



Fermentors: Types, Functions, Design and Control

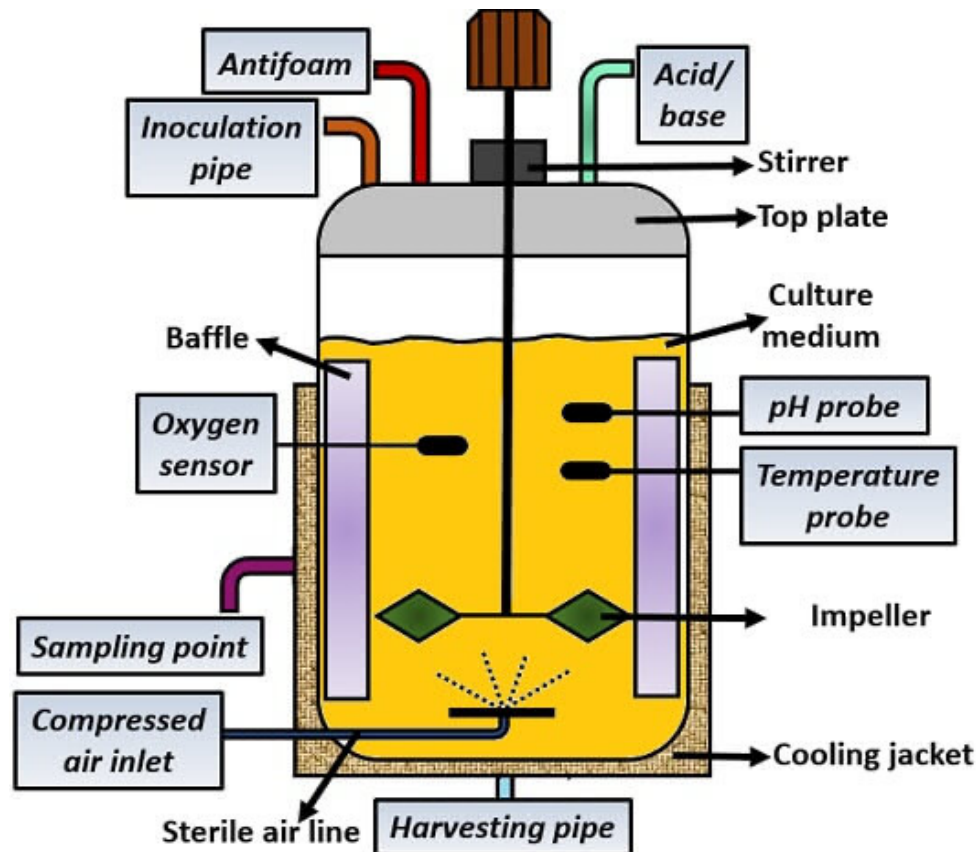
- **Reliable operation of fermentation system : fermentor design and fermentation process.**
- **Design should consider factors as space constraints, relationships between fermentor productivity and throughput rates of downstream equipment, validation requirements, utilities requirements, overall labor requirements and operating versus capital costs.**
- **Consistency, safety, cost, are of prime concern for production equipment.**

- **Fermentor is an optimal environment for cultivation of organisms will yield a desirable substance.**
- **Bioreactor is a vessel in which is carried out a chemical process which involves organisms or biochemically active substances derived from such organisms.**
- **Bioreactors: cylindrical, ranging in size from some liter to cube meters, and made of stainless steel.**
- **Bioreactor: used for growth and maintenance of population of mammalian/ insect cells**
- **Fermentor: used for growth and maintenance of population of bacterial/fungal cells.**

Bioreactor Configuration

Design Criteria

Objective of fermentor design is to produce fermentation systems necessary to build economical production facilities that satisfy performance criteria.



Design of a fermentor

Mechanical Aspects

- **Mechanical design aspects are important for operation of any fermentation plant.**
- **Practical aspects of vessel design are:**
 - **Space requirements: The vessel dimensions must be chosen to meet plant space limitations. Poor choice of equipment sizes can cause inordinately high building costs.**
 - **Transportation: Shop built vessels are usually less expensive and of higher quality than field built vessels.**
 - **Special heads: A hemispherical bottom gives better mixing and fewer shears than does a standard dished head.**

Process aspects

- **Aeration rate:** Airflow rate to fermentor must be generally one volume of air per liquid volume per minute (1 vvm).
- **Impeller tip speed:** Tip speed of a fermentor impeller must not exceed 7.6 m/s.
- **Arrest of fermentative metabolism:** At end of fermentation, fermentor broth must be cooled immediately and stored at 4°C, to arrest the fermentative metabolism.
- **Maximum production rate cell mass theory:** Process optimization is achieved by obtaining very high cell mass concentrations at very high growth rates.
- **Oxygen transfer rate:** Increasing OTR by increasing air flow rate and agitation could lead to foaming, increased gas holdup, higher gas velocities, higher vessel pressure, and oxygen enrichment.
- **Heat transfer rate:** Heat transfer usually is limiting constraint for highly aerobic large scale fermentors.

Jackets and coils

- Jackets are used for circulation of steam and cooling water during heating and cooling cycles of sterilization of fermentor.
- Since microbial reactions are exothermic, heat produced during fermentations leads to rise in temperature of broth, necessitating the need to maintain temperature at optimal value.
- Steam is used as heating fluid; and water, chilled water, or chilled brine is used as cooling fluids.
- Contact surface area of jacket with the fermentor should be maximal and pressure drop of circulating fluids in jacket should be minimal for better process performance.
- Layout of external jackets could be double jacket, full pipe, or half pipe, depending on required area for heat transfer, the heating or cooling medium, and circulation velocity.

Safety codes

Vessel must be fabricated in accordance with the Standard Code for unfired pressure vessels and tested at design conditions to insure that vessel can withstand all forces generated under specified operating conditions. If operation is required at high operating pressures, minimize the metal thickness to allow use of cold rolled sheet rather than plate. This results in better heat transfer, a better interior finish and lower price.

Material of construction

- **Stainless steel is employed material for fabrication of biotechnology equipment.**
- **Low carbon steels, SS 304L and SS 316L, are known worldwide as standard steels.**
- **Vessels used in biological processes are fabricated with 316 or 316L steel.**
- **Vessels widely used in food technology or harvest storage tanks are fabricated with cheaper and less corrosion resistant steel of grade 304 or 304L.**
- **Aseptic operation requires use of SS316, SS316L, SS304, or SS304L.**

Baffles

- **Welded to interior of vessel.**
- **Baffles usually take form of metal strips, roughly one tenth of vessel diameter in width, extending vertically down the height of the vessel and attached radially to wall.**
- **Removable baffles mean unsealed joints.**
- **Baffles should be set off from wall, to minimize solids build up and simplify cleaning.**
- **Slots between baffle and vessel wall prevent the formation of dead spots.**
- **Provision of baffles increases turbulence in liquid and results in more efficient utilization of power.**



Sparger

- Introduce air below liquid level in the fermentor vessel.
- Spargers with very small orifices is more efficient than a single orifice delivering same volume of air.
- Aerobic fermentations, e.g., penicillin, produce large quantities of mycelium and mechanical agitation ensure adequate dispersion of air and other nutrients in large scale fermentations.
- As degree of agitation is increased, relative efficiencies of of spargers tend to converge, and at high agitation levels, all spargers give approx. same performance.
- Types of spargers: nozzle spargers, orifice spargers, and porous spargers.



Nozzle and Manways

- **Nozzle design:**
 - ✓ To ensure aseptic connections to external piping
 - ✓ In order to facilitate free draining
 - ✓ For proper and safe cleaning of nozzles, protrusions inside vessel should be as minimal as possible.
 - ✓ Addition of feed through nozzles to fermentor to take care that added liquids do not dribble down interior surfaces.
 - ✓ Use of manways obviates need for full opening heads on larger vessels.

Piping and Valves

- **Piping materials:** Stainless steel, thermoplastics (polypropylene, polyethylene, polyvinylidene fluoride), carbon steel, copper, iron, glass, and lined pipe (glass and plastic liners).
- In sterile fermentation processes, lines for sterile air and lines for transferring sterile mash are the subject of special care during installation to prevent the formation of pockets where liquid can collect.
- Adequate slopes, continuous in one direction, have to be given in what would be normally horizontal lines.
- For sterilization, steam is introduced wherever possible at highest point or points in the system, with the steam condensate removed from the lowest points.
- Valves used on sterile lines have given cause for thought for a considerable time.
- For alcohol fermentation, use of the standard type of gate valve is normally acceptable.

Steam Locks

- **Good steam lock assembly should have following features:**
 - ☐ **Elimination of chances of dead spots with inefficient sterilization**
 - ☐ **Thorough steaming of sterile lines to be done during non usage to avoid contamination**
 - ☐ **Steam locks to be checked for leakage of steam during steaming**
 - ☐ **Self draining of condensate through steam traps**
 - ☐ **Easy cleaning and maintenance of the steam lock assembly**

Welds and joints

- **Vessel welds of high quality are required to adhere to code purposes, ensure maximum smoothness and cleanability, and minimize corrosion problems.**
- **Welding for aseptic fermentors should be carried out under an inert gas shield to minimize oxidation and flux residue, and create smoother, pit free welds.**

Surface treatment and finish

- **Surface treatment of a vessel is required for any surface that comes in contact with the product. It is imperative that all stainless steel surfaces are treated and cleaned in a way that prevents corrosion under the operating conditions. Stainless steels are corrosion resistant due to formation of microscopically thin, invisible chromium oxide layer, which occurs on clean metal and polished surfaces only.**
- **Mechanical Surface Treatment**
- **Chemical surface treatment: Two main types of chemical surface treatment are cauterization and passivation. Impurities that require cauterization may be interior surfaces with oxidation tints, welding slag residues, and fine scales or overlaps generated during the working process. Passivation is used either after cauterization or as a final treatment of ground, brushed, or polished steels with special surface structures.**
- **Electrochemical surface treatment: Electropolishing, or mirror polishing, is an electrochemical treatment which smoothes and polishes rough, dull surfaces. The vessel is immersed in an electrolyte and serves as an anode.**

Agitation system design

- Typical agitation equipment consists of prime mover (usually an electric motor) coupled to shaft through reduction gear.
- Impellers and baffles are fitted to shaft and vessel, respectively, to give desired liquid motion.
- Shaft may enter from the top, side or bottom, and is usually fitted with a mechanical seal at vessel wall.
- Number and location of impeller units depends on vessel.
- In a smooth walled tank, liquid swirls round in same general direction as agitator.
- As the impeller speed is increased, a vortex is formed and the liquid level at wall is raised above average liquid level.

Temperature Control

- Temperature control system is designed using PID control algorithms.
- Liquid temperature is sensed and compared it with desired temperature to form error signal.
- Error signal is processed using control algorithms to produce desired output to heater driver.
- Feed back control system operates on heating system to maintain the temperature at required set value by reducing the error towards zero.
- PID controllers are most commonly used controllers in temperature control.

pH control

- **Bioreactors actually use on-off control for pH.**
- **Consideration in pH control is hold time, which is required to provide time for neutralization reaction to go to completion.**

A comprehensive depiction of fermentor controls

