, in many parts of modern science the term biotechnology is now being used as a substitute for genetic modification and genetic engineering. In the United States in the late 1970-80s, new aspects of genetic engineering were being demonized by activists and the NHI began using the term 'biotechnology' when describing trans-species genetic modifications. The term was then picked up by the media and by politicians and, eventually, found its way into governmental documents and legislation.

In the broadest sense biotechnology applies the principles of technology to the biological sciences and applies the principles of living biological materials to technology. However, from a public aspect the term biotechnology is now more widely recognized from its genetic engineering association and as an icon of high technology. Few realize that which is recognized as traditional biotechnology generates huge worldwide wealth.

While engineers were using the term biotechnology by the late 1960s most biologists waited on the arrival of genetic engineering before it was more widely accepted. The term biotechnology held great fascination within business programs and in press coverage in the 1980-1990s, but undoubtedly the word biotechnology has, to some extent, become an overused buzzword, often with incorrect usage together with a plethora of definitions.

Biotechnology should not be viewed as a single scientific discipline but rather drawing upon a wide range of relevant subjects including microbiology, biochemistry, molecular biology, cell biology, plant biology, immunology, protein engineering, enzymology, mammalian cell culture and a wide range of process technologies **(**see also *Fundamentals in Biotechnology***)**. More relevantly, biotechnology can be viewed as a range of enabling technologies that will be applied in many industrial, environmental, agricultural, medical and veterinary sectors. As stated by McCormick, a former editor of *Nature Biotechnology* 'there is no such thing as biotechnology, there are biotechnologies. There is no biotechnology industry; there are industries that depend on biotechnologies for new products and competitive advantage.'

It is now becoming increasingly accepted that there should be a descriptive foreword when defining biotechnology, e.g. animal cell biotechnology, stem cell biotechnology, plant biotechnology, enzyme biotechnology *etc*. Clearly, the term biotechnology will never remain static and its usage and how it is defined will continue to evolve.

1.2. Biotechnology – A Three Component Central Core

When considering the historical evolution of biotechnological processes it can be seen that for most examples there will be a three component central core. Firstly, there will be the most applicable biological catalyst for the specific function or process followed by the creation of the best possible environment for the catalyst to perform (e.g. containment system or bioreactor with technical backup) and finally, for most advanced systems, the separation and purification of an essential product(s) (downstream processing).

It will be seen, especially with 'traditional biotechnology' that the most effective, stable and convenient form of catalyst will be the whole organism, especially microorganisms of many types. In more recent times, there has been increased use made of mammalian and animal cell cultures in 'new' biotechnology.

Microorganisms with their immense gene pool have shown an almost unlimited synthetic and degradative potential coupled with extremely rapid growth rates. Over time precise specific microorganisms have been selected, modified by mutations and in more recent years by a spectacular array of new molecular biology techniques yielding amazingly improved biological catalysts for biotechnological processes.

Before embarking on a detailed study of the phases of the historical evolution of modern-day biotechnologies, it must be noted that while biotechnology encompasses science, technology, industrial, medical and agricultural applications and increasing public policies, there is a growing unease with certain ways that we now 'use life processes'. This is now generating intense debate on the ethics and philosophy of biotechnology (see also *Public Policy Responses to Biotechnology – Why Genetic Modification arouses Concern: Social, Cultural and Political Impacts*).

It has often been written that biotechnology has its roots in the dawn of history and could be considered as a deliberate application of what we now know as 'microbiology'. While microorganisms were first observed microscopically by Anton van Leeuwenhoek in the seventeenth century the fermentative ability of microorganisms was not to be scientifically demonstrated by Pasteur until 1857-76.

When looking back on the historical evolution or development of biotechnology four distinct phases can be demonstrated:

- Biotechnological production of foods and beverages.
- Biotechnological production of biomass (bakers' yeast), brewers yeast, waste treatment processes and various solvents under non-sterile conditions.
- Biotechnological processes under conditions of sterility and the use of pure single cultures.
- The impact of applied genetics and recombinant DNA technology on biotechnology processes.

Biotechnological production of foods and beverages. Sumarians and Babylonians were drinking beer by 6000 BC; they were the first to apply direct fermentation to product development; Egyptians were baking leavened bread by 4000 BC; wine was known in the Near East by the time of the book of Genesis. Microorganisms were first seen in the seventeenth century by Anton van Leeuwenhoek who developed the simple microscope; the fermentative ability of microorganisms were demonstrated between 1857-76 by Pasteur – the father of biotechnology; cheese production has ancient origins, as does mushroom cultivation. Biotechnological processes initially developed under non- sterile conditions. Ethanol, acetic acid, butanol and acetone were produced by the end of the nineteenth century by open microbial fermentation processes. Waste-water treatment and municipal composting of solid wastes represents the largest fermentation capacity practised throughout the world. Introduction of sterility to biotechnological processes In the 1940s complicated engineering techniques were introduced to the mass production of microorganisms to exclude contaminating microorganisms. Examples include the production of antibiotics, amino acids, organic acids, enzymes, steroids, polysaccharides, vaccines and monoclonal antibodies. Applied genetics and recombinant DNA technology Traditional strain improvement of important industrial organisms has long been practised; recombinant DNA techniques together with protoplast fusion allow new programming of the biological properties of organisms.

Table 2. Historical Development of Biotechnology
Source: Smith (2009) *Biotechnology*. 5th Edition. Cambridge University Press

2. Biotechnology of Traditional Fermented Foods and Beverages

The very roots of modern biotechnology can be seen in traditional food and beverage fermentations. Fermented foods and beverages were derived from plant and animal sources and became an accepted and essential part of the diet in almost all parts of the world (see also *Fermented Foods and their Processing*). Use was made of a wide array of substrates applying techniques of the most primitive nature yet achieving an amazing range of sensory and textural qualities in the final products. Fermented foods include breads, cheeses, yoghurts, sauerkraut, soy sauce, tempeh, fermented fish, while fermented beverages include alcoholic beers, wines, saké, brandy, whisky and non-alcoholic teas, coffee and cocoa. The Egyptians, Sumerians and Babylonians produced alcoholic beverages from barley, sour-dough bread from rye occurred in Europe in 800 BC while accounts of fermented dairy products can be seen in early Sanskrit and Christian works.

2.1. Food Fermentations

Food fermentations in tropical countries have a long history of usage and almost certainly predated those in temperate zones. It is believed that tropical food fermentations may have spread from China to South East Asia over 3000-4000 years ago. The postulated range of fermented foods would include pickles, sauces (especially soya sauce), dried salted and unsalted fish and meats, leaven for fermentations and countless others.

For tropical civilization to grow and expand it was essential to have a constant supply of food and to have food reserves. Whereas in cold climates foods could be stored and preserved by chilling and freezing and by air and sun drying, tropical climates had difficulties in drying raw materials and foods could readily ‘rot’ overnight by microbial activity. Somehow, ancient societies were able to harness this high microbial metabolic activity associated with ‘rotting’ and turn it into beneficial biochemical transformations, yielding improved products, with stability, and acceptable taste and nutrition.

Contributions to the economy of food-winning

- Preserves perishable raw material at low cost, aids dehydration.
- Salvages waste otherwise not usable as food.
- Reduces cooking time, hence reducing demand on the food-winning time by reducing fuel demand.
- Enhances nutritional value by improving digestibility, protein value, and vitamin content.

Protective value

- Destroys toxic, undesirable or anti-digestive components of the raw material; this action increases the range of raw materials available as food.
- Adds positive antibiotic components, destroys harmful biota and protects against infection or infestation.

Psychological and social value

- Improves appearance and flavour, often imparting a meat-like flavour.
- Functions as appetite stimulant and condiment
- Imparts texture, fibre and bite/chewiness, makes the product enjoyable.

Table 3. Virtues Conferred on a Potential Food Material by Fermentative Processes
Source: Stanton. In Wood (1998) Vol. 2. *Microbiology of Fermented Foods*

With our modern understanding of such indigenous fermentations it is hard to contemplate how such village-level fermentations evolved and were repeatable, *viz*. selection and preparation of the raw materials, the conservation of the inoculum and the control of environmental parameters. In essence, food fermentations can be considered as the control of rotting (microbiology) by controlled rotting (applied microbiology).

Stanton has characterized fermented indigenous foods by four main determinates: people, environment, substrates and microorganisms.

2.1.1. People and Environment

The type of climate, or geographic area, was the dominant determinate on the type and range of food fermentations. While temperate civilizations left many artifacts symbolic of their fermentations, this had not happened to any noticeable level in the tropics. Cold climates show less forms of food fermentations, rather food preservations have relied on air/sun drying and ambient cold temperature storage. Temperate societies evolved a wide range of food preservation largely by drying and bacterial fermentation of milk and vegetables. In the humid tropics food microbial fermentations were the main means of food preservations.

2.1.2. Substrate

Substrates, largely define indigenous food fermentations. Old World tropical food fermentations made extensive use of rice, sorghum, and millet, many forms of peas and beans, yams, tree legumes, palm and cycads. New World food fermentations employed maize, cassava, palms, cocoa, agave and various fruits.

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Biographical Sketch

John Edward Smith (BSc. MSc., PhD., DSC) is Currently Emeritus Professor of Applied Microbiology in the newly-formed Institute of Pharmacy and Biomedical Sciences, University of Strathclyde. He is a Fellow of the Institute of Biology, Fellow of the Royal Society of Edinburgh and Founder Fellow of the International Academy of Food Science and Technology. Professor Smith is married to Evelyn and has two daughters and one son, and nine grandchildren.

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