BIOTECHNOLOGY

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Keywords: biotechnology, agriculture, medicine, industry, environment.

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Summary

The practice of biotechnology has often been described as the second oldest profession known to humankind. Biotechnology is a technology using biological systems and parts thereof. It has evolved from traditional practices into modern-day bioprocesses as a result of the use of gene technology [genetic engineering] and microbial machinery in fermentation processes to yield clean and green bioprocesses. The growing acreage of gene-based agriculture, the development of animal and plant factories for the production of biopharmaceuticals, the use of bioremediation technology, socio-ethical considerations and exercise of intellectual property rights are some of the features that characterize the practice of biotechnology at the start of the third millennium. Though biotechnology provides powerful tools for the sustainable development of agriculture and aquaculture and for the emergence of molecular medicine, it is necessary to emphasize that the practice of biotechnology is anchored in a sound knowledge of the basic fundamentals of the science which are often glossed over or ignored. Thus, biotechnology, enriched by inputs from other disciplines, generically embraces a variety of bioprocesses in which traditional and novel practices co-exist and reinforce one another, with an accompanying socio-economic impact in the industrial, environmental, agricultural, medical, pharmaceutical, energy, and food sectors of our everyday life. This introductory chapter covers the historical, current and future perspectives of biotechnology that have a bearing on a wide spectrum of humankind's activities that

range from food and fuel production to conservation of human health and the environment.

1. Historical Development

Biotechnology is a technology using biological systems and parts thereof. Since the basic unit of any biological system is the cell, any biotechnological approach will and does involve living and/or resting cells or their enzymes of many kinds, such as bacteria (prokaryotes), yeast, fungi, plants, and animals (eukaryotes), including man. Depending on the specific purposes and needs, wild-type cells, natural mutants, or genetically modified cells are employed. In most cases, the cells are not grown under natural conditions but are cultivated under more or less strict control in semi-artificial or artificial environments.

Biotechnology has its roots in fermentation, a process requiring a ferment to convert complex molecules into different chemical compounds. Fermentation itself has been practiced for many centuries. Bread, cheese, and pickled cabbage together with beer, mead, and wine making are believed to have occurred under the Egyptians, Romans, Greeks, and Germans around 5000 B.C. The Aztecs in Mexico harvested algae of the genus *Spirulina* for food from alkaline ponds. The origins of a variety of indigenous "fermented" foods and sauces in Africa and Asia using surface culture methods go back thousands of years.

The earliest report of the observation of micro-organisms is that of Antonie van Leeuwenhoek in 1680 describing them as "animalculus." It was in 1856, nearly 200 years later, when Louis Pasteur concluded that yeast cells (Leeuwenhoek's animalculus) are the ferment converting sugars into ethanol and carbon dioxide, that the connection between the living cell and the products were established. A further milestone in this development came in 1881, when the medical doctor Robert Koch pioneered the development of pure culture techniques and in 1897 when Buchner discovered the enzymes in yeast cells.

The establishment of pure culture techniques together with the now ever-increasing biochemical knowledge of unicellular functions (bacteria, yeast) led to the commercial exploitation of these "organic catalysts" in an industry, coining the name "industrial microbiology." The first successful culture of plant cells was achieved in the mid-1930s, but had to wait until the 1950s and 1960s before the development of cultivation techniques allowed further strain development. In a very similar development, the classical mammalian cell culture techniques started only in 1910, when Harrison and Carrel were able to establish complex media for growth. It was not until the late 1950s that many of the nutritional requirements of cultured mammalian cells were fully understood.

As soon as it was realized that not only micro-organisms, but also plants and mammalian cells, could be cultivated and used as organic catalysts in product formation, and that cells of either source could be manipulated by transferring genes from one to the other, that the term "industrial microbiology" had to be widened and became, around 1980, biotechnology.

It is of interest to realize that the word “biotechnology” itself has gone through an evolutionary development since the Hungarian agricultural economist Karl Ereky first introduced it in 1919. He coined his new word to cover the interaction of biology with technology. The first use of the word in the English language appeared in the journal *Nature* in 1933. The most important definition of biotechnology, however, was published in 1938, when Julian Huxley stated, “biotechnology will in the long run be more important than mechanical and chemical engineering.” In 1962, the *Journal of Microbiological Technology and Engineering* changed its name to *Biotechnology and Bioengineering*, whereby its editor, Elmer Gaden, used the word biotechnology representing “all aspects of the exploitation and control of biological systems.” It was only in the late 1970s and early 1980s that the word became more associated with genetic engineering.

It is therefore not surprising to realize why the first commercial applications of technology of biological systems occurred with microbial cells around 1900. It was at that time that the engineering profession got involved in microbial process development joining forces with the microbiologists, and thus the subject areas of industrial microbiology (or applied microbiology) and biochemical engineering evolved. Processes such as bread making, cheese manufacture, brewing, and distilling developed to meet modern commercial requirements for large-scale production, high and consistent quality, competitive cost, and product variety. During the First World War (1914–18) in Germany, baker’s yeast grown on sugarbeet molasses was produced as a protein supplement for human consumption (SCP) and during the Second World War (1939–45) it was *Candida utilis* grown on sulfite waste liquor from pulp and paper manufacture. Commercial production of lactic acid using *Lactobacillus delbrueckii* began in 1881 and citric acid around 1923. The latter began as a surface culture method (that is, solid substrate fermentation), with the submerged *Aspergillus niger* process being introduced after the Second World War.

It is often forgotten that the first cars ever built used ethanol as fuel, produced chemically as well as microbiologically. Industrial alcohol and acetone-butanol fermentations dominated until the 1950s, when oil became cheap and ethylene was introduced into the market.

This enormous development in the chemical and microbial fermentation industry led to the evolvement of the “chemical engineer” and “biochemical engineer,” creating the term “biochemical engineering” in the engineering sciences and “fermentation technology” in the biological sciences. This was particularly pronounced with the start of the antibiotic industries. Although Louis Pasteur suggested that the antagonistic effects of micro-organisms might have therapeutic potential, it was Alexander Fleming in 1928, exactly seventy-two years later, who observed that the fungus *Penicillium notatum* is able to kill the pathogenic bacterium *Staphylococcus aureus*. He was able to demonstrate that the product of the fungus, which he called penicillin, displayed inhibition toward many pathogenic bacteria. It took, however, until 1940 and the enormous casualties in the Second World War for the first commercial plant to be established in the United States, starting the ever-increasing search and production of antibiotics to combat infectious diseases and thus improving health care.

In the context of the antibiotic industry development it should also be of interest to realize that the ability to confer resistance to disease by vaccination was first described in 1798 and the first mass application of the first cholera vaccine was administered in 1885. Mass vaccinations against diphtheria started in the 1930s and further programs and the development of new vaccines happened in the 1950s. This resulted in the explosive development of the commercial production of antibiotics and vaccines around the same time, only fifty to sixty years ago.

The elucidation of the double helix structure of DNA in 1953 by James Watson and Francis Crick opened the floodgates for the development of gene technology in the field of genetics, which was given the name "genetic engineering." Since, by this time, cultivation techniques for biological cells of microbial, plant, and animal/mammalian origin had already been developed, the new gene technology soon spread to all biological systems. It involves the formation of new combinations of heritable material by insertion of foreign genes, produced outside the cell, into a host organism in which they do not naturally occur. The first experiments in which DNA fragments were joined *in vitro* and the recombinant molecule reintroduced into living cells were performed in 1973. Only two years later, the basic technology for the production of monoclonal antibodies from a single ancestor or clone was established. The basic information obtained in these experiments together with new findings in all fields of the biosciences as well as in the chemical, physical, and computer sciences have led to what is now the development of modern genetic engineering. This new powerful methodology can be regarded as a set of biological, genetic, biochemical, chemical, and physical procedures that enable the localization, isolation, characterization, modification, synthesis, and transfer of genetic material.

The application of gene technology or genetic engineering as a research tool has undoubtedly changed nearly all areas of the biosciences and has dramatically increased the rate at which data can be obtained. The enormous and rapid development in plant and animal cell cultivation, together with the new gene technology applicable to all biological systems, led bioscientists and biochemical engineers to realize, in the early 1980s, that the existing terminologies did not encompass this development and it was decided to combine fermentation technology, plant cell technology, animal cell technology, and gene technology under the one name "biotechnology." Therefore, over the past twenty years, all technological applications based on biological systems, whether small or large, rural or urban, medical or non-medical, natural or engineered, fall under this one name "biotechnology." What the inorganic catalyst represents for the chemical industries, finds its counterpart in the organic or biological catalyst of the biotechnology industries.

Often misunderstood, biotechnology is best considered as the integration of the natural and engineering sciences in order to achieve the application of organisms, cells, parts thereof, and molecular analogues for products and services. Biotechnology generically embraces a variety of bioprocesses in which the traditional and novel practices co-exist and reinforce one another with accompanying socio-economic impact in the industrial, environmental, agricultural, medical, pharmaceutical, energy, and food sectors of our everyday life. Genetically engineered strains have been designed to produce potent biopharmaceuticals, agrobiochemicals (such as biofertilizers), biopesticides, and bioremediation agents. Biotechnology has even been used to counteract deterioration of valuable objects of cultural heritage such as monuments, ancient books, and valuable paintings as well as outside strategic metals through improved microorganism-mediated bioleaching. Different components of the microbial world contribute through interlocking biogeochemical cycles to the recycling of nutrients in food chains in aquatic and terrestrial niches, and to the bioconversion of waste residues into useful products, reflecting the various kinds of physiological activities in the maintenance and management of the planet's biological fabric.

There is no doubt that the application of gene technology or genetic engineering of plant cells has made a tremendous impact on traditional agriculture. The implantation of genes for pest resistance should reduce the application of pesticides. Other genes have led to higher yields and to crops containing higher nutritional supplements. This field of plant genetical engineering will largely replace and speed up the natural breeding, mutation. and adaptation processes. This field, plus the successes in animal cell cloning to produce transgenic plants and animals has been revered for its potential to be the "Holy Grail" solution to any of the world's problems. This thought has also sent shockwaves through various communities, because it is feared that biological tinkering is both dangerous and uncontrollable, and perhaps even immoral.

With its transformative capacity in fostering and driving the world's economy, biotechnology has set in motion changing technical and market profiles for the health, pharmaceutical, agricultural, food, and environmental sectors. Coupled to this development come the revolutionary networking information technologies, bioinformatics, and its applications in novel fields, such as telemedicine, tissue engineering, edible vaccines, transgenic food market, DNA-chip computers, and bioprobes for use in space exploration**.** In fact, biotechnology will be a key and integral component of the network household of the future, which is already on the horizon. Such advances and benefits will be accompanied by concerns and problems that focus on biosafety, proprietary, and intellectual property rights and ethics. Cloning and the mimicking of life-sustaining processes and their interaction with the financial markets will be some of the issues that will continue to make the headlines.

Despite the ever-increasing new direction of biotechnology over the last two decades, it should not be forgotten that the practice of basic biotechnology from several hundred years ago is still with us. As outlined earlier, humans in various fields have unwittingly used microbes. The cultural heritage of virtually every civilization provides indelible testimony of the domestication of microbial fermentations. Traditional foods of strong cultural and national identity, such as *kefir* (Bulgaria), *chichi* (Venezuela), *taettemjolk* (Scandinavia), *dahi* (India), *mopwo* (Kenya), *leben* (Egypt and Syria), *tofu* and *tempeh* (Indonesia), *soy sauce* (South-east Asia) and many others are produced from fermentation processes going back several thousands of years. Such traditional knowledge reinforced by important research advances in the field of nutrition and food preservation has contributed to the production of quality-controlled fermented foods that are consumed by three-quarters of the world's population. Today, the preparation of fermented foods is widespread, especially in South-east Asia. Food products derived through the fermentative action of micro-organisms on seed, milk, meat, fish, and vegetables are delicacies that supply protein, and that fortify predominantly starchy staple diets with vitamins and other nutrients badly needed by millions of people subsiding on marginal incomes. Fermented foods such as *tempeh*, *ontjom*, and *tofu* are today commercially processed in industrialized societies as vegetable protein meat substitutes and as sources of meat-like flavors and sauces.

The start of the third millennium has therefore been marked by a paradox in the life sciences. Modern genetic engineering techniques and sophisticated culture skills honed into a fine art over the last two decades has given rise to a new agriculture. Crops have been genetically altered to increase yields for food and energy production, or for resistance to disease and pests, which in turn has led to a steady loss of the wild strains and of biological diversity. How will this affect our natural cycles of matter and the environment? Have we asked ourselves that question? How will genetic engineering affect traditional food production and will pests overcome the resistance of pest-resistant plants as bacteria developed resistant strains against antibiotics?

During the past two decades biotechnology has further expanded into socio-economics and the field of sustainability. David del Porto established in 1999 the co-efficient of sustainability as:

$$\text{sustainability} = \frac{\text{quality of life}}{\text{cost of living}}$$

This field of socio-economic biotechnology moves away from the purely commercial application into the rural and urban development level. Topics, such as "bio-integration," "multi-product development," and "urban- and farm-level applications," have emerged that may help to secure farm development and reduce the trend towards urbanization.

The introduction of biotechnology in the global economy has been marked by extensive public debates on the role of science and technology in global society. Policy makers around the world are beginning to understand the revolutionary implications of biotechnology for economic transformation.

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Biographical Sketches

Horst W. Doelle was born in 1932 and studied biology at the University of Jena, Germany (1950–4). He studied for his doctorate at the University of Göttingen, Germany (1955–7) in antibiotic production. After receiving his doctorate, he worked in the wine and brewing industry in Germany before taking up an appointment with CSIRO in Australia in 1960. After four years' wine research, he took up the challenge to build up microbial physiology and fermentation technology at the Department of Microbiology, the University of Queensland, Brisbane, Australia. He received his D.Sc. in 1976 and his D.Sc. *honoris causa* in 1998. He has participated in and conducted numerous training courses in developing countries. After twenty-nine years' teaching he retired in 1992. His research area was regulation of anaerobic/aerobic metabolism, microbial technology (*Zymomonas* ethanol technology), and socio-economic biotechnology using micro-organisms for waste management.

Edgar DaSilva, a graduate of the University of Bombay in microbiology and chemistry, was awarded the Bachelor of Science Degree (first class with honours) in 1962. In 1966 he obtained his M.Sc. and in 1969 his Doctorate for research studies on cyanobacteria. As a NORAD Fellow, his research on the marine algae at the Norwegian Seaweed Research Institute, Trondheim, Norway in 1970 was followed by a teaching assignment at the University of Helsinki, Finland. Two years later he joined the Institute of Physiology, University of Uppsala, Sweden, as a UNESCO Fellow. A former Vice-President of the World Federation of Culture Collections (WFCC), author of several scientific publications, and member of well-known microbiological societies. Dr DaSilva has been instrumental in the planning and implementation of programs within the framework of the UNESCO global network of microbial resources centres (MIRCENs) since 1977, and other allied biotechnologies. Currently he is the director, Section of Life Sciences, UNESCO, France.