

## Introduction to USP – What is a Bioreactor?

### Your Objectives:

At the end of the lesson, you should be able to distinguish different types of bioreactors.

### The Bioreactor vessel

A **large-scale bioreactor** is a closed mechanical system designed to contain and grow genetically engineered cells at large-scale commercial **volumes**. A bioreactor is built according to strict **sanitary** guidelines and is designed to control all **culture** parameters critical to cell growth.

A **stirred tank bioreactor** will typically be cylindrical with a curved **base**. Its curved base assists in the mixing of vessel contents.

The bioreactor vessel itself is a double-walled, glycol-jacketed, sanitary pressure vessel designed to provide primary containment for the cell culture.

The bioreactor **vessel wall** consists of four layers:

### Interior wall

The interior wall provides the sterile contact **surface** for the cell culture and is made of **stainless steel**. It is electropolished to produce a smooth, cleanable **finish\***. Electropolishing is an **electrochemical** method of smoothing, deburring, polishing and cleaning stainless steel. This process also improves **resistance** to corrosion.

\* A 'finish' is a particular surface texture (e.g. on wood, metals, or other materials) designed to give a **desired** condition.

### Glycol jacket

The glycol jacket is a heat-transfer surface welded to the outside of the interior wall. The jacket serves as a heat exchanger to **regulate** the cell culture temperature inside the bioreactor vessel.

Glycol jackets can be one of two types:

- dimpled
- half-pipe

Glycol is basically pumped into the base of the jacket and exits through the top. This flow path is designed to eliminate air pockets that might **decrease** the efficiency of the heat transfer.

## Insulation

Located between the glycol jacket and the outer sheath is a layer of fire-retardant insulation that reduces **heat** loss of the bioreactor **vessel**.

## Outer sheath

The outer sheath is the **visible** layer of the bioreactor. It envelops both insulation and glycol jacket. In contrast to the mechanically polished and electropolished interior wall, the surface of the outer sheath is finished by **mechanical** polishing only. The outer sheath is not part of any sterile operation, though.

Watch this useful YouTube video on fermentation processing:

<https://youtu.be/5eKdZ0dVCCo?t=144>

## Principle types of bioreactor

Stationary bioreactors (i.e. where cell cultures are not **agitated**)

- T-flasks, 6-well plates, microtitre plates, roller bottles, shake **flasks** (etc.)

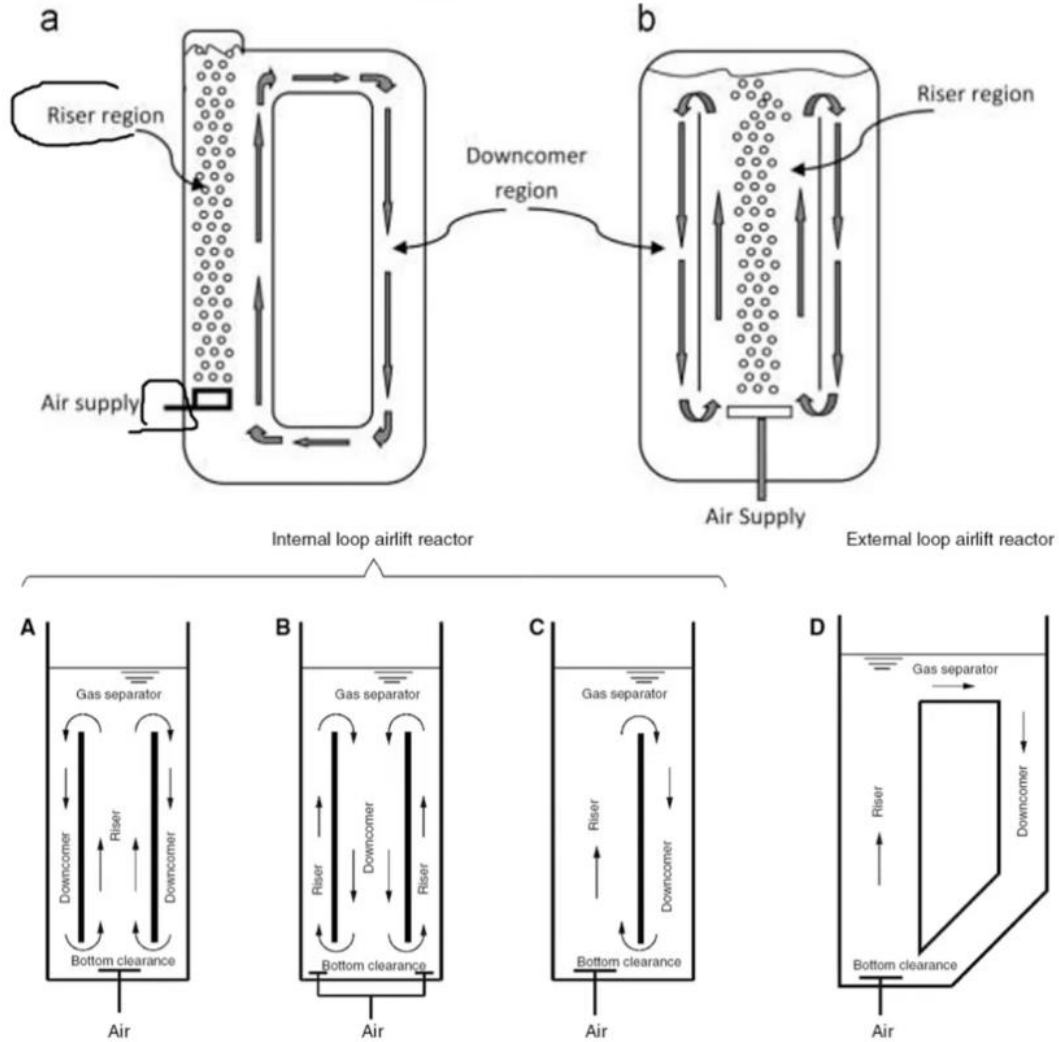
**Mechanically** agitated bioreactors

- Stirred tank bioreactors, spinner flasks, Wave bioreactors

Gas **agitated** bioreactors

- Airlift reactors\*

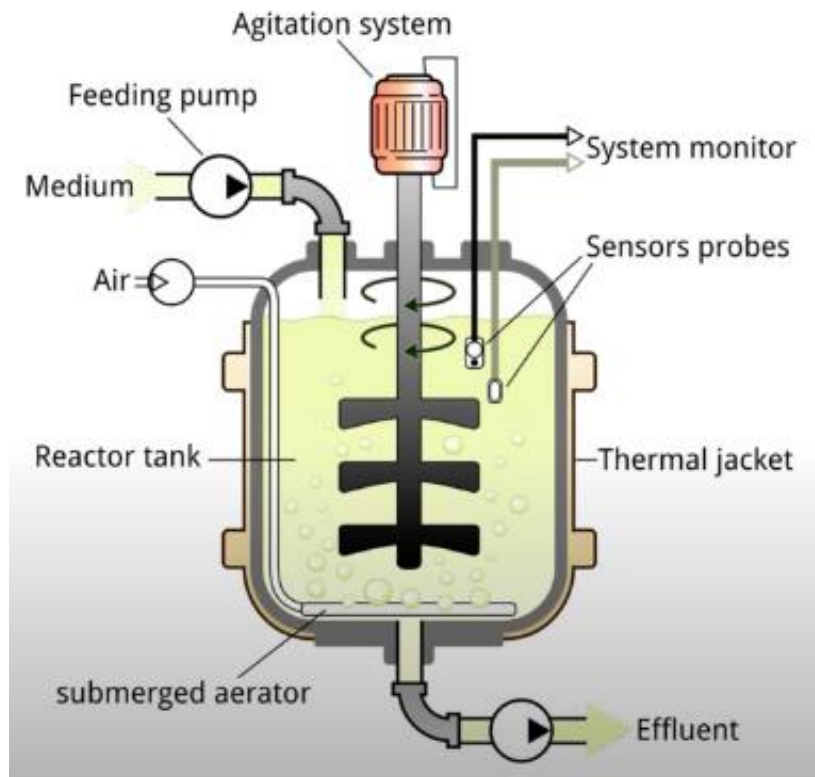
## Airlift Bioreactor



\* An ALR, or airlift reactor, is a pneumatically-driven bioreactor especially suitable for large-scale culture of immobilized plant cells.

## Fluid agitated bioreactors (stirred-tank)

- Fixed bed bioreactors, fluidized-bed bioreactors



## Membrane bioreactors

- Hollow fibre reactors, Transwells®

## Modes of operation of a bioreactor

- This is different to other types of bioreactors
- The four (4) different modes of operation are:
  - Batch
  - Fed-batch
  - Continuous
  - Perfusion
- All types of bioreactors can be operated in any of the four modes of operation.
- The modes of operation are determined by whether, and how, a medium is supplied to the culture.