# INDUSTRIAL MICROBIOLOGY AND BIOTECHNOLOGY

Sibi G.

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# Preface

Microbes provide rapid generation times, genetic flexibility, unequalled experimental scale and manageable study systems. The practice of industrial microbiology has its roots deep in antiquity. Long before their discovery, microorganisms were exploited to serve the needs and desires of humans. They preserved milk, fruits and vegetables, and enhanced the quality of life by the resultant beverages, cheeses, bread, pickled foods and vinegar. Industrial biotechnology encompasses the exploitation of the genetic and biochemical machinery of useful microorganisms (bacteria, fungi, yeasts and microalgae) and of higher cells, for the synthesis of bulk and fine chemicals (including vitamins and related factors), pharmaceuticals, enzymes, biomaterials and energy, using renewable resources rather than fossil ones.

A comprehensive index section will assist in navigating through this book when searching for specific topics. The book is divided into two sections and arranged in 33 well illustrated chapters. Part I describes, the use of bioprocessing to make industrial products. Part II describes, the use of microorganisms for the manufacture of organic acids, vitamins, amino acids, enzymes, biopolymers, nutraceuticals, polysaccharides and biosensors.

The book will be useful to industrial microbiologists and students interested in the application of microorganisms for useful purposes. No longer will people think of microbes only as undesirable agents of disease or sources of antibiotics to combat such diseases. They will learn of the useful application of these wonderful creatures to make their lives more enjoyable and healthy, and to contribute to our ever-growing increase in human life expectancy.

***Bangalore*** ***Sibi G***
***India***

# Contents

# CHAPTER - 1

# INTRODUCTION

## Structure



## 1.0 INTRODUCTION

Industrial microbiology is defined as the study of the large-scale and profit motivated production of microorganisms or their products for direct use, or as inputs in the manufacture of other goods. Industrial microbiology is primarily associated with the commercial exploitation of microorganisms, and involves processes and products that are of major economic, environmental and social importance throughout the world. The key aspect of industrial microbiology is relating to production of valuable microbial products via fermentation processes. These include traditional fermented foods and beverages, such as bread, beer, cheese and wine, which have been produced for thousands of years. In addition, over the last hundred years or so, microorganisms have been further employed in the production of numerous chemical feed stocks, energy sources, enzymes, food ingredients and pharmaceuticals.

Originally, the term “fermentation” was used to describe anaerobic processes to convert starch grains into alcohol, a process still used in first-generation biofuels. Fermentation was a non-sterile, empirical endeavour. The first real commercial industrial fermentation application was vinegar production from wine by a continuous “fill and draw” method during the Renaissance in France. Wine in large barrels was allowed to be oxidized by a floating mat of aerobic bacteria. A large part of the liquid containing the acetic acid was then removed from the barrel and replaced with fresh wine; this process step was repeated as long as the oxidative biomass remained active. Today, the term fermentation stands synonymously for any submerged cultivation in a bioreactor, which is now dominated by aerobic processes. Today’s “living factories” comprise wild type, mutated, and recombinant microbial, fungal, plant, animal, mammalian, and stem cells.

Bioprocessing examines the commercial fermentation operations and requirements for large-scale cultivation of microorganisms. This involves the acquisition and development of suitable production strains that must then be provided with nutrients, especially appropriate carbon and energy sources. The object of any industrial fermentation is then to optimize either growth of the organism or the production of a target microbial product. This is normally achieved by performing fermentations under rigorously controlled conditions in large fermenters with culture capacities often in excess of several thousand litres.

The birth of industrial microbiology largely began with the studies of Louis Pasteur. In 1857, he demonstrated beyond doubt that alcoholic fermentation in beer and wine production was the result of microbial activity, rather than being a chemical process. Pasteur also noted that certain organisms could spoil beer and wine, and that some fermentations were aerobic, whereas others were anaerobic. He went on to devise the process of pasteurization, a major contribution to food and beverage preservation, which was originally developed to preserve wine. Today, pasteurization is the routine process of milk preservation.

In the 1940s, initial boost to industrial biotechnology was given by the discovery of antibiotics. In 1929, Alexander Fleming, a british scientist discovered *Penicillium notatum*, a fungus, produced a antibacterial substance through his observations on cultures of *Staphylococcus aureus* that were contaminated with the fungus. The bacterial growth was not found around the colonies in the plate producing clear zones of inhibition. He named the antibacterial substance as penicillin.

Another significant landmark was the discovery of streptomycin by Selman Waksman in 1944. He isolated this antibiotic from the actinomycete, *Streptomyces griseus*. Since penicillin was effective against Gram positive bacteria, there was no drug that could control Gram negative bacteria. Streptomycin was effective against both Gram positive and Gram negative bacteria. The first fungal antibiotic discovered was nystatin in 1950 by two women scientists, Elizabeth Hazen and Rachel Brown.

More recent progress includes the ability to produce monoclonal antibodies for analytical, diagnostic, therapeutic and purification purposes, pioneered by Milstein and Kohler in the early 1970s.

## 1.1 HISTORICAL OVERVIEW OF FERMENTATION

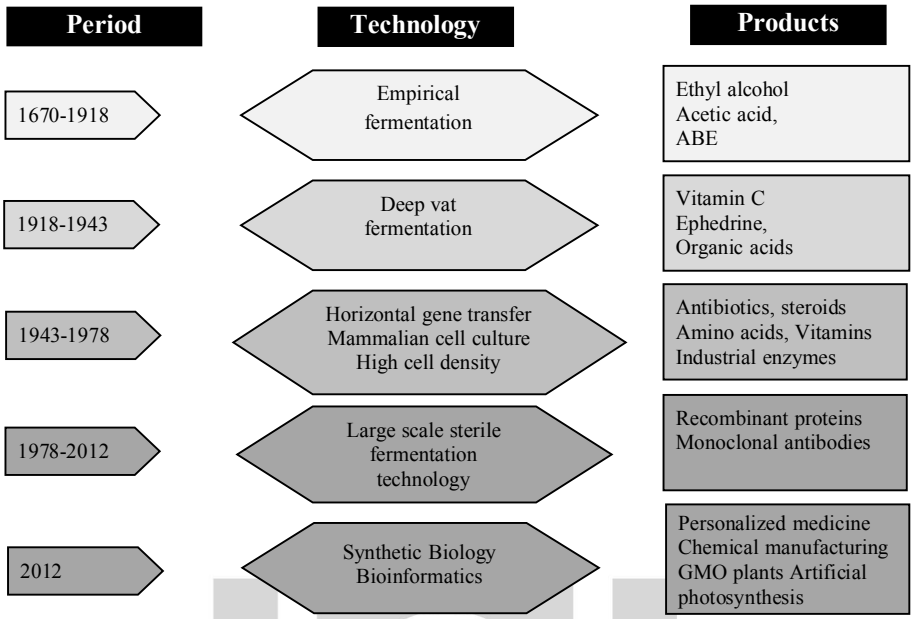


**Fig. 1.1: Historical overview of fermentation**

There are three basic methods for biotechnological production using living matter.

1. The first refers to mass cultivation and production by making use of cells in a highly controlled, closed bioreactor.
2. The use of genetically modified higher plants that produce recombinant products in their leaves, fruits, roots, or other parts is a second option. Transgenic plants are under serious consideration for what is called molecular farming or plant-made pharmaceuticals for products such as insulin, lactoferrin, trypsin, secondary metabolites, and non-pharmaceutical products such as bioplastics.
3. Genetically modified mammals can be used to produce therapeutic proteins in their milk, urine, blood, or other body liquids.

Elements that can influence the success of a large-scale culture :

1. Genotype of the cell that is controlled and steered by the physicochemical environment within the bioreactor, for which a whole arsenal of in-line sterilizable sensors are available for control.
2. Composition of the culture medium, which is ideally chemically defined and simple. Moreover, when formulating a culture medium recipe, the coalescence characteristics of the medium, which affect kLa, or the foaming behaviour, must be taken into consideration early.
3. Cultivation conditions (T, pH, $pO_2$, $pCO_2$, mixing time and shear), which are maintained by the bioreactor's capacity for heat, gas, and momentum transfer. In most cases, ad hoc hardware changes to industrial bioreactors are limited to changing turbines and impellers only.
4. Operating mode such as batch, fed-batch, continuous, or perfusion.

## 1.2 ECONOMICS AND SCALE OF MICROBIAL PRODUCT FERMENTATIONS

The type of fermentation used, as well as its size, duration, and nutrient profile, will depend critically on the nature of the microbial product. For "low-value, high-volume" products, such as citric acid and xanthan gum, high-capacity fermentors (often up to 800 $m^3$ in volume) are generally used. However, the duration of the fermentation process and the costs of nutrients and utilities (heating, cooling, and air) are the critical factors in the overall profitability of this business.

Medium-value, medium-volume products, such as antibiotics are typically made in fermentors that are considerably smaller (100 - 200 $m^3$), and again the duration and the utility and nutrient costs are significant factors.

High-value ; low-volume products, such as recombinant therapeutic proteins are made in small (approximately 400 L, i.e., 0.4 $m^3$) fermentors for which the cost of the nutrients and utilities is a minor factor in the overall feasibility and profitability.

For all but the high-value products, nutrient costs (especially of the primary carbon source) are critical. Depending on the vagaries of world commodity markets, complicated further by artificially imposed trade tariffs, the availability and, in turn, cost of nutrients can fluctuate at alarming rates.

## 1.3 APPLICATIONS OF INDUSTRIAL MICROBIOLOGY AND BIOTECHNOLOGY

Applications are as follows :

1. It is applied in quality control department of foods, beverages, pharmaceutical, dairy and chemical industries.
2. It can be applied in waste disposal and sewerage treatment systems and its research and development.
3. Antibiotics and antimicrobial products are produced, which are important for treatment of various diseases.
4. Various health care products like insulin, antibodies and hormones are produced.
5. Research and development is carried out in diagnostic assay systems and r-DNA technology. These techniques are used in the development of vaccines and various metabolites production to avoid and treat various diseases.

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