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Faculty Of Engineering & Tecxhnology

Bioprocess Engineering BBT-611

Submitted By-
Namrata Singh
Department Of Biotechnology

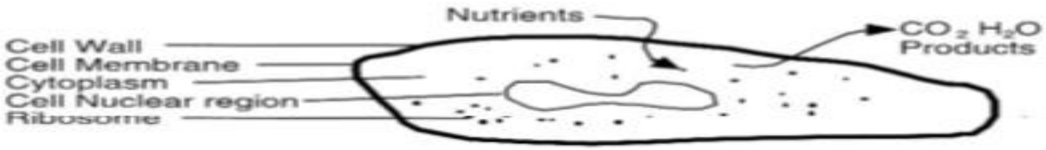
What is Bioreactors?

“An apparatus for growing organisms (yeast, bacteria, or animal cells) under controlled conditions. Used in industrial processes to produce pharmaceuticals, vaccines, or antibodies. Also used to convert raw materials into useful byproducts such as in the bioconversion of corn into ethanol.”

Basis:

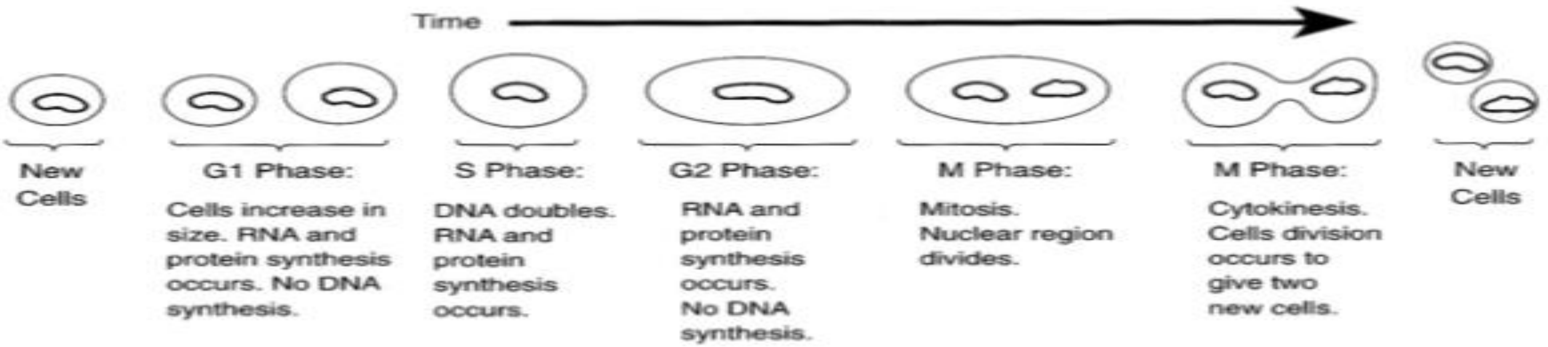
- They are systems or devices that supports a biologically active environment
- They are vessels in which a chemical process is carried out which involves organisms or biochemically active substances derived from such organisms
- They can be either aerobic or anaerobic
- They are commonly cylindrical, ranging in size from liters to cubic meters, and are often made of stainless steel
- They supply a homogeneous (same throughout) environment by constantly stirring the contents.
- They give the cells a controlled environment by ensuring the same temperature, pH, and oxygen levels.

Industrial Bioreactors



(a)

(b)



[Cells] + [Carbon source] + [Nitrogen source] + [Oxygen source] + [Phosphate source] + ⋯

→ Culture media conditions (pH, temperature, etc.) →

[CO_2] + [H_2O] + [Products] + [More cells]

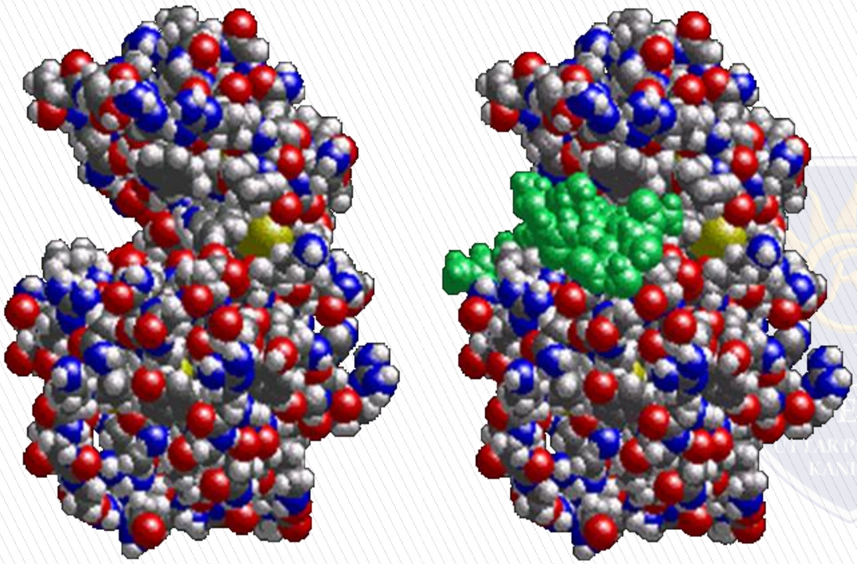
Limiting substrate:

•The substrate or substrate(s) (energy source, carbon source and/or nutrient source) which is/are first exhausted in batch growth. This substrate(s) has a direct influence on the kinetics of cell growth.

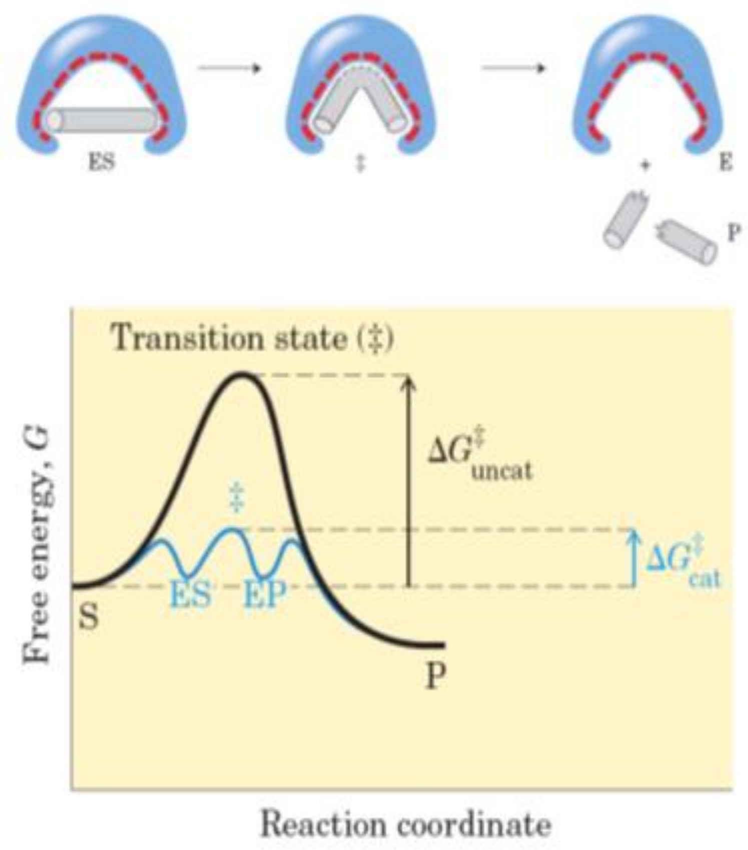
In excess:

•The substrate or substrate(s) (energy source, carbon source and/or nutrient source) which is/are not exhausted at the end of batch growth. This substrate(s) has no effect on the kinetics of cell growth.

Biological Catalyst-Enzymes



$$E + S \rightleftharpoons ES \rightleftharpoons EP \rightleftharpoons E + P$$



Reaction Rate For Enzymes

Michaelis-Menten kinetics

Maud Menten and Leonor Michaelis

Michaelis-Menten kinetics

$v0=rP=-rS=Vmax[S]/Km+[S]$

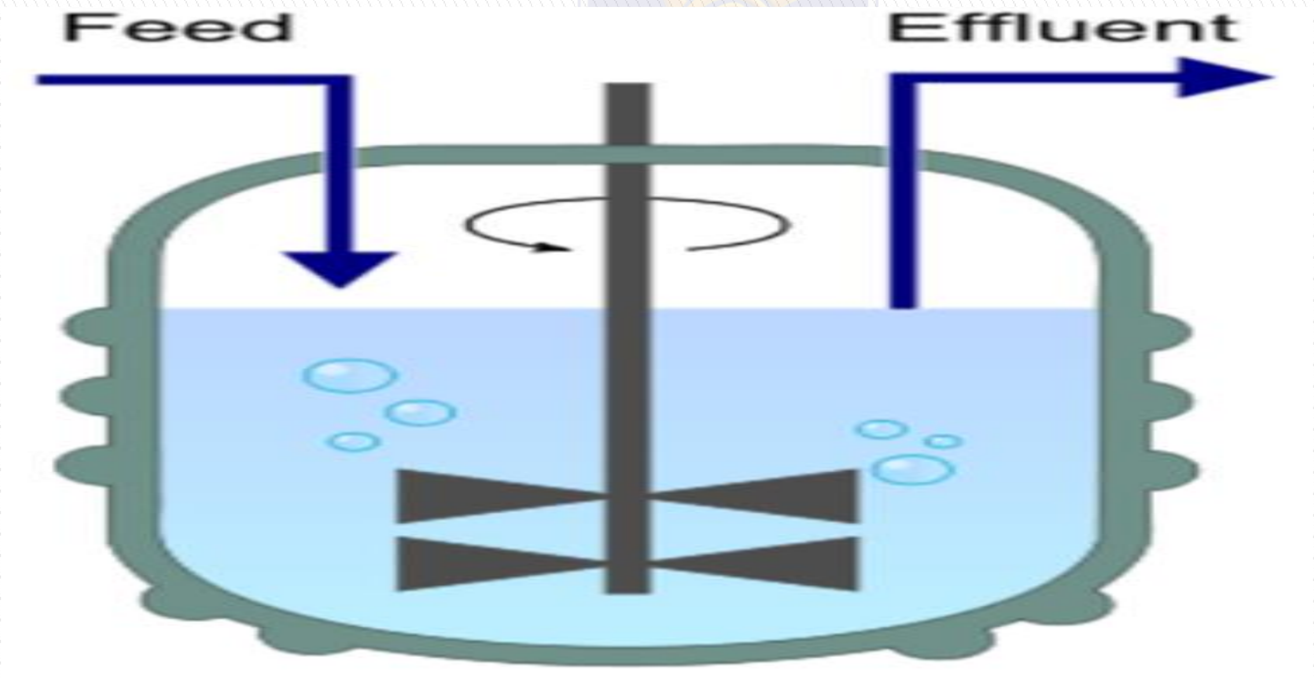
where, v0 is the initial 'reaction velocity', rp is the rate of production of the product, rs is the rate of production of the substrate, S is substrate, P is product, and [] represents concentration.

This equation governs the initial reaction rates (i.e., not including the reversion of products).

Reactor types

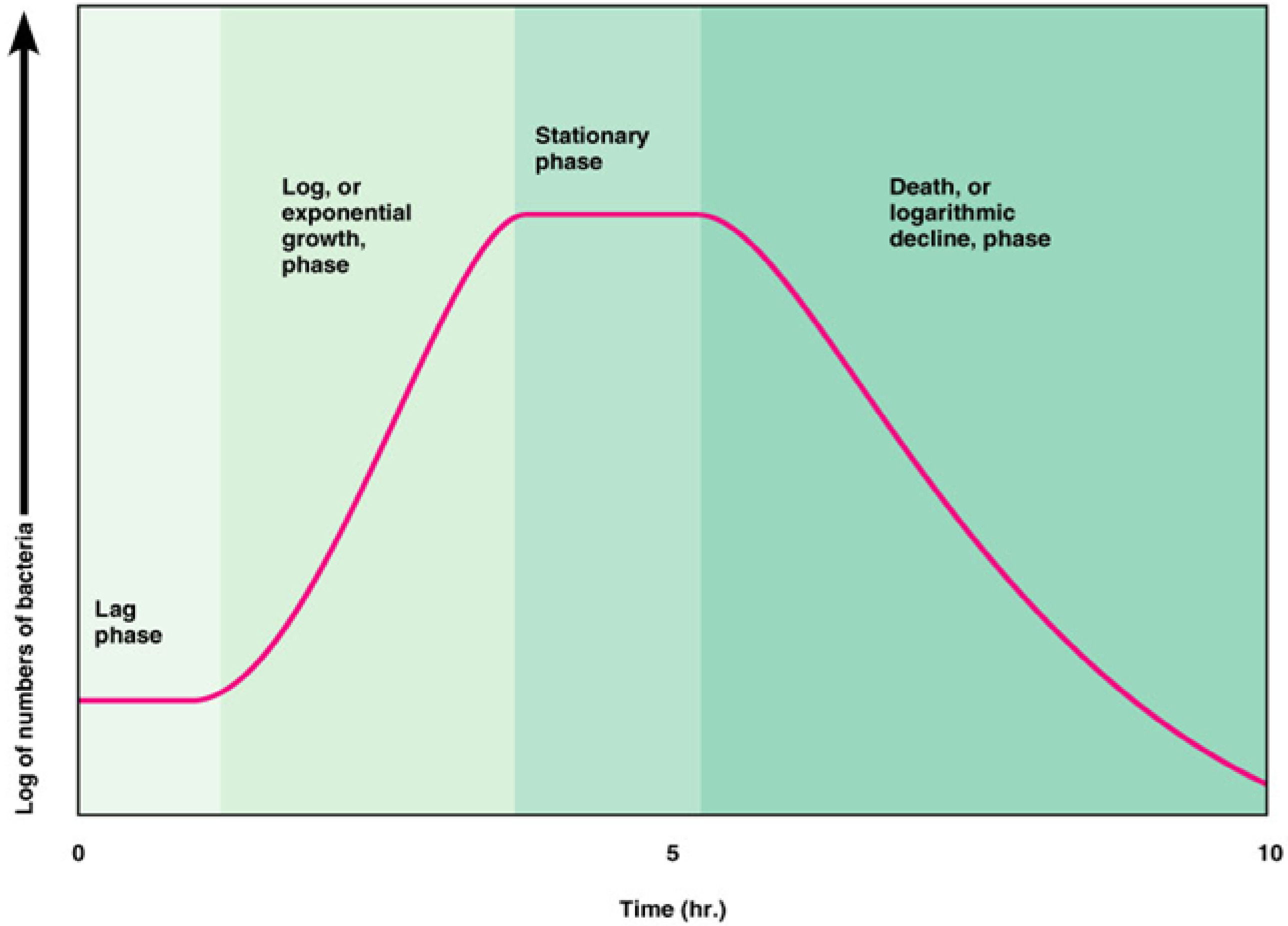
•Chemostat (chemical environment is static)

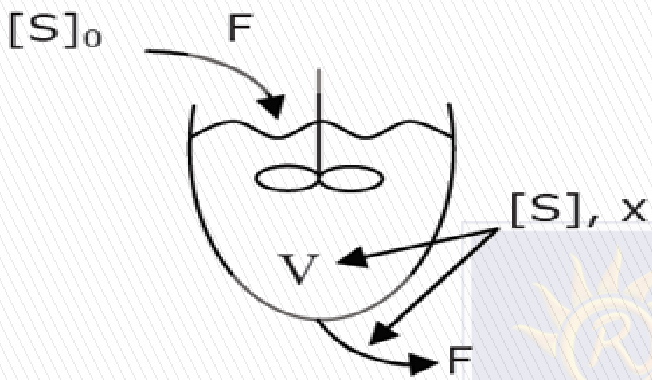
•A bioreactor to which fresh medium is continuously added, while culture liquid is continuously removed to keep the culture volume constant



Bioreactor Design

- Oxygenation for aerobic microorganisms
- Temperature management
- Methods for monitoring the culture
- Sterility


Log of numbers of bacteria
Lag phase
Log, or exponential growth, phase
Stationary phase
Death, or logarithmic decline, phase
0
5
10
Time (hr.)

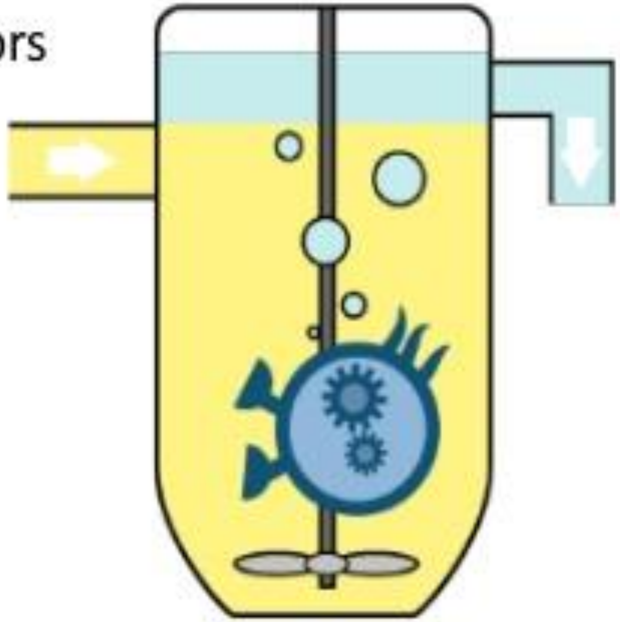


where

- [S] is the concentration of growth limiting substrate
- F or V˙ is the volumetric flow rate of S into the chemostat
- V is the reactor volume
- x is the biomass per unit volume (x = biomass/V)
- μ is the biomass growth rate
- τ is the residence time in the reactor (τ=V/F)
- D is the dilution rate (D=F/V)
- Cell growth kinetics: rx=μx

BIOREACTORS TYPES

1. Continuous Stirred Tank Bioreactors
2. Bubble Column Bioreactors
3. Airlift Bioreactors
4. Fluidized Bed Bioreactors
5. Packed Bed Bioreactors
6. Photo-Bioreactors



1. Continuous Stirred Tank Bioreactor

The most important type of bioreactor for industrial production processes.

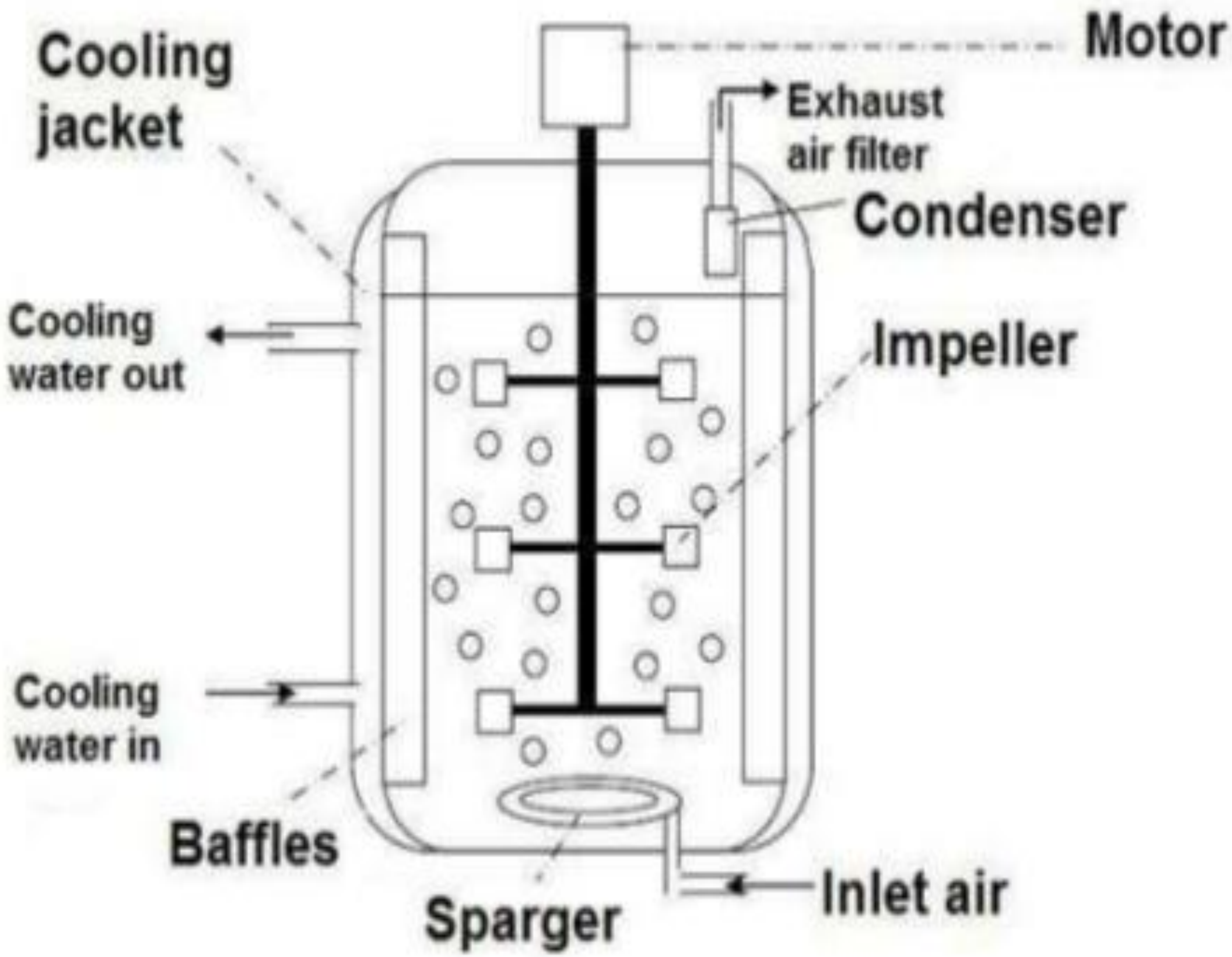
Low capital and operating costs.

Depending largely on the amount of heat to be removed, the stirrer may be top- or bottom driven.

Tanks are fitted with baffles, which prevent large central vortex as well as to improve mixing.

High agitation and aeration cause major problems such as foaming, which may lead to unknown contamination.

Stirred tank bioreactor


Cooling
jacket
Motor
Exhaust
air filter
Condenser
Cooling
water out
Impeller
Cooling
water in
Baffles
Sparger
Inlet air

2. Bubble Column Bioreactor

Used in production of Baker's yeast, beer and vinegar.

Also used in aeration and treatment of wastewater.

In bubble columns, the hydrodynamics and mass transfer depend on the size of bubbles and how they are released from the sparger.

3. Airlift Bioreactor

Mixing is accomplished without any mechanical agitation.

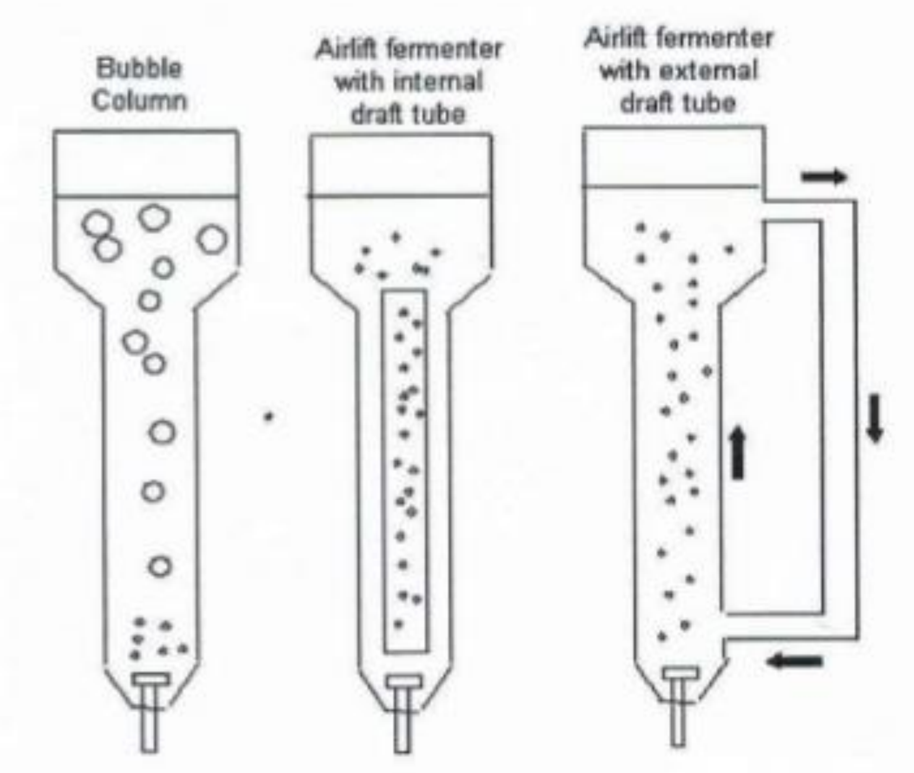
Used for tissue culture because the tissues are sensitive to shear stress, thus normal mixing is not possible.

Air is fed into the bottom of a central draught tube through a sparger ring. The flow passes up through the draft tube to the head space of the bioreactor, where excess air, by-product and CO_2 disengage.

In general, airlift bioreactors the following features:

- Internal loop or
- External loop
- Draft tubes

Airlift Bioreactor



Airlift Bioreactor Advantages

Low shear, which means it can be used for plant and animal cells.

Since there is no agitation, sterility is easily maintained.

In a large vessel, the height of the liquid can be as high as 60m, the pressure at the bottom of the vessel will increase the oxygen solubility, thus increase the mass transfer.

Extremely large vessel can be constructed.

Disadvantage of Airlift Bioreactor

High capital cost with large scale vessel.

High energy cost. Although an agitator is not required, a greater air throughput is necessary, and the air has to be at higher pressure, especially if large scale.

As the microorganism circulate through the bioreactor, the conditions change, and it is impossible to maintain consistent levels of carbon source, nutrients and oxygen throughout the vessel.

The separation of gas from the liquid is not very efficient when foam is present.

4. Immobilized Bioreactor

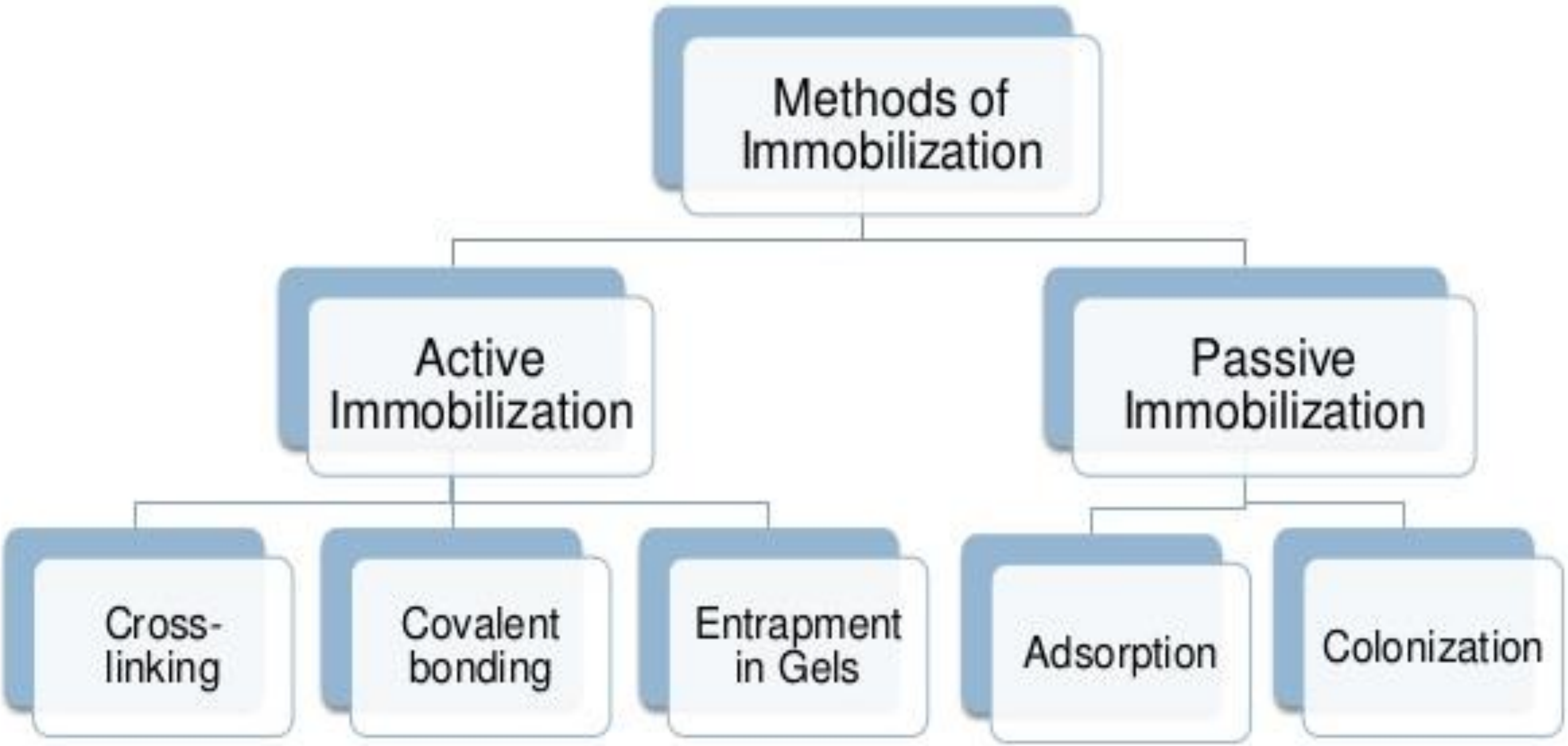
Enzymes, viable cells, plant cells and animal cells can be immobilized.

It can be divided into stirred tank reactors, fixed bed reactors, fluidized bed reactors. These reactors can also be combined or modified.

The choice of reactor design for an ICB would depend on:

- Mass transfer requirements, eg. Oxygen supply and gas removal
- Particle characteristics, eg. In stirred tank reactor, damage to the particle is greater than in packed bed reactor.
- Kinetic considerations

Methods of Immobilization



Advantages of Immobilized Bioreactor

Application to multi-step enzyme reaction may be possible.

The enzyme activity yield on immobilization is high.

Operational stability is generally high.

Operations for enzyme extraction and/or purification are unnecessary.

High cell densities can be employed.

Cell densities and enzyme activities can be expected to be maintained over a long period of operation.

Products can be easily removed from immbilized cells

Immobilized cells appear to be less susceptible to microbial contamination.

Disadvantages of Immobilized Bioreactor

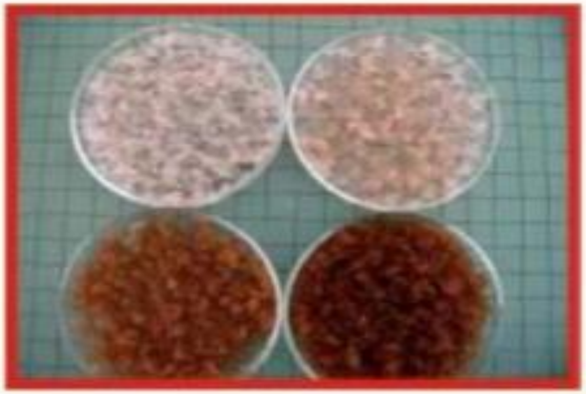
The cells may contain numerous catalytically active enzymes, which may catalyze unwanted side reactions.

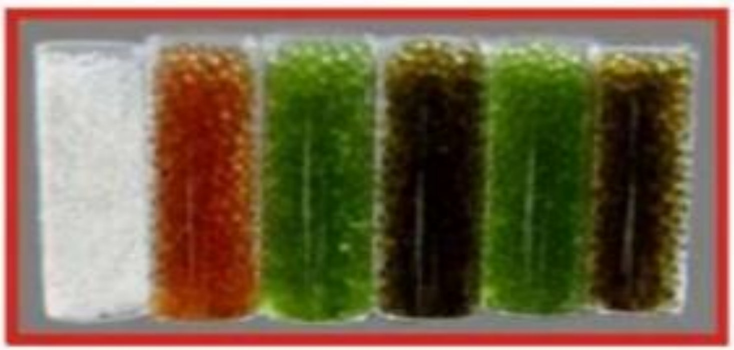
The cell membrane itself may serve as a diffusion barrier, thus reducing productivity.

Contamination by cells leaking out from carriers may occur.

The physiological state of the microorganism cannot be controlled.

Immobilized Plant Cell Culture





Immobilized yeast cells

Membrane Reactor

A membrane reactor is a flow reactor within which membranes are used to separate cells or enzymes from the feed or product streams.

Usually a continuous system.

Products may also be removed continuously, but in some applications they must be harvested intermittently or at the end of the run.

Polymeric microfiltration (0.1 – 5 μm) or ultrafiltration (20 – 1000 Å) membranes are most commonly used.

Membranes are obtained in hollow-fiber or flatsheet form.

Application in enzymatic reaction, production of primary and secondary metabolites by microorganisms and plant cells, generation of antibodies by mammalian cells.

Application of Membrane Reactor

A consequence of the retention of cells or enzymes within the reactors. This allows the reactors to be continuously perfused without worrying about washout.

Membrane also provide an in-situ separation of the cells or enzymes from the product.

Compared to immobilization technique, no chemical agents or harsh conditions are employed.

Challenges in Membrane Reactor

Cells and enzymes entrapped within membrane reactors are subject to diffusion and convection that can render their distribution heterogeneous.

An uneven flow distribution among the various channels in a membrane reactor can have significant effect.

Photobio Reactor

Designed for applications such as wastewater treatment, water quality management, remediation of contaminated soil.

Organisms used: green and blue-green (bacteria) algae, photoautotrophs, photoheterotrophs

Culture systems utilizing ponds or rectangular tanks with limited mixing.

Deep channeled culture systems with a closed circulating loop and better mixing.

Photobioreactor