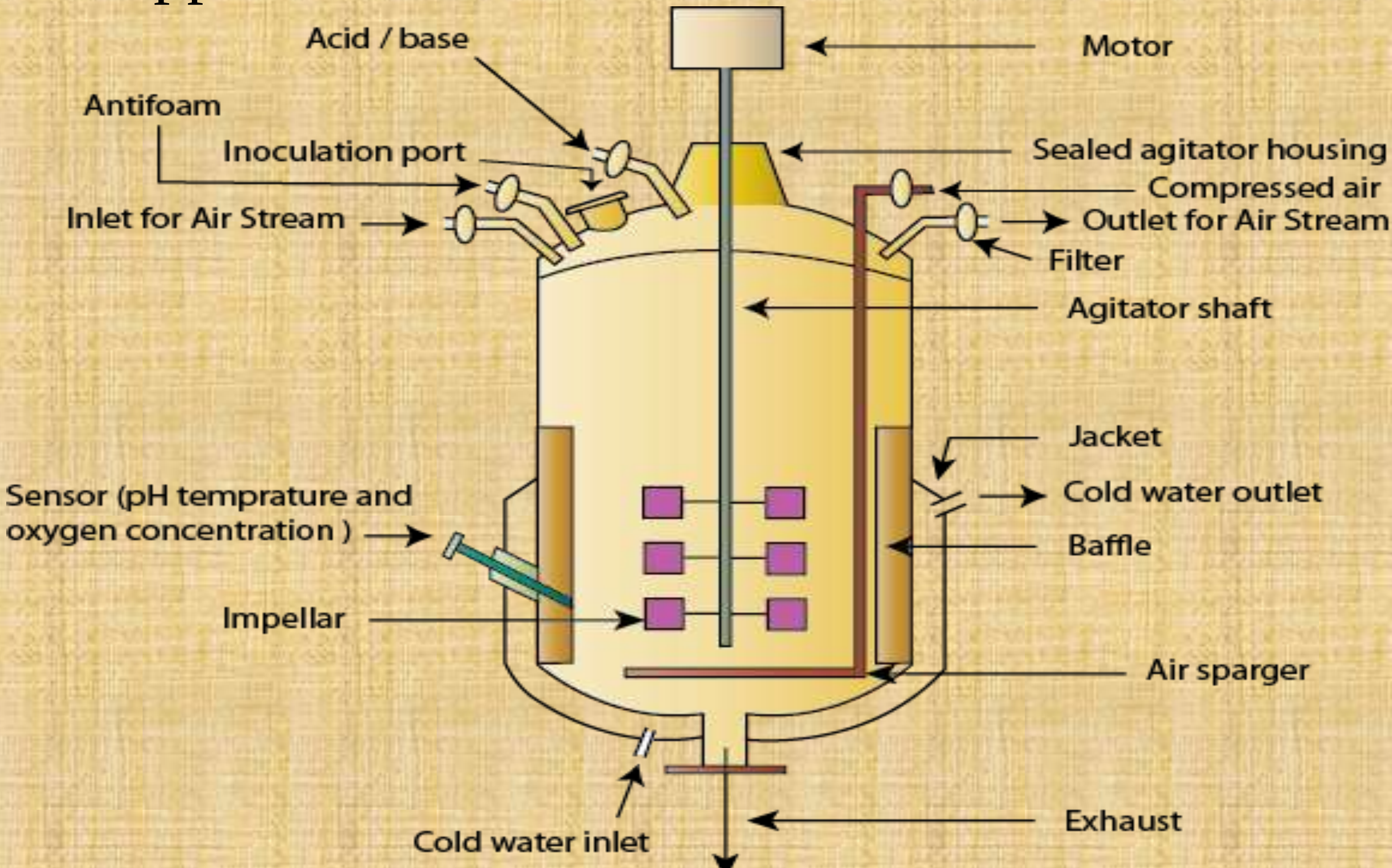
WHAT IS A BIOREACTOR?

- An apparatus (usually jacketed cylindrical SS vessel) for growing organisms such as bacteria, viruses, or yeast that are used in the production of pharmaceuticals, antibodies, or vaccines, or for the bioconversion of organic wastes.
- Under optimum conditions of gas (air, oxygen, nitrogen, and carbon dioxide) flow rates, temperature, pH, dissolved oxygen level, and agitation speed, the microorganisms or cells will reproduce at a rapid rate

In other words……

A bioreactor is a vessel or a device designed to sustain and support life of cell and tissue cultures.



TYPES OF BIOREACTORS

The major types are:

(1) Continuous Stirred Tank Bioreactors

(2) Bubble Column Bioreactors

(3) Airlift Bioreactors

(4) Fluidized Bed Bioreactors

(5) Packed Bed Bioreactors

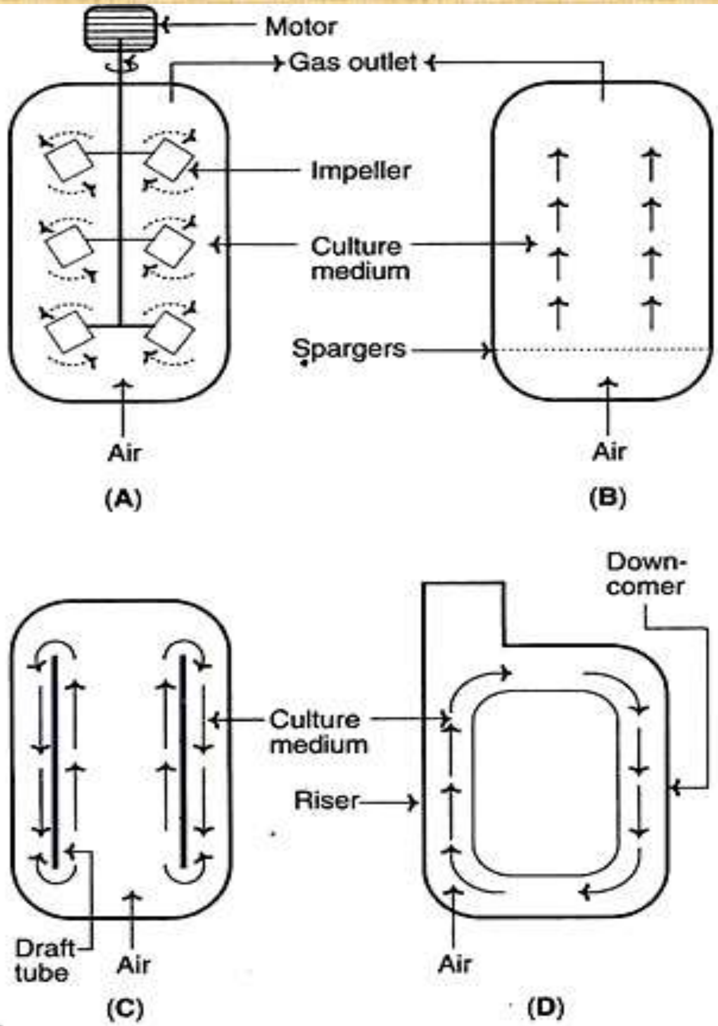


Fig. 19.1 : Types of bioreactors (A) Continuous stirred tank bioreactor (B) Bubble column bioreactor (C) Internal-loop airlift bioreactor (D) External-loop airlift bioreactor.

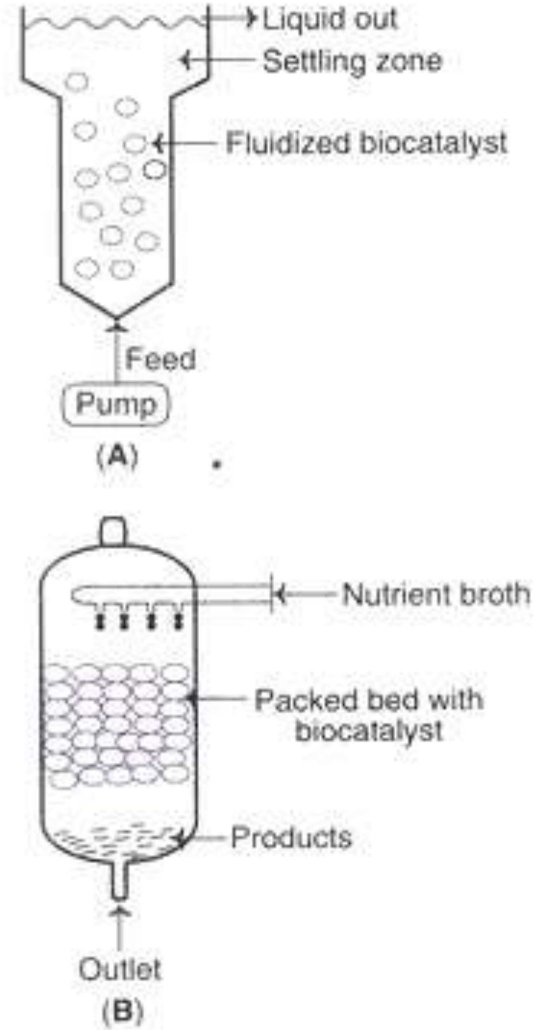


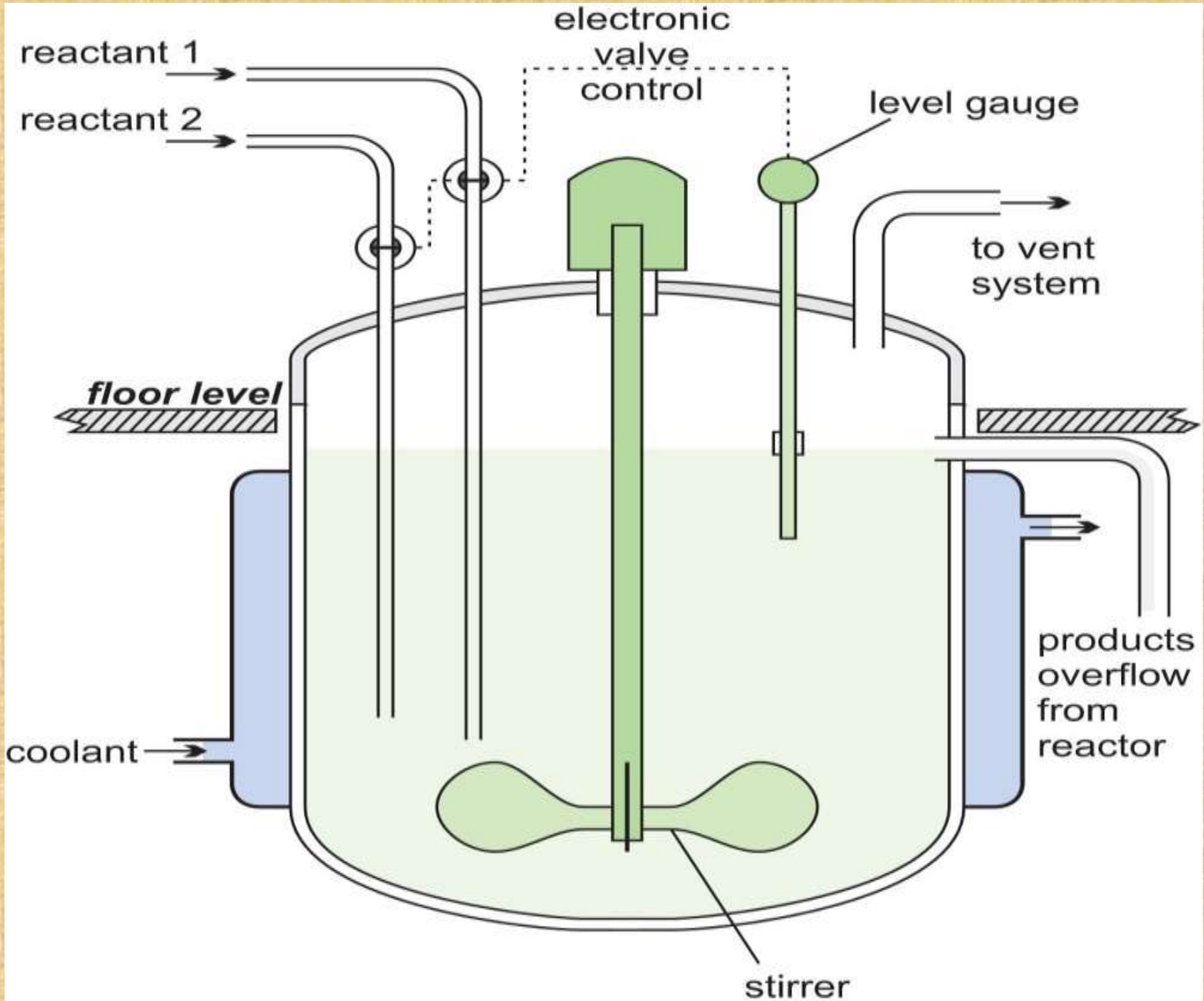
Fig. 19.3 : Types of bioreactors (A) Fluidized bed bioreactor (B) Packed bed bioreactor.

CONTINUOUS STIRRED TANK REACTORS

DEFINITION:

The Continuous Stirred Tank bioreactor is the classical design and still the most widely used bioreactor. Most production facilities and FDA approved production processes for biopharmaceuticals are based on the stirred tank bioreactors. The scale-up process from laboratory to production sized systems is therefore based on this design as well. This cylindrical bioreactor uses a top or bottom mounted rotating mixing system. The aspect ratio is usually between 3-5.

- ❖In Continuous Stirred Tank Bioreactor, the contents of the vessel no longer vary with time, this applies to the hold up of micro-organisms and the concentration of the components of the medium in the fermentor.
- ❖Steady state conditions can be achieved by either **Chemo static** or **Turbid static** principles which is used to control the flow rate.
- ❖ Both these methods have been employed in practice, though the former is obviously the simpler from every view point.


electronic
valve
control
reactant 1
reactant 2
level gauge
to vent
system
floor level
products
overflow
from
reactor
coolant
stirrer

FEATURES

1. Microbial reactors have impellers to provide agitation and generally have baffles from the walls to prevent vortexing of the fluid.
2. High mechanical stress in the stirrer shaft, bearings and seal.
3. Bioreactors for animal cell cultures usually do not have baffles (to reduce turbulence).
4. The aspect ratio (height-to-diameter ratio) of the vessel is 3-5 for microbial cultures but is normally less than 2 for animal cell culture.
5. Sparger: gas is sparged at the bottom using a perforated pipe ring sparger.
6. Different types of impellers (Rustom disc, concave bladed, marine propeller etc.) are in use.

MECHANISM

- ❖In stirred tank bioreactors, the air is added to the culture medium under pressure through a device called sparger.
- ❖The sparger may be a ring with many holes or a tube with a single orifice.
- ❖The sparger along with impellers (agitators) enables better gas distribution system throughout the vessel.
- ❖The bubbles generated by sparger are broken down to smaller ones by impellers and dispersed throughout the medium.
- ❖This enables the creation of a uniform and homogeneous environment throughout the bioreactor, which enables the bioprocess reaction to efficiently perform.
- ❖The bioprocess endures the desired product through the vent.

ADVANTAGES

1. Continuous operation
2. Good temperature control
3. Easily adapts to two phase runs
4. Good control over parameters and environment
5. Simplicity of construction
6. Flexible and Low operating (labor) cost and investment needs
7. Easy to clean
8. Can cope up with high concentrations due to superior heat transfer
9. Efficient gas transfer to growing cells and mixing of the contents

DISADVANTAGES

1. The need for shaft seals and bearings.
2. Size limitation by motor size, shaft length and weight.
3. Foaming is often a problem.
4. Consumption of power is more due to the mechanical pressure pumps.

APPLICATIONS

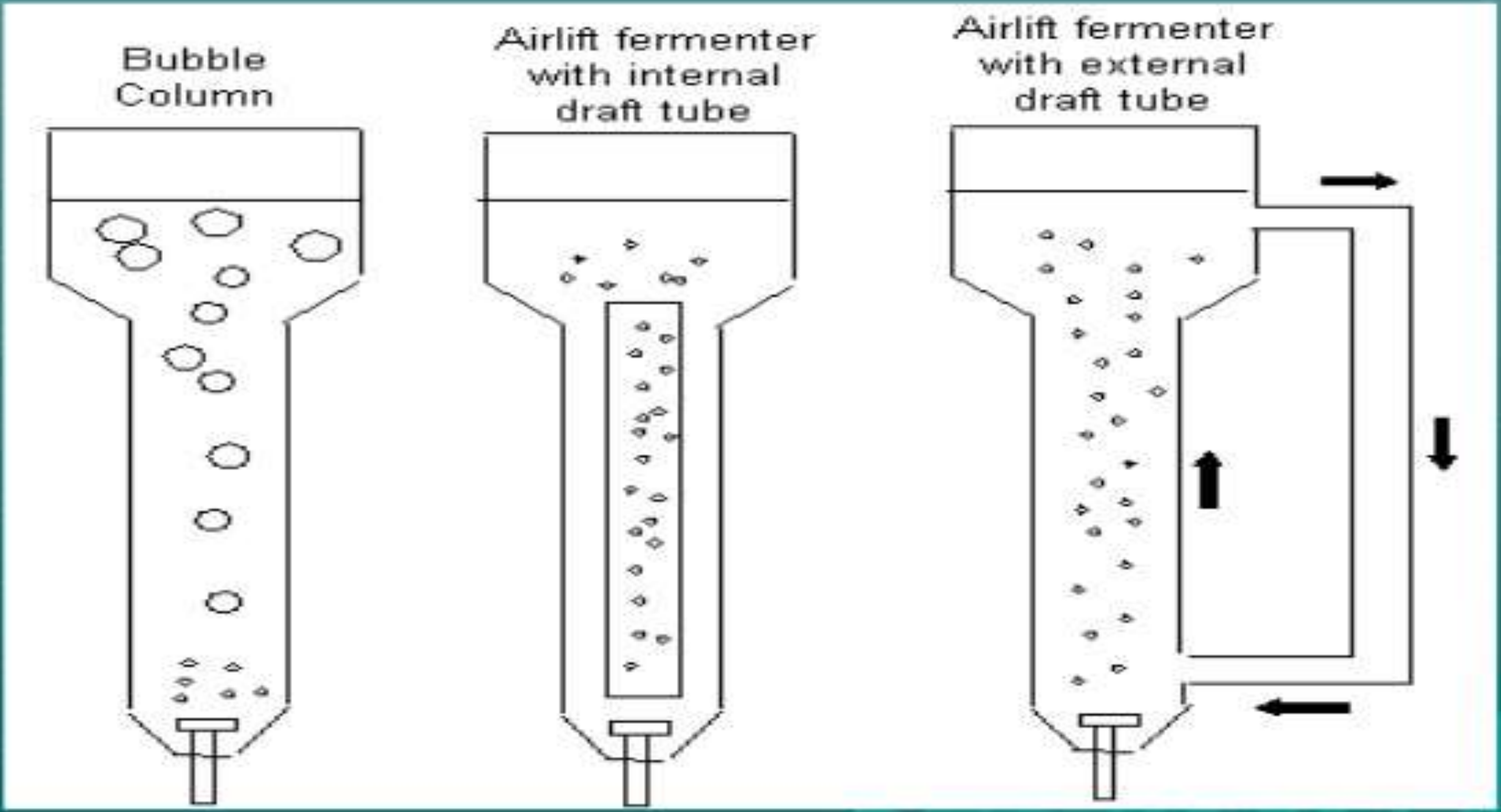
1. The most successful continuous systems to date have been those employing yeasts and bacteria, in which the desired products are the cells.
2. Production of primary metabolites, enzymes and amino acids.
3. The production of alcohol(product clearly associated with growth or energy producing mechanisms).
4. The most widely used is the activated sludge process used in waste water treatment industry.

BUBBLE COLUMN BIO-REACTORS

DEFINITION:

1. Bubble column bioreactors are tall column bioreactors where gas is introduced in the bottom section for mixing and aeration purposes.
2. The vessel used for bubble column bioreactors is usually cylindrical with an aspect ratio of 4-6.

Bubble driven bioreactors



FEATURES

1. Usually the height-to-diameter ratio is 4-6.
2. Gas is sparged at the base through perforated pipes or plates or metal porous spargers.
3. O_2 transfer, mixing and other performance factors are influenced mainly by gas flow rate and rheological properties of the fluid.
4. Mixing and mass transfer can be improved by placing perforated plates or vertical baffles in the vessel.
5. Does not have a draft tube.

MECHANISM

1. In the bubble column bioreactor, the air or gas is introduced at the base of the column through perforated pipes or plates, or metal micro porous spargers and causes a turbulent stream to enable gas exchange.
2. The flow rate of the air/gas influences the performance factors —O_2 transfer, mixing.
3. The bubble column bioreactors may be fitted with perforated plates to improve performance.
4. The reactants are compacted in the presence of finely dispersed catalyst and thus produce the products using fermentation method.

ADVANTAGES

1. Have high volumetric productivity and excellent heat management.
2. Better utilization of the plate area and flow distrubution.
3. Self regulating.

DISADVANTAGES

1. Less efficient than other bioreactors
2. Does not have draft tube
3. Higher catalyst consumption than the fixed bed
4. Higher installation cost and difficult to design

APPLICATIONS

1. The reactor is commonly used in the culture of shear sensitive organisms. E.g.: mould and plant cells
2. Productions of chemicals and pharmaceuticals.
3. Also for fermentation processes.

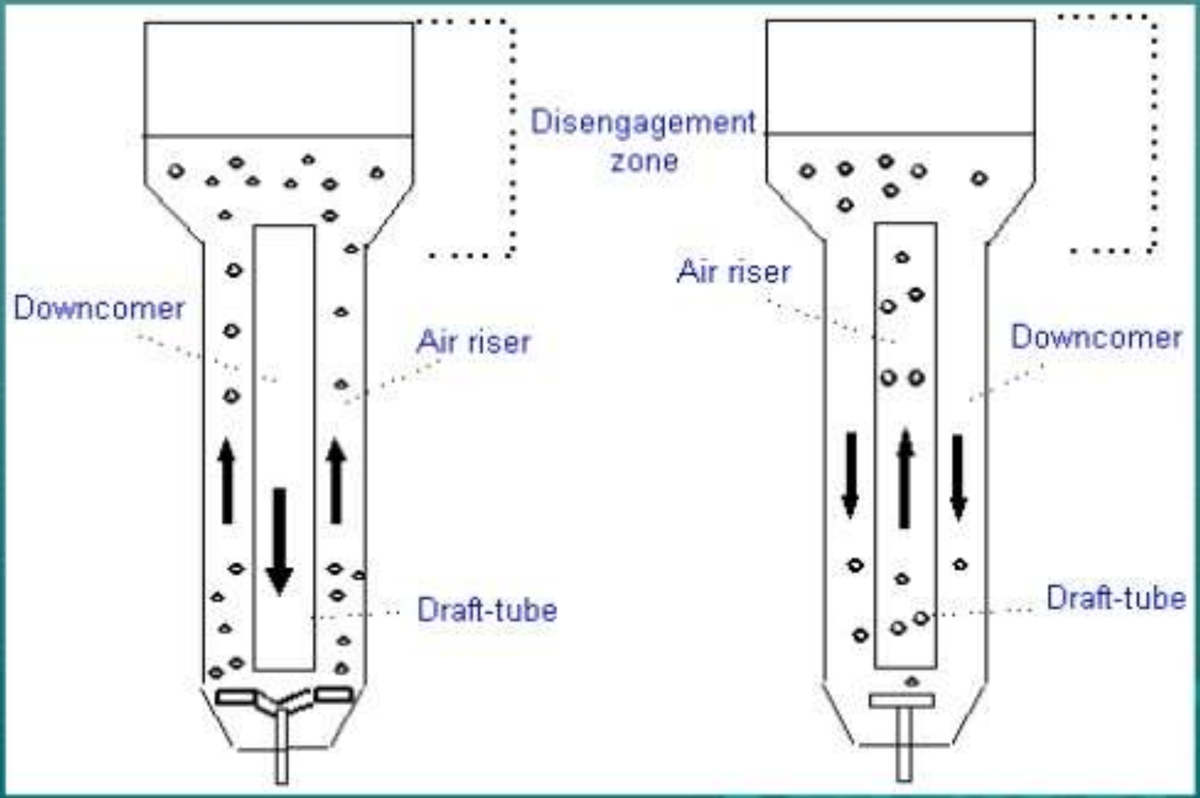
AIR-LIFT BIO-REACTORS

DEFINITION:

Air-lift bioreactors are similar to bubble column reactors, but differ by the fact that they contain a draft tube. The draft tube is always an inner tube (this type of air-lift bioreactor is called “air-lift bioreactor with an internal loop”) or an external tube (called “air-lift bioreactor with an external loop”), which improves circulation and oxygen transfer and equalizes shear forces in the reactor.

- Internal-loop airlift bioreactor has a single container with a central draft tube that creates interior liquid circulation channels. These bioreactors are simple in design, with volume and circulation at a fixed rate for fermentation.
- External loop airlift bioreactor possesses an external loop so that the liquid circulates through separate independent channels.
- These reactors can be suitably modified to suit the requirements of different fermentations.
- In general, the airlift bioreactors are more efficient than bubble columns, particularly for more denser suspensions of microorganisms.
- This is mainly because in these bioreactors, the mixing of the contents is better compared to bubble columns.

Airlift bioreactor



FEATURES

1. Separated as two zones: the sparged zone is called the riser, and the zone that receives no gas is the downcomer.
2. The bulk density in the riser region is lower than that in the downcomer region, causing the circulation (so circulation is enhanced if there is little or no gas in the downcomer).
3. For optimal mass transfer, the riser to downcomer cross-sectional area ratio should be between 1.8 and 4.3.
4. The rate of liquid circulation increases with the square root of the height of the airlift device. Consequently, the reactors are designed with high aspect ratios.
5. A gas-liquid separator in the head-zone can reduce the gas carry-over to the downcomer and hence increase the

MECHANISM

1. In general, the performance of the airlift bioreactors is dependent on the pumping (injection) of air and the liquid circulation.
2. It is different from the Stirred tank bioreactor that needs the heat coat or plate surrounding the tank to make warm bioreactor. It is clear enough that the Airlift bioreactor has greater heat-removal compare to Stirred tank.

I. Two-stage airlift bioreactors are used for the temperature dependent formation of products.
II. Growing cells from one bioreactor (maintained at temperature 30°C) are pumped into another bioreactor (at temperature 42°C).
III. There is a necessity for the two-stage airlift bioreactor, since it is very difficult to raise the temperature quickly from 30°C to 42°C in the same vessel.
IV. Each one of the bioreactors is fitted with valves and they are connected by a transfer tube and pump.
V. The cells are grown in the first bioreactor and the bioprocess proper takes place in the second reactor.

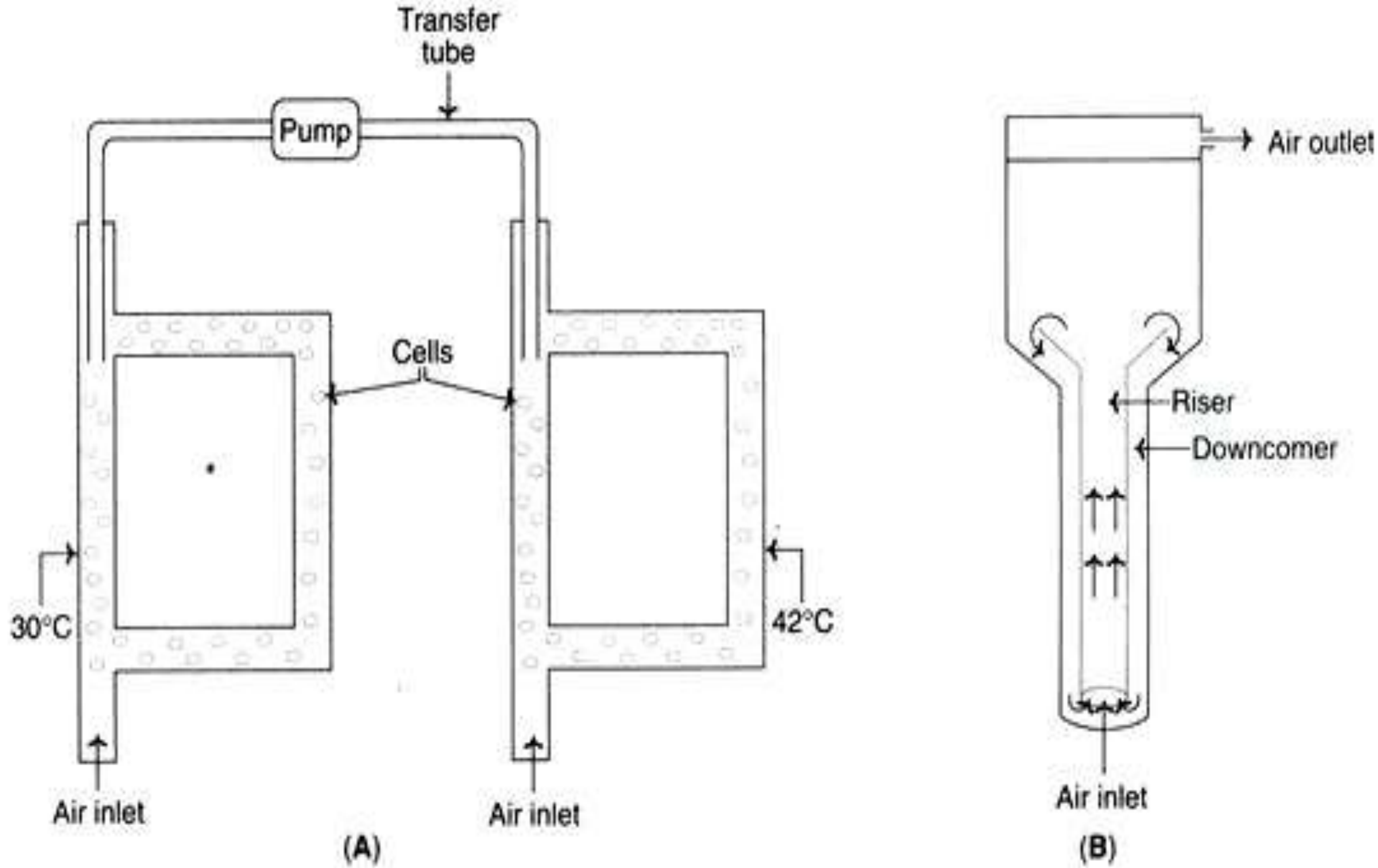


Fig. 19.2 : Types of bioreactors (A) Two–stage airlift bioreactor (B) Tower bioreactor.

ADVANTAGES

1. Highly energy efficient and productivities are comparable to those of stirred tank bioreactors.
2. Simple design with no moving parts or agitator for less maintenance, less risk of defects.
3. Easier sterilization (no agitator shaft parts)
4. Low Energy requirement vs. stirred tank Obviously doesn’t need the energy for the moving parts (agitator shaft).
5. Greater heat-removal vs. stirred tank
   At the Airlift bioreactor it doesn’t need the heat plate to control the temperature, because the Draught-Tube which is inside the bioreactor can be designed to serve as internal heat exchanger.

DISADVANTAGES

1. Greater air throughput and higher pressures needed.
2. The agitation on the Airlift bioreactor is controlled by the supply air to adjust the supply air then the higher pressure needed.
3. the higher pressure of air needed then more energy consumption needed and more cost must pay.
4. Inefficient break the foam when foaming occurs
5. No bubbles breaker, There are no blades that used as a breaker the bubbles which produced from the air supply (sparger).

APPLICATIONS

1. The reactor is commonly used in the culture of shear sensitive organisms.
2. Airlift bioreactors are commonly employed for aerobic bioprocessing technology. They ensure a controlled liquid flow in a recycle system by pumping.
3. Due to high efficiency, airlift bioreactors are sometimes preferred e.g., methanol production, waste water treatment, single-cell protein production.

FIXED BED BIO-REACTORS

DEFINITION:

Fluidized bed bioreactor is comparable to bubble column bioreactor except the top position is expanded to reduce the velocity of the fluid. The design of the fluidized bioreactors (expanded top and narrow reaction column) is such that the solids are retained in the reactor while the liquid flows out. These bioreactors are suitable for use to carry out reactions involving fluid suspended biocatalysts such as immobilized enzymes, immobilized cells, and microbial flocks.

❖This is a characteristic of beds of regular particles suspended in an up flowing liquid stream.

❖If an additional gas phase is involved, there is a tendency for the particles in the bed to become less evenly distributed.

❖The fermentor consists of a vertical cylinder with an aspect ratio is 10:1.

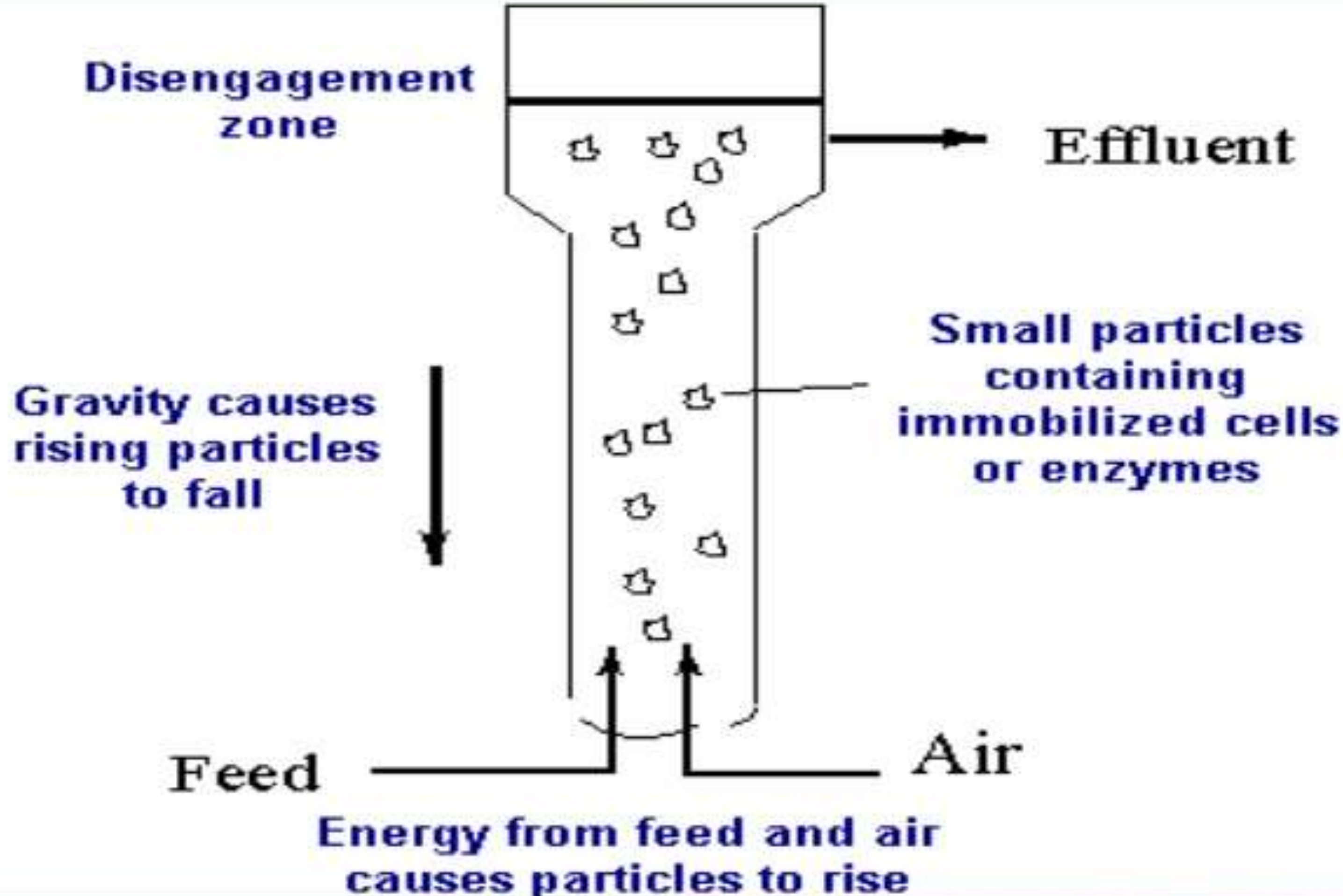
❖At the top of the tower a separator is provided to induce the gas bubbles produced by the reaction, to coalesce and escape from the liquid phase.

❖There are two important features of the beds of mixed particle sizes:

(i) The increase in porosity from the bottom to the top of the bed, and

(ii) The decreased particle movement when compared with beds containing particles of constant size.

Fluidized bed reactors



FEATURES

1. Suitable for reactions involving a fluid-suspended particulate biocatalyst such as immobilized enzyme and cell particles.
2. Similar to the bubble column reactor except that the top section is expanded to reduce the superficial velocity of the fluidizing liquid to a level below that needed to keep the solids in suspension.
3. Consequently, the solids sediment in the expanded zone and drop back, hence the solids are retained in the reactor whereas the liquid flows out.
4. The properties include:
   1. Extremely high surface area contact between fluid and solid per unit bed volume
   2. High relative velocities between the fluid and the dispersed solid phase.
   3. High levels of intermixing of the particulate phase.
   4. Frequent particle-particle and particle-wall collisions.

MECHANISM

- For an efficient operation of fluidized beds, gas is spared to create a suitable gas-liquid-solid fluid bed.
- It is also necessary to ensure that the suspended solid particles are not too light or too dense (too light ones may float whereas to dense ones may settle at the bottom), and they are in a good suspended state.
- Recycling of the liquid is important to maintain continuous contact between the reaction contents and biocatalysts. This enable good efficiency of bioprocessing.

ADVANTAGES

1. Uniform Particle Mixing
2. Uniform Temperature Gradients
3. Ability to Operate Reactor in Continuous State

DISADVANTAGES

1. **Increased Reactor Vessel Size**
2. **Pumping Requirements and Pressure Drop**
3. **Particle Entrainment**
4. **Lack of Current Understanding**
5. **Erosion of Internal Components**
6. **Pressure Loss Scenarios**

APPLICATIONS

1. These reactors can utilize high density of particles and reduce bulk fluid density.
2. Fluidized beds are used as a technical process which has the ability to promote high levels of contact between gases and solids.
3. In a fluidized bed a characteristic set of basic properties can be utilized, indispensable to modern process and chemical engineering
4. The food processing industry: fluidized beds are used to accelerate freezing in some individually quick frozen (IQF) tunnel freezers.

5. The fluid used in fluidized beds may also contain a fluid of catalytic type.
6. Fluidized beds are also used for efficient bulk drying of materials.
7. Fluidized bed technology in dryers increases efficiency by allowing for the entire surface of the drying material to be suspended and therefore exposed to the air.

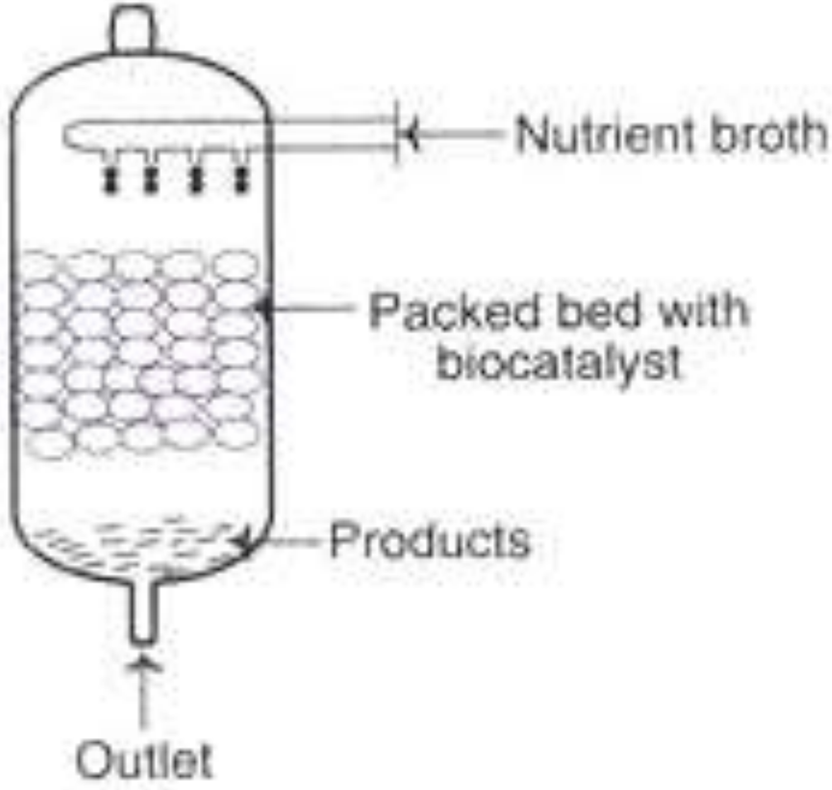
PACKED BED BIO-REACTORS

DEFINITION:

A bed of solid particles, with biocatalysts on or within the matrix of solids, packed in a column constitutes a packed bed bioreactor. The solids used may be porous or non-porous gels, and they may be compressible or rigid in nature. A nutrient broth flows continuously over the immobilized biocatalyst. The products obtained in the packed bed bioreactor are released into the fluid and removed. While the flow of the fluid can be upward or downward, down flow under gravity is preferred.

- ❖The concentration of the nutrients (and therefore the products formed) can be increased by increasing the flow rate of the nutrient broth.
- ❖Because of poor mixing, it is rather difficult to control the pH of packed bed bioreactors by the addition of acid or alkali.
- ❖However, these bioreactors are preferred for bioprocessing technology involving product-inhibited reactions.
- ❖The packed bed bioreactors do not allow accumulation of the products to any significant extent.

(A)



(B)

*Fig. 19.3 : Types of bioreactors (**A**) Fluidized bed bioreactor (**B**) Packed bed bioreactor.*

FEATURES

1. A bed of particles are confined in the reactor. The biocatalyst (or cell) is immobilized on the solids which may be rigid or macroporous particles.
2. A fluid containing nutrients flows through the bed to provide the needs of the immobilized biocatalyst. Metabolites and products are released into the fluid and removed in the outflow.
3. The flow can be upward or downward. If upward fluid is used, the velocity can not exceed the minimum fluidization velocity.

ADVANTAGES

1. Higher conversion per unit mass of catalyst than other catalytic reactors
2. Low operating cost
3. Continuous operation
4. No moving parts to wear out
5. Catalyst stays in the reactor
6. Reaction mixture/catalyst separation is easy
7. Design is simple
8. Effective at high temperatures and pressures

DISADVANTAGES

1. Undesired heat gradients
2. Poor temperature control
3. Difficult to clean
4. Difficult to replace catalyst
5. Undesirable side reactions

APPLICATIONS

1. These are used with immobilized or particulate biocatalysts.
2. High conservation per weight of catalyst than other catalytic reactors. Thus mostly preferred fermentor.
3. Used is waste water treatment.