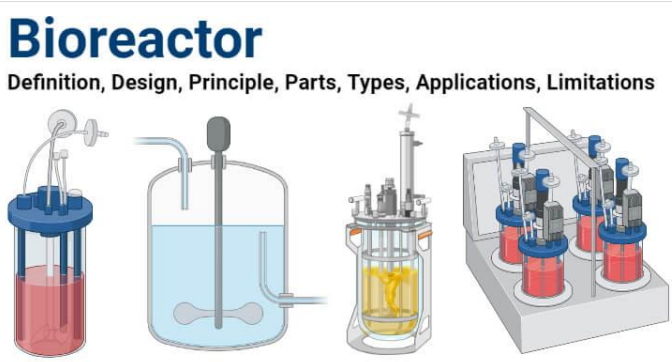
A bioreactor is a type of fermentation vessel that is used for the production of various chemicals and biological reactions.

It is a closed container with adequate arrangement for aeration, agitation, temperature and pH control, and drain or overflow vent to remove the waste biomass of cultured microorganisms along with their products.

A bioreactor should provide for the following:

1. Agitation (for mixing of cells and medium),
2. Aeration (aerobic fermentors); for O2 supply,
3. Regulation of factors like temperature, pH, pressure, aeration, nutrient feeding, and liquid leveled.
4. Sterilization and maintenance of sterility, and
5. Withdrawal of cells/medium

Bioreactors are used for the production of biomass, metabolites, and antibiotics.



Bioreactor Design

- The design and mode of operation of a bioreactor are based on the production of an organism, optimum conditions required for desired product formation, product value, and its scale of production.
- A good bioreactor design will help to improve productivity and provide higher quality products at lower prices.
- A bioreactor is a device that consists of various features such as an agitator system, an oxygen delivery system, a foam control system, and a variety of other systems such as temperature & pH control system, sampling ports, cleaning, and sterilization system, and lines for charging & emptying the reactor.
- The material used for the construction of a bioreactor must have the following important properties:
- It should not be corrosive.

- It should not add any toxic substances to the fermentation media.
- It should tolerate the steam sterilization process.
- It should be able to tolerate high pressure and resist pH changes.
  - The sizes of the bioreactor vary widely depending on the application.
  - Some bioreactors are designed for small scale fermenters and some for large scale industrial applications from the microbial cell (few mm3) to shake flask (100-1000 ml) to the laboratory-scale fermenter (1 – 50 L) to pilot level (0.3 – 10 m3) to plant scale (2 – 500 m3) for large volume).

Bioreactor Principle

- The bioreactor is the heart of any biochemical process as it provides an environment for microorganisms to obtain optimal growth and produce metabolites for the biotransformation and bioconversion of substrates into desirable products.
- The reactors can be engineered or manufactured based on the growth requirements of the organisms used.
- Reactors are machines that can be made to transform biological-based materials into desirable products.
- They can be used for the production of various enzymes and other bio-catalysis processes.

Parts of the bioreactor and their function

- These reactors have been designed to maintain certain parameters like flow rates, aeration, temperature, pH, foam control, and agitation rate.
- The number of parameters that can be monitored and controlled is limited by the number of sensors and control elements incorporated into a given bioreactor
- Other factors should be kept in mind before designing a fermenter as described below and demonstrated in the figure below.

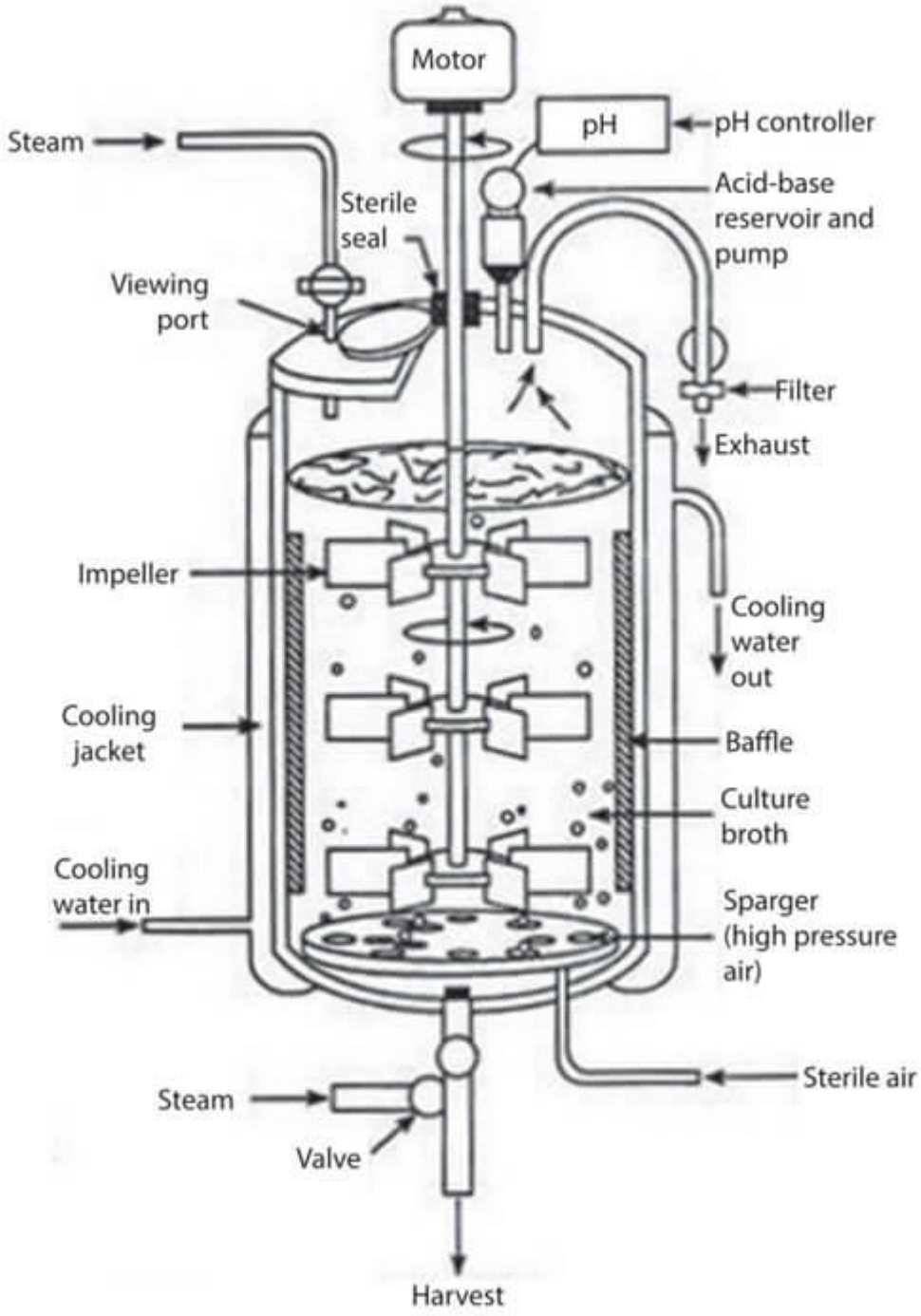


Figure: Bioreactor. Image Source: Kuila, A., & Sharma, V. (2018). Principles and applications of fermentation technology. John Wiley & Sons, Inc.

1. Fermenter Vessel

- A fermenter is a large cylinder closed at the top and bottom connected with various pipes and valves.
- The vessel is designed in such a way that it allows to work under controlled conditions.
- Glass and stainless steels are two types of fermenter vessels used.
- The glass vessel is usually used in small-scale industries. It is non-toxic and corrosion-proof.
- Stainless steel vessel is used in large scale industries. It can resist pressure and corrosion.

2. Heating and Cooling Apparatus

- The fermentor vessel's exterior is fitted with a cooling jacket that seals the vessel and provides cooling water.
- Thermostatically controlled baths or internal coils are generally used to provide heat while silicone jackets are used to remove excess heat.
- A cooling jacket is necessary for sterilization of the nutrient medium and removal of the heat generated during fermentation in the fermentor.

3. Aeration System

- An aeration system is one of the very important parts of a fermentor.
- It is important to choose a good aeration system to ensure proper aeration and oxygen availability throughout the culture.
- It contains two separate aeration devices (sparger and impeller) to ensure proper aeration in a fermentor.
- The stirring accomplishes two things:
- It helps to mix the gas bubbles through the liquid culture medium and
- It helps to mix the microbial cells through the liquid culture medium which ensures the uniform access of microbial cells to the nutrients.

4. Sealing Assembly

- The sealing assembly is used for the sealing of the stirrer shaft to offer proper agitation.
- There are three types of sealing assembly in the fermenter:
- Packed gland seal
- Mechanical seal
- Magnetic drives

5. Baffles

- The baffles are incorporated into fermenters to prevent a vortex improve aeration in the fermenters.
- It consists of metal strips attached radially to the wall.

6. Impeller

- Impellers are used to provide uniform suspension of microbial cells in different nutrient mediums.
- They are made up of impeller blades attached to a motor on the lid.
- Impeller blades play an important role in reducing the size of air bubbles and distribute them uniformly into the fermentation media.
- Variable impellers are used in the fermenters and are classified as follows.
- Disc turbines
- Variable pitch open turbine

7. Sparger

- A sparger is a system used for introducing sterile air to a fermentation vessel. It helps in providing proper aeration to the vessel.
- The sparger pipes contain small holes of about 5-10 mm, through which pressurized air is released.
- Three types of sparger are used
- Porous sparger
- Nozzle sparger

- Combined sparger–agitator

8. Feed Ports

- They are used to add nutrients and acid/alkali to the fermentor.
- Feed ports are tubes made up of silicone.
- In-situ sterilization is performed before the removal or addition of the products.

9. Foam-Control

- The level of foam in the vessel must be minimized to avoid contamination, this is an important aspect of the fermentor.
- Foam is controlled by two units, foam sensing, and a control unit.
- A foam-controlling device is mounted on top of the fermentor, with an inlet into the fermentor.

10. Valves

- Valves are used in the fermentor to control the movement of liquid in the vessel.
- There are around five types of valves are used, that is,
- globe valve,
- butterfly valve,
- a ball valve, and
- diaphragm valve.
- A safety valve is built-in in the air and pipe layout to operate under pressure

11. Controlling Devices for Environmental Factors

- A variety of devices are utilized to control environmental elements like temperature, oxygen concentration, pH, cell mass, essential nutrient levels, and product concentration.

12. Use of Computer in Fermenter

- For an efficient process, monitoring, and data collecting, fermentors are generally coupled with modern automated and semi-automated computers and databases.

Types of bioreactor

The fermentor (bioreactor) types used extensively in industries are

1. Continuous stirred tank fermentor

- A continuous stirred tank bioreactor is made up of a cylindrical vessel with a central shaft controlled by a motor that supports one or more agitators (impellers).
- The sparger, in combination with impellers (agitators), allows for improved gas distribution throughout the vessel.
- A stirred tank bioreactor can be operated continuously in the fermentor, temperature control is effortless, construction is cheap, easy to operate, resulting in low labor cost, and it is easy to clean.
- It is the most common type of bioreactor used in industry.

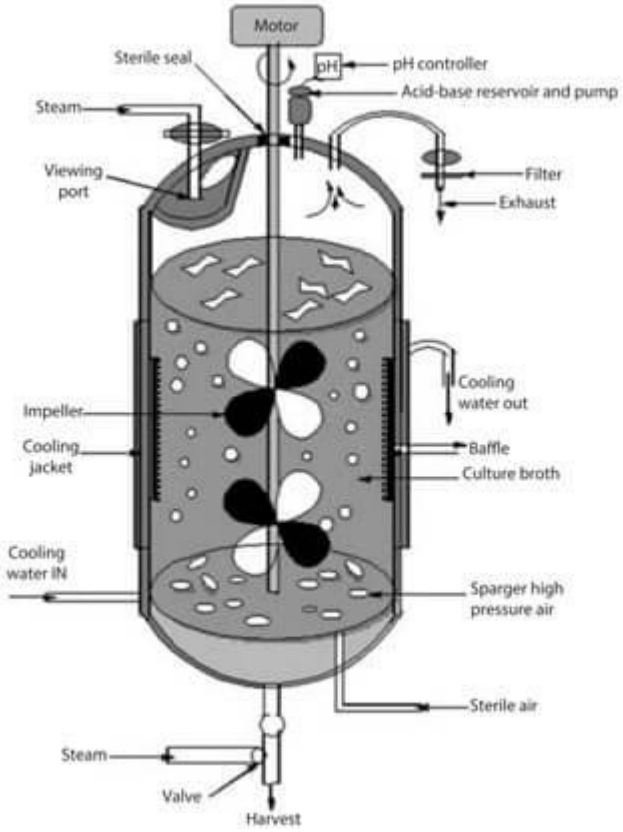


Figure: Continuous stirred tank fermentor. Image Source: Saran, S., Malaviya, A., & Chaubey, A. (2019). Introduction, scope and significance of fermentation technology. *High Value Fermentation Products*, 1–25. https://doi.org/10.1002/9781119460053.ch1

2. Airlift fermentor

- The airlift reactor is generally used for gas-liquid or gas-liquid-solid contact devices. It is also known as a tower reactor.
- A bioreactor using an airlift system divides the fluid volume into two zones to improve circulation, oxygen transfer, and equalize forces in the reactor
- In a two-zone system, only one zone is sparged with gas. The zone where the gas is sparged is the riser; the zone in which it is not sparged in the downcomer.
- Airlift bioreactors are used for aerobic bioprocessing technology so that they can provide a controlled liquid flow in a recycling system using pumps.
- This equipment has several advantages such as its simplicity of design because it doesn't contain any moving parts or agitators, its easy sterilization, its low energy requirements, and its low cost.

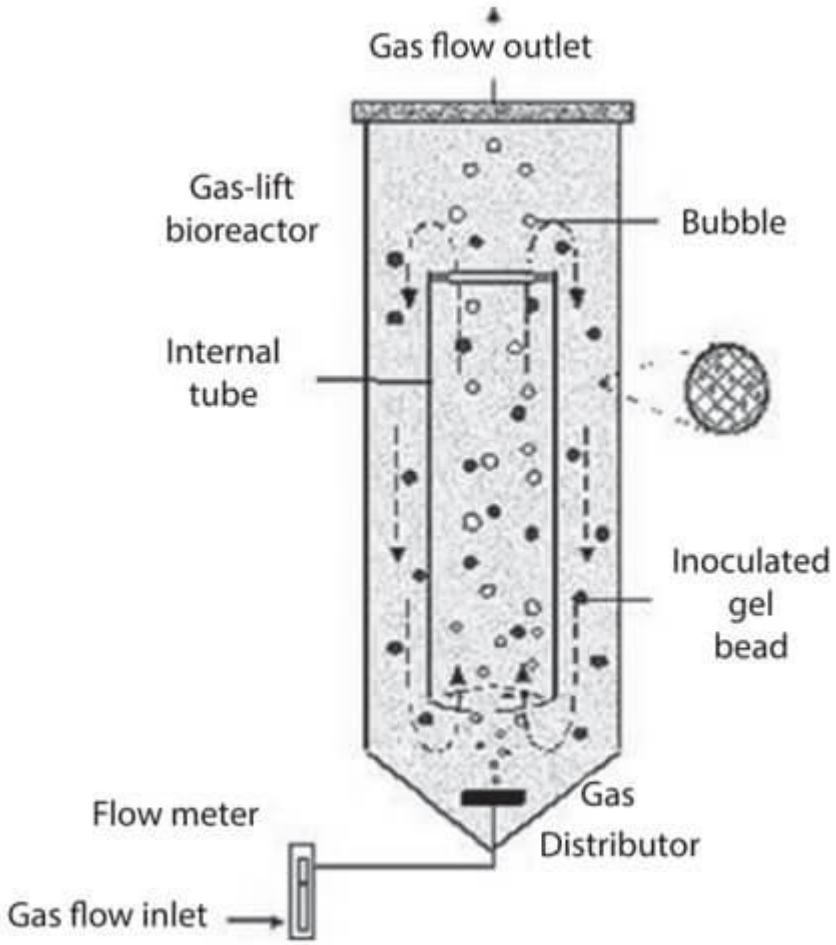


Figure: Airlift fermentor. Image Source: Kuila, A., & Sharma, V. (2018). Principles and applications of fermentation technology. John Wiley & Sons, Inc.

3. Bubble column fermentor

- The bubble column fermentor consists of a cylindrical vessel equipped with a gas sparger that pushes gas bubbles into a liquid phase or a liquid-solid suspension.
- The base of the column air or gas is introduced via perforated pipes or plates, or metal micro porous sparger.
- The rheological properties of the fluid and the gas flow rate have a significant influence on the mixing of O2 and other performance factors.
- To improve mass transfer and modify the basic design of the vessel, internal devices such as horizontal perforated plates, vertical baffles, and corrugated sheet packings placed are in the vessel.
- These reactors are simple in construction, easy maintenance, and have a low operating cost
- Bubble columns reactors are used in biochemical processes such as fermentation and biological wastewater treatment. It is also used in many chemical, petrochemical, and biochemical industries.

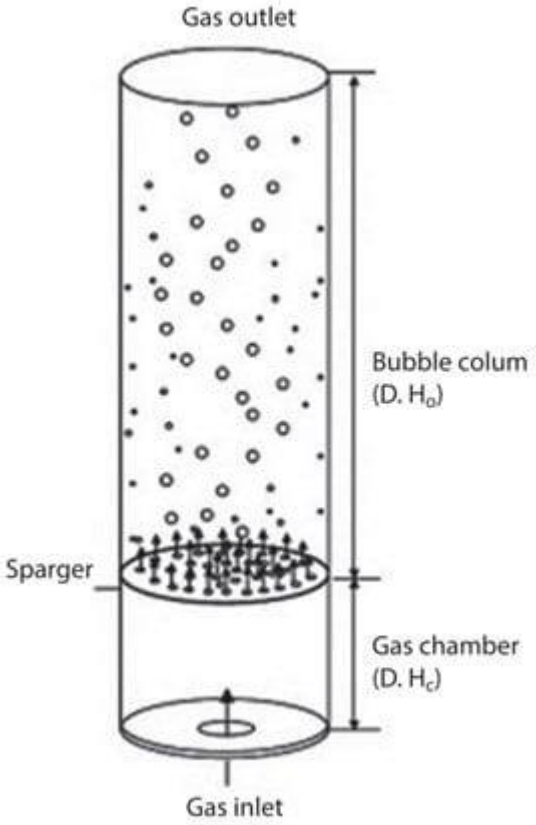


Figure: Bubble column fermentor. Image Source: Kuila, A., & Sharma, V. (2018). Principles and applications of fermentation technology. John Wiley & Sons, Inc.

4. Fluidized-bed fermentor

- Fluid bed bioreactors constitute packed beds with smaller particles. This prevents problems such as clogging, high liquid pressure drop, channeling, and bed compaction associated with packed bed reactors.
- Catalyst is laid on the bottom of the reactor and the reactants are pumped into the reactor through a distributor pump to make the bed fluidized.
- In these reactors, the cells are immobilized small particles which move with the fluid as a result, mass transfer, oxygen transfer, and nutrition to the cells are enhanced.
- The bioreactors can be used for reactions involving fluid-suspended biocatalysts, such as immobilized enzymes, immobilized cells, and microbial flocs.
- Its main advantages include its ability to maintain even temperatures, easy replacement and regeneration of the catalyst, continuity, and automaticity of operation, and reduced contact time between gas and solid, compared to other catalytic reactors.

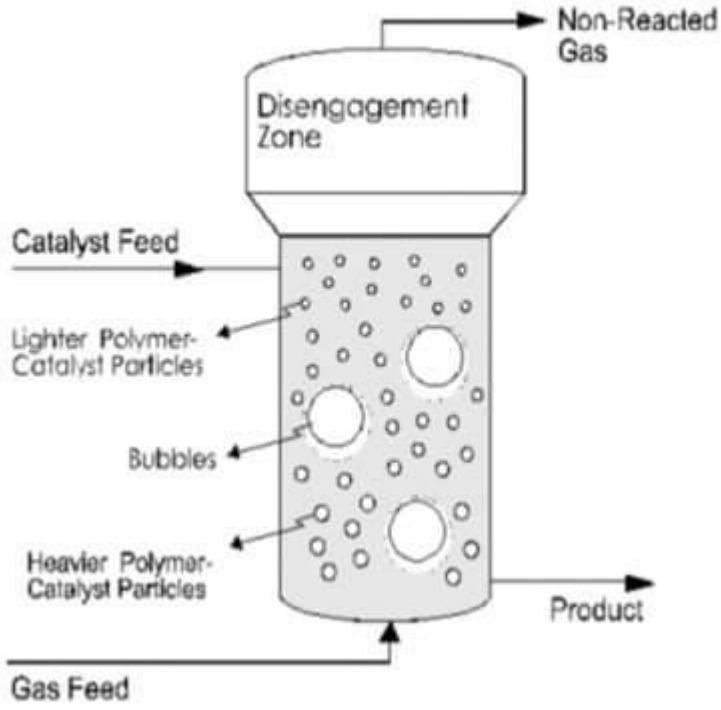


Figure: Fluidized-bed fermentor. Image Source: Singh, J., Kaushik, N., & Biswas, S. (2014). Bioreactors – Technology & Design Analysis. April 2016.

5. Packed bed fermentor

- A packed bed fermentor is a bed of solid particles, having biocatalyst on or within, the matrix of solids.
- It can either be run in the submerged mode (with or without aeration) or the trickle flow mode.
- Frequently used in chemical processing processes such as absorption, distillation, stripping, separation process, and catalytic reactions, packed bed reactors are also called fixed bed reactors.
- In packed-bed bioreactors, the air is introduced through a sieve that supports the substrate.
- This reactor has many benefits, like a high conversion rate for the catalyst, ease of operation, low construction and operation costs, increased contact between reactant and catalyst, and the ability to work in high temperatures and pressures.

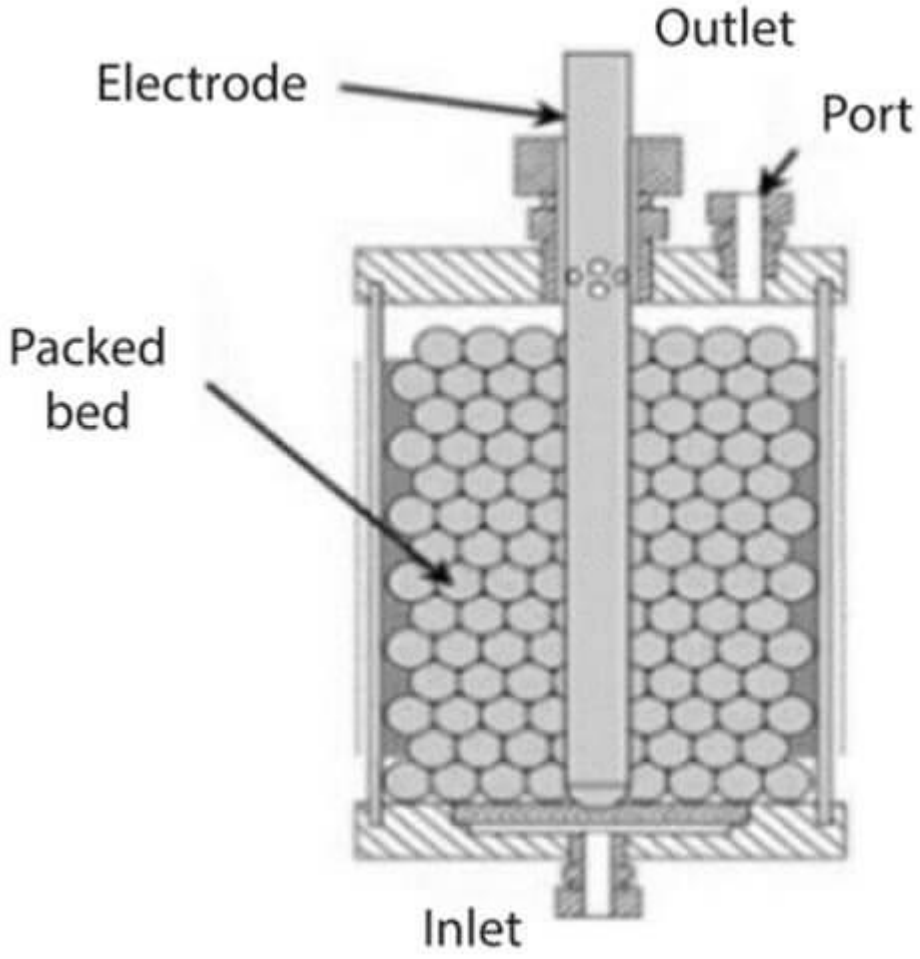
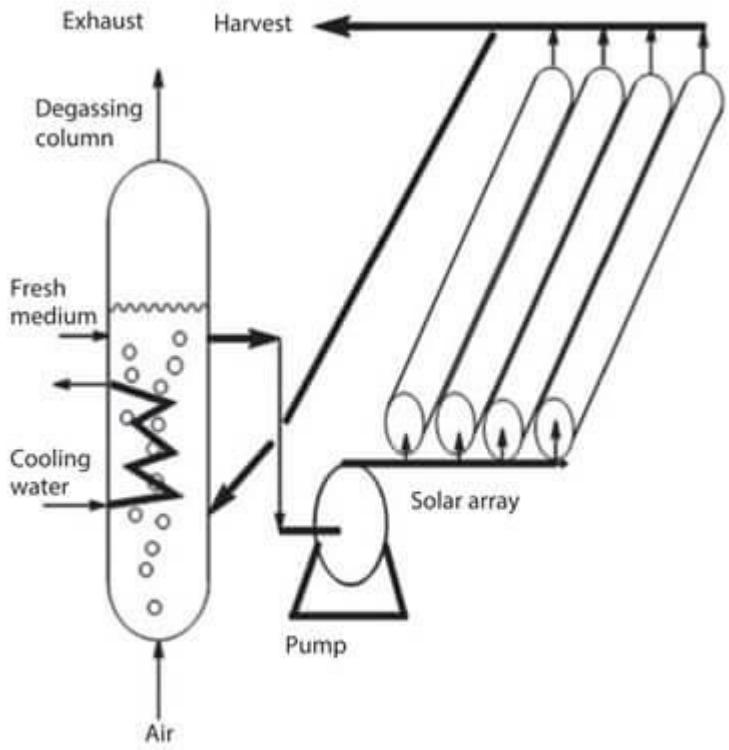


Figure: Packed bed fermentor. Image Source: Kuila, A., & Sharma, V. (2018). Principles and applications of fermentation technology. John Wiley & Sons, Inc.

6. Photobioreactor



A tubular photobioreactor with parallel run horizontal tubes.

Figure: Photobioreactor. Image Source: Singh, J., Kaushik, N., & Biswas, S. (2014). Bioreactors – Technology & Design Analysis. April 2016.

- A photobioreactor is a specialized unit for fermentation that is either illuminated by direct sunlight or artificially illuminated
- They are made up of glass or more commonly transparent plastic and the tubes or flat panels is consist of light receiving systems.
- In this bioreactor, centrifugal pumps or airlift pumps can be used to circulate the medium through solar receivers.
- Photo-bioreactors are usually operated in a continuous mode at a temperature in the range of 25–40 °C.
- Photobioreactors are used for the photosynthetic culture of microalgae and cyanobacteria to produce products such as astaxanthin and β-carotene.

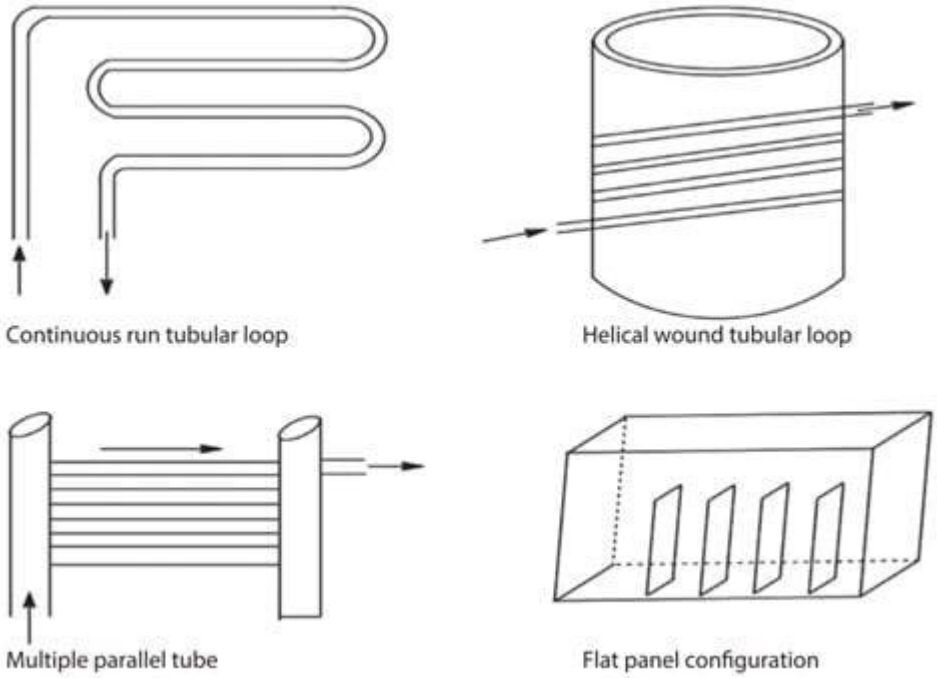


Figure: Types of photobioreactor. Image Source: Singh, J., Kaushik, N., & Biswas, S. (2014). Bioreactors – Technology & Design Analysis. April 2016.

7. Membrane bioreactor

- This system combines traditional treatment with membrane filtration, resulting in the removal of organics and suspended solids as well as the removal of high nutrient levels.
- Membranes in this system are submerged in an aerated biological reactor. The pore size of the membrane ranges from 0.035 microns to 0.4 microns.
- With pure oxygen, the benefits of this bioreactor are enhanced resulting in even higher rate biological treatment systems that provide compact control of COD, microorganisms.

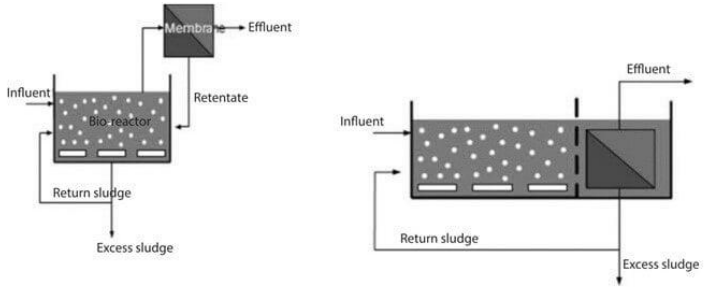


Figure: Membrane bioreactor. Image Source: Kuila, A., & Sharma, V. (2018). Principles and applic