ChEn5751
PERFUSION AND IMMOBILIZED CELL CULTURE PROCESSES

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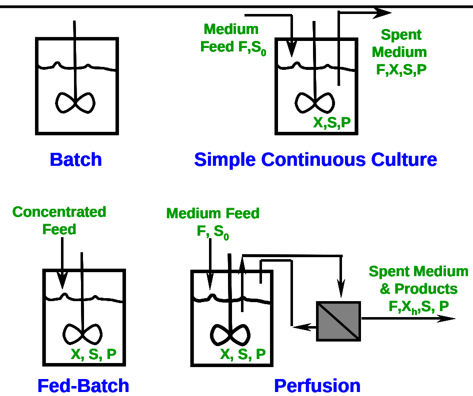
Outline

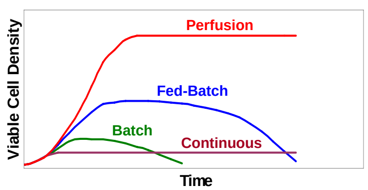
I. CELL RETENTION DEVICES
- A. Process mode, productivity and cell retention
- B. External vs internal cell retention, cell immobilization
- C. Cell retention devices
  1. Sedimentation
  2. Centrifugation
  3. Membrane separation

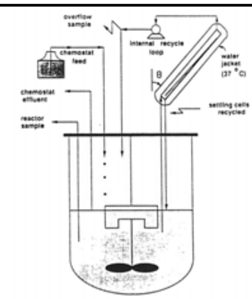
II. THE EFFECT OF CONCENTRATION FACTOR AND RETENTION TIME

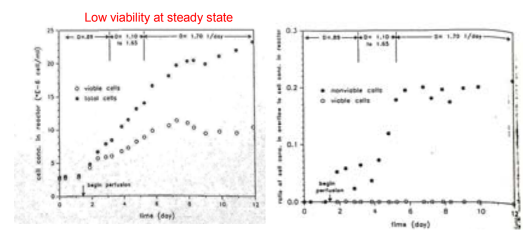
III. ENVIRONMENTAL PROCESSES AND CELL IMMOBILIZATION

IV. CELL IMMOBLIZATION METHOD



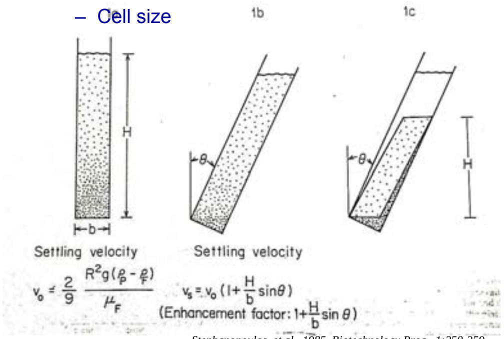




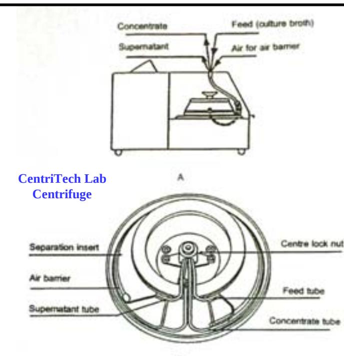


Batt, et al., 1990, Biotech. Prog., 6:458-464

- Operating parameters
  - Cell Density
  - Perfusion rate
  - Settling area
    - Length of the plates
  - Settler cross section - linear velocity
  - Incline angle
    - compromise between return rate and settling distance
  - Cell size



Stephanopoulos, et al., 1985, Biotechnology Prog., 1:250-259



THE EFFECT OF CONCENTRATION FACTOR AND RETENTION TIME

- Typically cell concentration with recycle is many times of that without recycle
- The same throughput (Dx_2) can be accomplished by different recirculation rate (αF) using different concentration factor c.
- c should be large enough to reduce αF. A high recirculation rate exposes cells to more frequent perturbation in the cell separation device.
- At large scale the recirculation stream needs cooling and imposes perturbation or stress

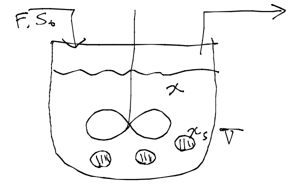
Cell Immobilization for Cell Retention

- Another way of retaining cells is via cell immobilization on supports which are easily retained in the reactor
- Immobilized cells grow in (or on) the solid support, may also grow in the liquid phase
- This is in contrast to using immobilized cells as biocatalysts, in those applications, non-growing but catalytically active cells are used.

Examples of Cell Immobilization as Cell Retention Method

- Microcarriers for animal cell culture
- Alginate/Agarose/Carragenan
- Biofilm

Analysis of Immobilized Cell Culture System



Reactor volume V
liquid phase volume εV
Solid phase volume $(1-\varepsilon)V$
x : cell concentration in liquid phase
x_s: cell concentration in solid phase
μ ; μ_s
S ; S_s
d_p: average particle diameter

k_d: detachment rate constant of solid phase cell into liquid phase.
Assume the reverse rate is very slow.

$$\varepsilon V \frac{dx}{dt} = \varepsilon V \mu x - Fx + k_d x_s \cdot (1-\varepsilon) V$$

$$(1-\varepsilon) V \frac{dx_s}{dt} = (1-\varepsilon) V \mu_s x_s - k_d x_s (1-\varepsilon) V$$

$$\varepsilon V \frac{dS}{dt} = F(S_0 - S) - \varepsilon V \cdot \frac{\mu x}{Y_{x/s}} - k_l (S - S_s)(1-\varepsilon)\frac{6V}{d_p}$$

$$(1-\varepsilon) V \frac{dS_s}{dt} = k_l (S - S_s)(1-\varepsilon)\frac{V \cdot 6}{d_p} - \frac{\mu_s x_s}{Y_{x/s}}$$

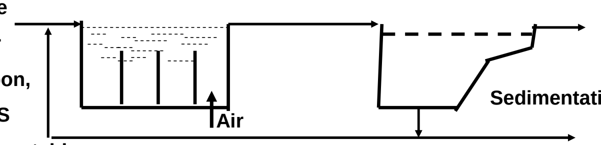
↑ assume uniform concn

Environmental Biological Treatment

- BOD (biochemical oxygen demand)
- COD (chemical oxygen demand)

Activated Sludge Plant with Recycle

Waste water (Carbon, N, P, S Sedimentable Solids)



Activated sludge: Microbial grown particulate in waste water treatment plant.