BIOREACTOR ENGINEERING
Chapter 8
Bioreactor/Fermenter Systems

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Chapter Description

- Topic Outcome
  - Classify types of bioreactor/fermenter and its operation mode.

- References

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  - Liu, S. (2013) Bioprocess Engineering: Kinetics, Biosystem, Sustainability and Reactor Design. Elsevier.
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Topic Outline

- Introduction
- Types of Bioreactor/Fermenter

Introduction

Fermenter versus Bioreactor

Fermenter	Bioreactor
For growth of bacterial and fungal cells which are: • robust (they have strong cell walls) • fast growing and double in just 20 min • very high oxygen demand	For growth of mammalian and insect cells which are: • fragile (they have shear sensitive cell membranes) • slow in growth (they have 24 h doubling time) • have low oxygen demand
Taller vessels for bacterial processes to improve oxygen mass transfer (H/D = 2.5-3.0)	Shorter vessels for mammalian cell culture to improve mixing. (H/D = 1.5)
Media is thermally sterilized in the fermenter	Media is filter sterilized into the bioreactor

Introduction

What is a Bioreactor/Fermenter?

- An apparatus for growing microorganisms under controlled conditions.
- Used to convert raw materials into useful products.
- Used in industrial processes to produce pharmaceuticals, vaccines, or antibodies.
- Varying in size, complexity and cost.

Types of Bioreactor/Fermenter

- Standing culture
  - T-flask (SmF)
  - Fernbach flask (SmF)
  - Tray chamber (SmF and SSF)
- Shake flask
  - Baffled (SmF)
  - Unbaffled (SmF)
- Mechanical stirred tank bioreactor
  - Nonsparged (SmF and SSF)
  - Sparged (SmF and SSF)

Types of Bioreactor/Fermenter

- Bubble driven bioreactor
  - Bubble column (SmF)
  - Airliftt bioreactor (SmF)
- Packed bed bioreactor (SmF and SSF)
  - Trickle flow bioreactor (SmF)
- Fluidized bed reactor (SmF and SSF)

Types of Bioreactor/Fermenter

Standing culture

- The medium is neither gassed nor agitated.
- Using surface aeration, hence poor rate of oxygen transfer.
- Commonly used in small scale laboratory system (when oxygen supply is not critical).
- E.g., biochemical tests for identification of bacteria (test-tubes containing 5-10 mL of media).

Types of Bioreactor/Fermenter

Standing culture - T flask (SmF) and Fernback flask (SmF)

- Used in small scale culture.
- Surface aeration rate can be increased by using larger volume flask (increase the surface area for oxygen transfer).

Types of Bioreactor/Fermenter

Standing culture - Tray chamber (SmF and SSF)

- Not restricted to the laboratory.
- SmF: Example: *Aspergillus niger* grown on the surface of liquid media in shallow trays.
- SSF: Example: Production of koji by *Aspergillus oryzae* on soy beans, mushroom cultivation.

Types of Bioreactor/Fermenter

Shake flask - Unbaffled flask & Baffled flask (SmF)

- Commonly used for small scale cell cultivation.
- Agitation breaks liquid surface and provides greater surface area for oxygen transfer.
- Shaking encourages bubbles become entrained into the medium to further increase the oxygen transfer rate.
- High level of foam formation in the baffled flask is due to high level of gas entrainment.
- The rate of oxygen transfer in shake flask depends the
  - Agitation rate
  - Liquid volume
  - Shake flask design

Types of Bioreactor/Fermenter

Mechanical stirred tank bioreactor

- Commonly used in industrial application.
- Low capital cost, low operating cost, and flexible.
- An external motor is used to agitate the growth medium with impellers.

Types of Bioreactor/Fermenter

Mechanical stirred tank bioreactor - Nonsparged (SmF)

- Nonsparged stirred tank bioreactor can supply sufficient aeration for microbial fermentations with liquid volumes up to 3 L.
- Oxygen is transferred from the headspace of bioreactor.
- Agitation continually breaks the liquid surface and increases the surface area for oxygen transfer.

Types of Bioreactor/Fermenter

Mechanical stirred tank bioreactor - Nonsparged (SSF)

- Consists of a drum of cylindrical cross section lying horizontally.
- The drum is partially filled with a bed of substrate, and air is blown through the headspace.
- In rotating drums, the whole drum rotates around its central axis to mix the bed.
- In stirred drums, the bioreactor body remains stationary and paddles mounted on a shaft running along the central axis of the bioreactor rotate within the drum.

Types of Bioreactor/Fermenter

Mechanical stirred tank bioreactor - Sparged (SmF)

- Liquid volumes greater than 3 L (can go up to >500,000 L).
- Air sparging is required to introduce bubbles into the culture for effective oxygen transfer
- Agitation is used to break up bubbles and thus further increases $k_L a$.
- Sparged bioreactor requires lower agitation speeds for aeration efficiencies comparable to non-sparged bioreactor.

Types of Bioreactor/Fermenter

Mechanical stirred tank bioreactor - Sparged (SSF)

- Stirred-bed bioreactor is similar to the static packed bed that a bed of substrate sits on a perforated base plate and air is forcefully blown through the bed from the bottom, an agitator is inserted at the top and provides continuous or intermittent mixing.
- Rocking-drum bioreactor consists of three concentric cylinders
  - an inner perforated cylinder, an outer perforated cylinder, and an outer solid cylinder.
  - The substrate sits in the space between the two perforated cylinders.

Types of Bioreactor/Fermenter

Bubble driven bioreactor - Bubble column (SmF) and Airliftt bioreactor (SmF)

- Aeration and mixing are achieved by air sparging (without mechanical agitation).
- Commonly used in the culture of shear sensitive organisms.
- Bubble driven bioreactor is generally tall (H:D between 8:1 and 20:1) to enhance oxygen transfer rate.
  - leads to high gas hold-ups.
  - long rising bubble residence times.
  - a region of high hydrostatic pressure near the sparger at the base of the fermenter.

Types of Bioreactor/Fermenter

Packed bed bioreactor (SmF)

- Cells or enzymes are immobilized by adsorption on or entrapment in non-moving solid (e.g, plastic blocks, concrete blocks, wood shavings, and porous gel).
- The liquid feed is pumped through the surface of the solids where the immobilized cells convert the substrates into products.

Types of Bioreactor/Fermenter

Packed bed bioreactor (SmF) - Trickle flow bioreactor

- The liquid medium trickles over the solid particles. In these reactors, the particles are not immersed in the liquid.
- Oxygen transfer is enhanced by ensuring that the cells are covered by only a very thin layer of liquid.

Types of Bioreactor/Fermenter

Packed bed bioreactor (SSF)

- A typical packed-bed bioreactor consists of a column of cylindrical or rectangular cross section, oriented vertically, with a perforated base plate on the bottom which supports a bed of substrate.
- Air is blown up through the base plate.

Types of Bioreactor/Fermenter

Fluidized bed bioreactor (SmF)

- Cells or enzymes are immobilized in/on the surface of light particles (e.g., microcarriers beads for animal cell culture).
- Mixing is assisted by the action of a pump.
- Able to maintain high cell concentrations and good mass transfer rates in continuous cultures.

Types of Bioreactor/Fermenter

Fluidized bed bioreactor (SSF)

- Gas-solid fluidized beds. In this bioreactor air is blown upwards through a perforated base plate at sufficient velocity to fluidize the substrate bed.

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