Chapter 9: Operating Bioreactors

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Presentation Outline:

- Choosing Cultivation Methods
- Modifying Batch and Continuous Reactors
- Immobilized Cell Systems

Choosing the Cultivation Method

The Choice of Bioreactor Affects Many Aspects of Bioprocessing.

1. Product concentration and purity
2. Degree of substrate conversion
3. Yields of cells and products
4. Capitol cost in a process (>50% total capital expenses)

Further Considerations in Choosing a Bioreactor.

1. Biocatalyst. (immobilized or suspended)
2. Separations and purification processes

Batch or Continuous Culture?

These choices represent extremes in bioreactor choices

Productivity →for cell mass or growth-associated products

Batch Culture: assume $k_d = 0$ and $q_p = 0$

$$r_b = \text{rate of cell mass production in 1 batch cycle}$$

$$r_b = \frac{X_m - X}{t_c} = \frac{Y^M_{X/S} S_o}{t_c}$$

$$t_c = \text{batch cycle time} = \frac{1}{\mu_{max}} \ln\frac{X_m}{X_o} + t_l$$

Exponential growth time

Lag time
Harvest &
Preparation

Batch or Continuous Culture? (cont.)

Continuous Culture: assume $k_d = 0$ and $q_p = 0$

r_c = rate of cell mass production in continuous culture

$$r_c = D_{opt} X_{opt}$$

$$\text{set } \frac{dDX}{dD} = 0 \quad \Rightarrow \quad D_{opt} = \mu_{max}\left(1 - \sqrt{\frac{K_S}{K_S + S_o}}\right)$$

$$X_{opt} = Y^M_{X/S}\left(S_o - \frac{K_S D_{opt}}{\mu_{max} - D_{opt}}\right) = Y^M_{X/S}\left(S_o + K_S - \sqrt{(K_S(S_o + K_S)}\ \right)$$

$$D_{opt}X_{opt} = Y^M_{X/S}\,\mu_{max}\left(1 - \sqrt{\frac{K_S}{K_S + S_o}}\right)\left(S_o + K_S - \sqrt{(K_S(S_o + K_S)}\ \right)$$

$$\approx \boxed{Y^M_{X/S}\,\mu_{max}\,S_o} \text{ when } K_S \ll S_o$$

Batch or Continuous Culture? (cont.)

Comparing Rates in Batch and Continuous Culture

$$\frac{r_c}{r_b} = \frac{Y^M_{X/S}\,\mu_{max}\,S_o}{Y^M_{X/S}\,S_o \Big/ \left(\frac{1}{\mu_{max}}\ln\frac{X_m}{X_o} + t_l\right)} = \ln\frac{X_m}{X_o} + t_l\mu_{max}$$

A commercial fermentation with

$$\frac{X_m}{X_o} = 20,\ t_l = 5 \text{ hr, and } \mu_{max} = 1.0 \text{ hr}^{-1}$$

$$\boxed{\frac{r_c}{r_b} = 8} \Rightarrow$$

Continuous culture method is ~ 10 times more productive for primary products (biomass & growth associated products

Batch or Continuous Culture? (cont.)

Why is it that most commercial bioprocess are Batch??

1. Secondary Product Productivity → is > in batch culture
   (SPs require very low concentrations of S, $S << S_{opt}$)
2. Genetic Instability → makes continuous culture less productive
   (revertants are formed and can out-compete highly selected and and productive strains in continuous culture.)
3. Operability and Reliability
   (sterility and equipment reliability > for batch culture)
4. Market Economics
   (Batch is flexible → can product many products per year)

Batch or Continuous Culture? (cont.)

Most Bioprocesses are Based on Batch Culture

(In terms of number, mostly for secondary, high value products)

High Volume Bioprocesses are Based on Continuous Culture

(mostly for large volume, lower value, growth associated products -- ethanol production, waste treatment, single-cell protein production)

Modified Bioreactors: Chemostat with Recycle

To keep the cell concentration higher than the normal steady-state level, cells in the effluent can be recycled back to the reactor.

Advantages of Cell Recycle

1. Increase productivity for biomass production
2. Increase stability by dampening perturbations of input stream properties

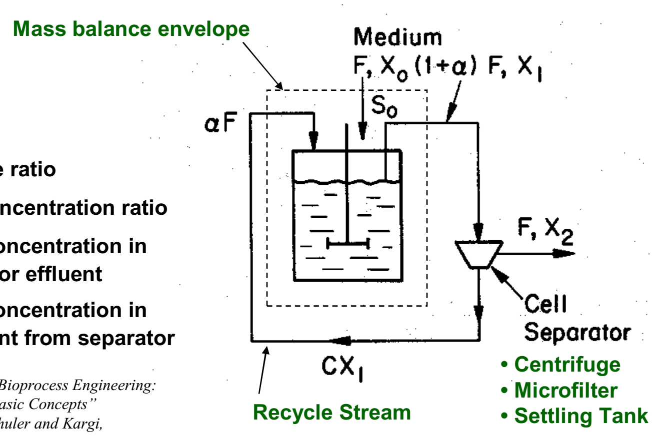
Chemostat with Recycle: Schematic Diagram Figure 9.1

α = recycle ratio

C = cell concentration ratio

X_1 = cell concentration in reactor effluent

X_2 = cell concentration in effluent from separator



"Bioprocess Engineering: Basic Concepts" Shuler and Kargi, Prentice Hall, 2002

Chemostat with Recycle: Biomass Balance

$$FX_o + \alpha FCX_1 - (1+\alpha)FX_1 + V_R \mu X_1 = V_R \frac{dX_1}{dt}$$

at steady-state ($\frac{dX_1}{dt} = 0$) and sterile feed ($X_o = 0$)

$$\alpha FCX_1 - (1+\alpha)FX_1 + V_R \mu X_1 = 0$$

and solving for μ

$$\mu = [1+\alpha(1-C)]D$$

Since $C > 1$ and $\alpha(1-C) < 0$, then $\mu < D$

A chemostat can be operated at dilution rates higher than the specific growth rate when cell recycle is used

Chemostat with Recycle: Biomass Balance

$$\mu = [1+\alpha(1-C)]D$$

Monod Equation, $\mu = \frac{\mu_{max} S}{K_S + S}$

Substitute Monod Eqn. into above, solve for S

$$S = \frac{K_S D(1+\alpha(1-C))}{\mu_{max} - D(1+\alpha(1-C))}$$

Chemostat with Recycle: Substrate Balance

$$FS_o + \alpha FS - (1+\alpha)FS - V_R \frac{\mu X_1}{Y^M_{X/S}} = V_R \frac{dS}{dt}$$

at steady state $\left(\frac{dS}{dt} = 0\right)$

$$FS_o + \alpha FS - (1+\alpha)FS - V_R \frac{\mu X_1}{Y^M_{X/S}} = 0$$

and solving for X_1

$$X_1 = \frac{D}{\mu} Y^M_{X/S}(S_o - S); \quad \text{But } \frac{D}{\mu} = \frac{1}{[1+\alpha(1-C)]}$$

$$X_1 = \frac{Y^M_{X/S}(S_o - S)}{[1+\alpha(1-C)]} = \frac{Y^M_{X/S}}{[1+\alpha(1-C)]}\left[S_o - \frac{K_S D(1+\alpha(1-C))}{\mu_{max} - D(1+\alpha(1-C))}\right]$$

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Chemostat with Recycle: Comparison Figure 9.2

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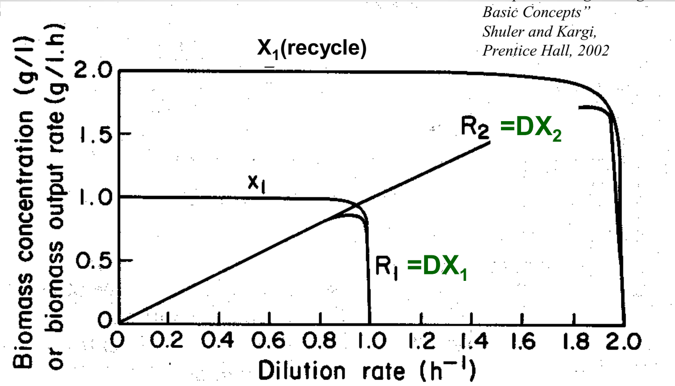

α=0.5, C=2.0, μ_{max}=1.0 hr^{-1}, K_S=0.01 g/L, $Y^M_{X/S}$=0.5

X_1 = cell concentration in reactor effluent with no recycle

X_1(recycle) = cell concentration in effluent with recycle

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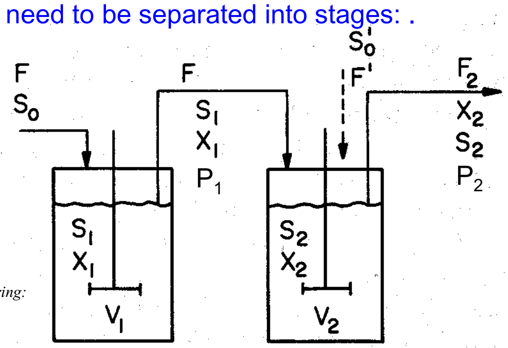
Multiple Chemostat Systems

Applicable to fermentations in which growth and product formation need to be separated into stages: .



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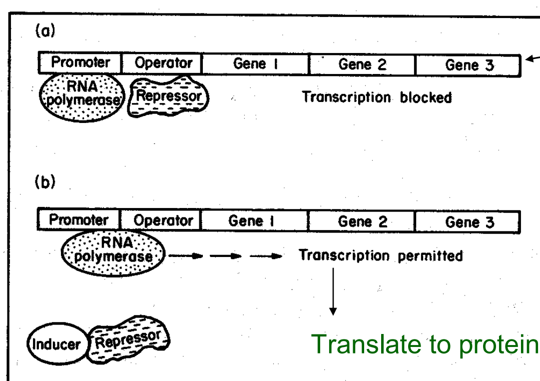
Growth stage   Product formation stage

Multiple Chemostat Systems (cont.)

1. Genetically Engineered Cells:



Recombinant DNA

"Bioprocess Engineering: Basic Concepts" Shuler and Kargi, Prentice Hall, 2002

Translate to protein product

Multiple Chemostat Systems (cont.)

Features of Genetically Engineered Cells:

→ have inserted recombinant DNA (plasmids) which allow for the production of a desired protein product.

→ GE cells grow more slowly than original non-modified strain (due to the extra metabolic burden of producing product).

→ Genetic Instability causes the GE culture to (slowly) lose ability to produce product. The non-plasmid carrying cells or the cells with mutation in the plasmid (revertants) grow faster.

Multiple Chemostat Systems (cont.)

Genetically Engineered Cells (cont.):

In the first stage, only cell growth occurs and no *inducer* is added for product formation. The GE cells grow at the maximum rate and are not out-competed in the first chemostat by *revertant* cells. When cell concentrations are high, an inducer is added in the latter (or last) chemostat to produce product at a very high rate.

Multiple Chemostat Systems (cont.)

2-Stage Chemostat System Analysis

Stage 1 - cell growth conditions, k_d=0, q_p=0, steady-state

$$\mu_1 = \frac{\mu_{max} S_1}{K_S + S_1} = D_1 \quad \text{from biomass balance}$$

$$\text{rearranging, } S_1 = \frac{K_S D_1}{\mu_{max} - D_1} \quad \text{where } D_1 = \frac{F}{V_1}$$

$$X_1 = Y^M_{X/S} (S_o - S_1) \quad \text{from substrate balance}$$

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Multiple Chemostat Systems (cont.)

2-Stage Chemostat System Analysis

Stage 2 - product formation conditions, k_d=0, $F^{'}$=0, steady-state

$$FX_1 - FX_2 + V_2 \mu_2 X_2 = V_2 \frac{dX_2}{dt} = 0 \quad \text{biomass balance}$$

$$\mu_2 = \frac{\mu_{max} S_2}{K_S + S_2} = D_2 \left(1 - \frac{X_1}{X_2}\right) \quad \text{where } D_2 = \frac{F}{V_2}$$

$$FS_1 - FS_2 - V_2 \frac{\mu_2 X_2}{Y^M_{X/S}} - V_2 \frac{q_P X_2}{Y_{P/S}} = V_2 \frac{dS_2}{dt} = 0 \quad \text{substrate balance}$$

$$FP_1 - FP_2 + V_2 q_P X_2 = V_2 \frac{dP_2}{dt} = 0 \quad \text{product balance}$$

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Multiple Chemostat Systems (cont.)

2-Stage Chemostat System Analysis

Stage 2 - product formation conditions, $k_d=0$, $F'=0$, steady-state

$$\mu_2 = \frac{\mu_{max} S_2}{K_S + S_2} = D_2 \left(1 - \frac{X_1}{X_2}\right) \quad \text{biomass balance}$$

$$S_2 = S_1 - \left(\frac{\mu_2 X_2}{D_2 Y^M_{X/S}} + \frac{q_P X_2}{D_2 Y_{P/S}} \right) \quad \text{substrate balance}$$

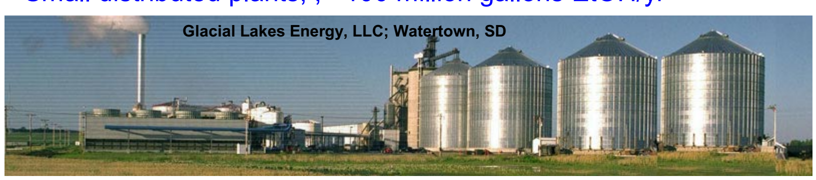
2 equations, 2 unknowns (S_2, X_2)

$$FP_1 - FP_2 + V_2 q_P X_2 = V_2 \frac{dP_2}{dt} = 0 \quad \text{product balance}$$

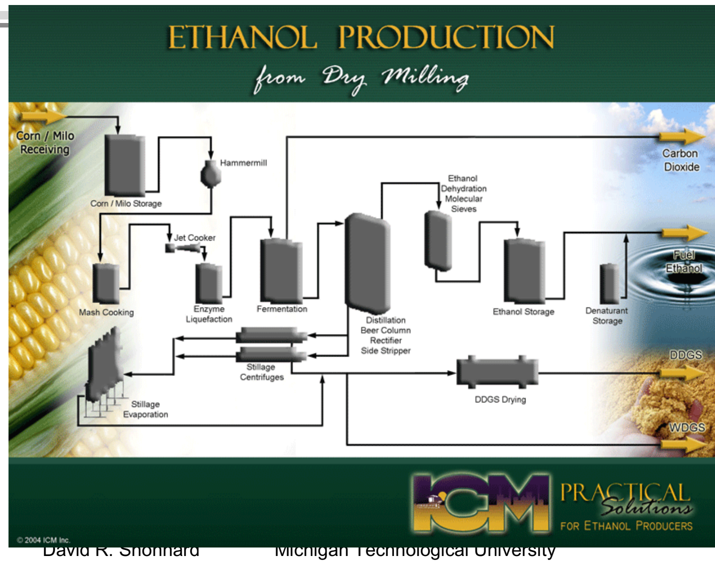
use X_2 in product balance to solve for P_2

Examples of Batch / Continuous Bioreactors: Ethanol Production from Corn

- 3.5 billion gallons EtOH / yr in the US
- Small distributed plants; , <100 million gallons EtOH/yr



Examples of Batch / Continuous Bioreactors: Ethanol Production from Corn



Fed-Batch Operation

Useful in Antibiotic Fermentation

→ reactor is fed continuously (or intermittently)
reactor is emptied periodically

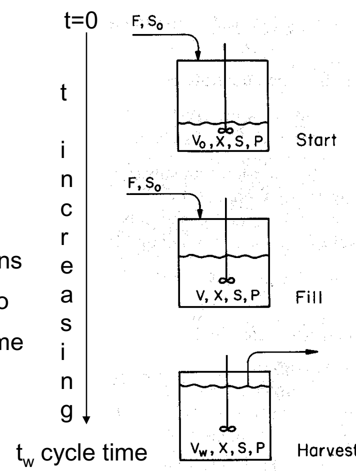
→ purpose is to maintain low substrate concentration, S

→ useful in overcoming *substrate inhibition* or *catabolic repression*, so that product formation increases.

Fed-Batch Operation (cont.)

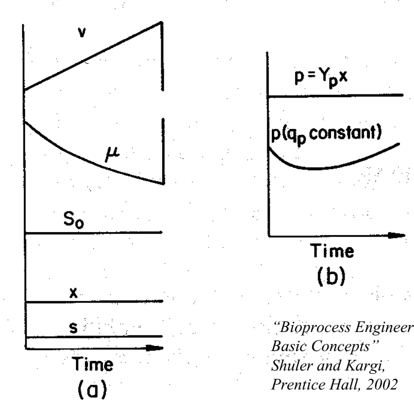
"Bioprocess Engineering: Basic Concepts" Shuler and Kargi, Prentice Hall, 2002

Before t = 0, almost all of the substrate, S_o, in the initial volume, V_o, is converted to biomass, X_m, with little product formation ($X=X_m \approx Y_{X/S}S_o$) and $P \approx 0$.
At t=0, feed is started at a low flow rate such that substrate is utilized as fast as It enters the reactor. Therefore, S remains very low in the reactor and X continues to maintain at $\approx Y_{X/S}S_o$ over time. The volume increases with time in the reactor and Product formation continues.



Fed-Batch Operation (cont.)

Behavior of X, S, P, V, and μ over time



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Fed-Batch Operation (cont.)

Analysis of Fed-Batch Operation

Volume: $$\frac{dV}{dt} = F \quad \Rightarrow \quad V = V_o + Ft$$

Biomass: $$\cancel{FX_o}^{\,0} + V\mu X = \frac{d(XV)}{dt} = V\cancel{\frac{dX}{dt}}^{\,0} + X\frac{dV}{dt}$$

$$V\mu X = X\frac{dV}{dt} \quad \Rightarrow \quad \mu = \frac{1}{V}\frac{dV}{dt} = \frac{F}{V} = D$$

$$\boxed{\mu = \frac{F}{V} = \frac{F}{V_o + Ft} = \frac{D_o}{1 + D_o t}}$$

Fed-Batch Operation (cont.)

Analysis of Fed-Batch Operation (cont.)

Total Biomass: X_t (g cells) vs time

$$\frac{dX}{dt} = 0 \quad \text{or} \quad \frac{d\left(\frac{X_t}{V}\right)}{dt} = \frac{V\left(\frac{dX_t}{dt}\right) - X_t\left(\frac{dV}{dt}\right)}{V^2} = 0$$

rearranging $$\frac{dX_t}{dt} = \frac{X_t}{V}\frac{dV}{dt} = X_m F = Y_{X/S} S_o F$$

integrating $$\boxed{X_t = X_{to} + Y_{X/S} S_o F t} = (V_o + Ft) X_m$$

Fed-Batch Operation (cont.)

Analysis of Fed-Batch Operation (cont.)

Product Formation: total product, $P_t = PV$

For many secondary products, the specific rate of product formation is a constant $= q_P$

$$\frac{dP_t}{dt} = q_P X_t = q_P (V_o + Ft) X_m$$

$$\text{integrating, } P_t = P_{to} + q_P X_m (V_o + \frac{Ft}{2})t$$

$$\text{or} \quad P = \frac{P_o V_o}{V} + q_P X_m (\frac{V_o}{V} + \frac{Dt}{2})t$$

$$\text{or} \quad P = \frac{P_o V_o}{(V_o + Ft)} + q_P X_m (\frac{V_o}{(V_o + Ft)} + \frac{Ft}{2(V_o + Ft)})t$$

Immobilized Cell Systems; 9.4

Restriction of cell mobility within a confined space

Potential Advantages:

1. Provides high cell concentrations per unit of reactor volume.
2. Eliminates the need for costly cell recovery and recycle.
3. May allow very high volumetric productivities.
4. May provide higher product yields, genetic stability, and shear damage protection.
5. May provide favorable microenvironments such as cell-cell contact, nutrient-product gradients, and pH gradients resulting in higher yields.

Immobilized Cell Systems; 9.4

Potential Disadvantages/Problems:

1. If cells are growing (as opposed to being in stationary phase) and/or evolve gas (CO_2), physical disruption of immobilization matrix could result.

2. Products must be excreted from the cell to be recovered easily.

3. Mass transfer limitations may occur as in immobilized enzyme systems.

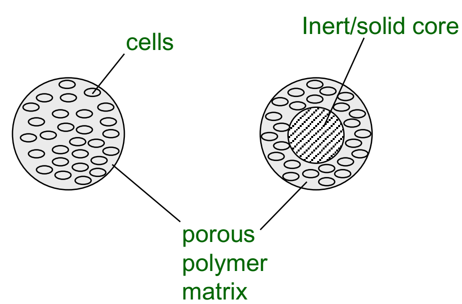
Methods of Immobilization

Active Immobilization:

1. Entrapment in a Porous Matrix:

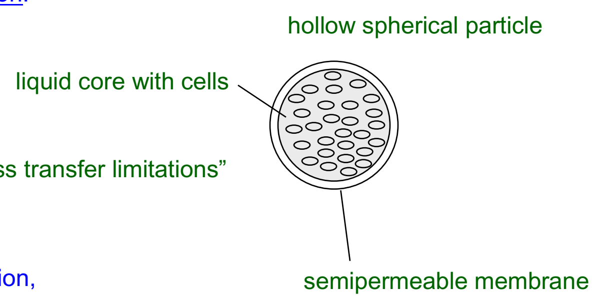
Polymeric Beads:

Polymers:
agar, alginate
κ-carrageenan
polyacrylamide
gelatin, collagen



Methods of Immobilization (cont.)

Encapsulation:

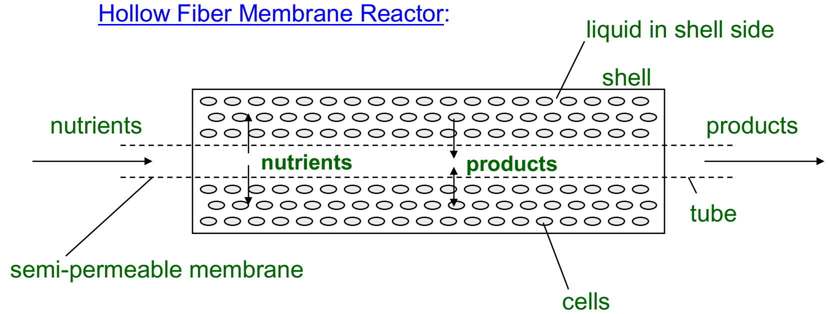


"less severe mass transfer limitations"

Membrane:
nylon, collodion,
polystyrene,
polylysine-alginate hydrogel
Cellulose acetate-ethyl acetate

Methods of Immobilization (cont.)

Hollow Fiber Membrane Reactor:

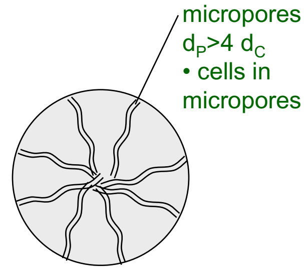


Methods of Immobilization (cont.)

2. Cell Binding to Inert Supports:

Micro-porous Supports:

"mass transfer limitations occur"

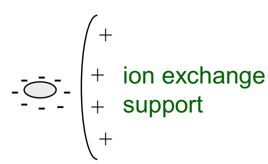


porous glass, porous silica, alumina
ceramics, gelatin, activated carbon
Wood chips, poly propylene ion-exchange resins
(DEAE-Sephadex, CMC-), Sepharose

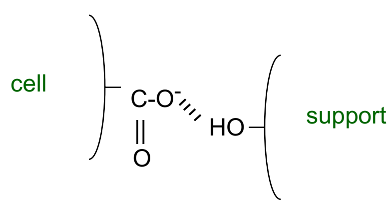
Methods of Immobilization (cont.)

Binding Forces:

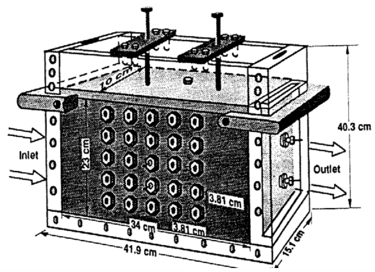
Electrostatic Attraction

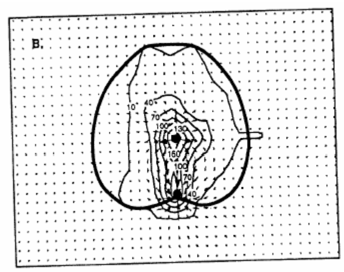


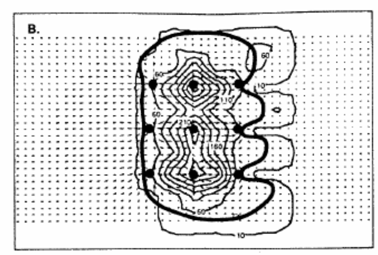
Hydrogen Bonding



Adhesion of bacteria to Sand Particles: Eliminating Electrostatic Repulsion







Methods of Immobilization (cont.)

Binding Forces:

Covalent Bonding: (review enzyme covalent bonding)

Support materials: CMC-carbodiimide
support functional groups
-OH, $-NH_2$, -COOH

Binding to proteins on cell surface

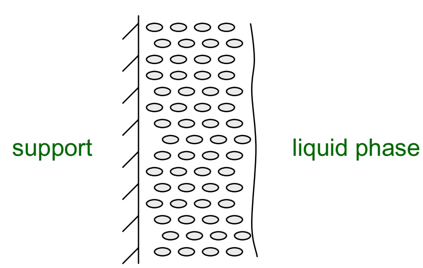
Methods of Immobilization (cont.)

Overview of Active Cell Immobilization Methods:

Support	Adsorption Capacity	Adsorption Strength
Porous silica	low	weak
Wood chips	high	weak
Ion-exchange resins	high	moderate
CMC	high	high

Methods of Immobilization (cont.)

Passive Immobilization:



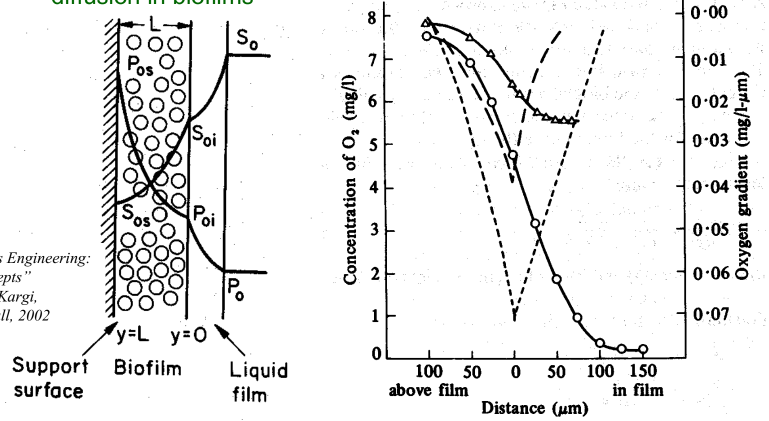
- wastewater treatment
- mold fermentations
- fouling of processing equipment

Biofilm (biopolymer + polysaccharides)

Analysis of Biofilm Mass Transfer Figures 9.1, 9.12

Substrate/product diffusion in biofilms

O_2 diffusion in biofilms



"Bioprocess Engineering: Basic Concepts"
Shuler and Kargi, Prentice Hall, 2002

Analysis of Biofilm Mass Transfer (cont.)

Differential Substrate Balance:

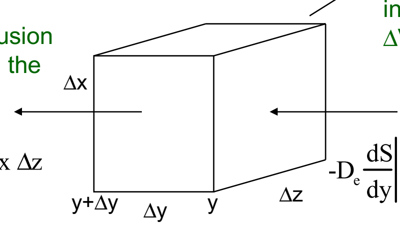
Material volume in biofilm, $\Delta V = \Delta x \, \Delta y \, \Delta z$

Rate of diffusion out through the area $\Delta x \, \Delta z$

$$-D_e \left.\frac{dS}{dy}\right|_{y+\Delta y} \Delta x \, \Delta z$$

Rate of diffusion in through the area $\Delta x \, \Delta z$

$$-D_e \left.\frac{dS}{dy}\right|_{y} \Delta x \, \Delta z$$



Rate of substrate consumption in the volume $\Delta V = \Delta x \, \Delta y \, \Delta z$ (due to cell growth, or product formation)

$$\frac{1}{Y^M_{X/S}} \frac{\mu_{max} S}{K_S + S} X \, \Delta x \, \Delta y \, \Delta z$$

$$\frac{1}{Y_{P/S}} \frac{q_p S}{K_S + S} X \, \Delta x \, \Delta y \, \Delta z$$

Analysis of Biofilm Mass Transfer (cont.)

Differential Substrate Balance at Steady-State:

Rate of diffusion in through the area Δx Δz − Rate of diffusion out through the area Δx Δz − Rate of substrate consumption in the volume ΔV = Δx Δy Δz = 0

$$-D_e \left.\frac{dS}{dy}\right|_y \Delta x\, \Delta z - \left(-D_e \left.\frac{dS}{dy}\right|_{y+\Delta y} \Delta x\, \Delta z\right) - \frac{1}{Y^M_{X/S}} \frac{\mu_{max}\, S}{K_S + S} X\, \Delta x\, \Delta y\, \Delta z = 0$$

Divide through by Δx Δy Δz and switch order of first 2 terms

$$\frac{D_e \left.\frac{dS}{dy}\right|_{y+\Delta y} - D_e \left.\frac{dS}{dy}\right|_y}{\Delta y} - \frac{1}{Y^M_{X/S}} \frac{\mu_{max}\, S}{K_S + S} X = 0$$

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Analysis of Biofilm Mass Transfer (cont.)

Differential Substrate Balance at Steady-State:

$$D_e \frac{d^2S}{dy^2} = \frac{1}{Y^M_{X/S}} \frac{\mu_{max}\, S}{K_S + S} X \qquad \text{eqn 9.49}$$

Boundary Conditions

$S = S_{oi}$ at $y = 0$ (at the biofilm / liquid interface)

$\frac{dS}{dy} = 0$, at $y = L$ (at the biofilm / support interface)

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Analysis of Biofilm Mass Transfer (cont.)

Dimensionless Substrate Balance at Steady-State:

$$\frac{d^2\bar{S}}{d\bar{y}^2} = \frac{\phi^2 \bar{S}}{1+\beta\bar{S}} \quad \text{eqn 9.51}$$

A numerical solution is required

$$\text{where} \quad \bar{S} = \frac{S}{S_o}, \quad \bar{y} = \frac{y}{L}, \quad \beta = \frac{S_o}{K_S},$$

$$\text{and } \phi = L\sqrt{\frac{\mu_{max} X}{Y^M_{X/S} D_e K_S}} \quad \text{"Thiele Modulus"}$$

Analytical solution is possible for 0 order and 1st order kinetics

Boundary Conditions

$$\bar{S} = 1 \quad \text{at } \bar{y} = 0 \text{ (at the biofilm / liquid interface)}$$

$$\frac{d\bar{S}}{d\bar{y}} = 0, \quad \text{at } \bar{y} = 1 \text{ (at the biofilm / support interface)}$$

Analysis of Biofilm Mass Transfer (cont.)

Zero Order Substrate Consumption Kinetics:

$$\frac{d^2\bar{S}}{d\bar{y}^2} = \frac{\phi^2 \bar{S}}{1+\beta\bar{S}}, \text{ for } \beta >> 1, \text{ and } \phi < 1$$

$$\frac{d^2\bar{S}}{d\bar{y}^2} = \frac{\phi^2}{\beta} \quad \text{zero-order substrate consumption kinetics}$$

$$\frac{d}{d\bar{y}}\frac{d\bar{S}}{d\bar{y}} = \frac{\phi^2}{\beta} \Rightarrow \int d\left(\frac{d\bar{S}}{d\bar{y}}\right) = \int \frac{\phi^2}{\beta} d\bar{y}$$

$$\frac{d\bar{S}}{d\bar{y}} = \frac{\phi^2}{\beta}\bar{y} + C_1$$

Analysis of Biofilm Mass Transfer (cont.)

Zero Order Substrate Consumption Kinetics:

Boundary condition # 2, at $\bar{y} = 1, \; \frac{d\bar{S}}{d\bar{y}} = 0$

$$0 = \frac{\phi^2}{\beta}(1) + C_1 \quad \Rightarrow \quad C_1 = -\frac{\phi^2}{\beta}$$

$$\frac{d\bar{S}}{d\bar{y}} = \frac{\phi^2}{\beta}\bar{y} - \frac{\phi^2}{\beta} \qquad \text{integrate again, } \int d\bar{S} = \int\left(\frac{\phi^2}{\beta}\bar{y} - \frac{\phi^2}{\beta}\right)d\bar{y}$$

$$\bar{S} = \frac{\phi^2}{2\beta}\bar{y}^2 - \frac{\phi^2}{\beta}y + C_2$$

Analysis of Biofilm Mass Transfer (cont.)

Zero Order Substrate Consumption Kinetics:

Boundary condition #1, at $\bar{y} = 0, \; \bar{S} = 1$

$$1 = \frac{\phi^2}{\beta}(0^2) - \frac{\phi^2}{\beta}(0) + C_2 \quad \Rightarrow \quad C_2 = 1$$

$$\bar{S} = \frac{\phi^2}{2\beta}\bar{y}^2 - \frac{\phi^2}{\beta}\bar{y} + 1 \quad \text{or} \quad \boxed{\bar{S} = \frac{\phi^2}{\beta}\left(\frac{\bar{y}^2}{2} - \bar{y}\right) + 1}$$

for $\frac{\phi^2}{\beta} << 1$

Biofilm Effectiveness

The effectiveness factor is calculated by dividing the rate of substrate diffusion into the biofilm by the maximum substrate consumption rate.

Solve for the Effectiveness Factor, η

$$N_S A_S = -A_S D_e \left.\frac{dS}{dy}\right|_{y=0} = \eta\left(\frac{\mu_{max} S_o X}{Y^M_{X/S}(K_S + S_o)}\right)(A_S L)$$

Rate of substrate diffusion into biofilm through an area A_S at the surface at y = 0

Volumetric rate of substrate consumption within the biofilm in a volume ($A_S L$)

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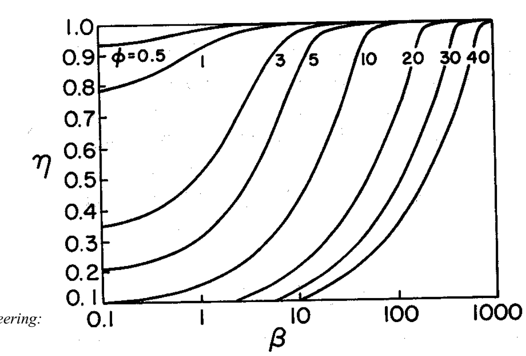
Effectiveness Factor

Biofilm is most effective for β >>1

η increases as ϕ decreases for any value of β



"Bioprocess Engineering: Basic Concepts" Shuler and Kargi, Prentice Hall, 2002

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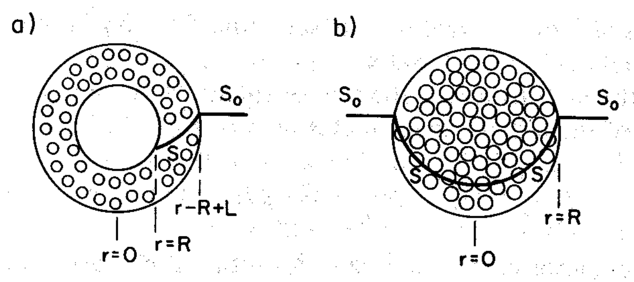
Spherical Particle of Immobilized Cells
Figure 9.14



"Bioprocess Engineering: Basic Concepts"
Shuler and Kargi,
Prentice Hall, 2002

V_P is particle volume
A_P is particle area

Analysis of Mass Transfer in Spherical Particle

Dimensionless Substrate Balance at Steady-State:

$$\frac{d^2\bar{S}}{d\bar{r}^2} + \frac{2}{\bar{r}}\frac{d\bar{S}}{d\bar{r}} = \frac{\phi^2\,\bar{S}}{1+\beta\bar{S}} \qquad \text{eqn 9.58}$$

where $\bar{S} = \frac{S}{S_o}$, $\bar{r} = \frac{r}{R}$, $\beta = \frac{S_o}{K_S}$,

and $\phi = R\sqrt{\frac{\mu_{max}X}{Y^M_{X/S}D_eK_S}}$ "Thiele Modulus"

Boundary Conditions

$\bar{S} = 1$ at $\bar{r} = 1$ (at the particle / liquid interface)

$\frac{d\bar{S}}{d\bar{r}} = 0,$ at $\bar{r} = 0$ (at the particle center)

Particle Effectiveness

If all of the particle cells "see" substrate at a concentration S_o or high enough to grow maximally, then the particle is said to have an effectiveness of 1.

Rate of S consumption by a single particle

$$N_S A_P = -A_P D_e \left.\frac{dS}{dr}\right|_{r=R} = \eta \left(\frac{\mu_{max} S_o X}{Y^M_{X/S} (K_S + S_o)} \right) V_P$$

Rate of substrate diffusion into particle through an area A_P at the surface at r = R

Volumetric rate of substrate consumption within the particle in a volume (V_P)

Particle Effectiveness (cont.)

Equation 9.58 can be solved analytically for limiting cases:

Case 1, for $S_o \ll K_S$ (very dilute substrate)

$$\eta = \frac{1}{\phi}\left[\frac{1}{\tanh 3\phi} - \frac{1}{3\phi}\right]$$

$$\phi = \frac{V_P}{A_P}\sqrt{\frac{\mu_{max} X}{Y^M_{X/S} D_e K_S}} \quad \text{"Thiele Modulus"}$$

Particle Effectiveness (cont.)

Equation 9.58 can be solved analytically for limiting cases:

Case 2, for S_o>>K_S (very concentrated substrate)

$$D_e\left[\frac{d^2S}{dr^2} + \frac{2}{r}\frac{dS}{dr}\right] = \frac{\mu_{max} S}{Y^M_{X/S}(K_S + S)} X = \frac{\mu_{max} X}{Y^M_{X/S}}$$

Boundary Conditions

$S = S_o$ at $r = R$ (at the particle / liquid interface)

$\frac{dS}{dr} = 0,$ at $r = 0$ (at the particle center)

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Particle Effectiveness (cont.)

Equation 9.58 can be solved analytically for limiting cases:

Case 2, for S_o>>K_S

Use a variable transformation, S=S'/r

$$\frac{1}{r}\frac{d^2S'}{dr^2} = \frac{\mu_{max} X}{Y^M_{X/S} D_e}$$

Solution for S is;

$$S = S_o - \frac{\mu_{max} X}{6\, Y^M_{X/S} D_e}(R^2 - r^2)$$

At a critical radius (r_{cr}), $S = 0$

$$0 = S_o - \frac{\mu_{max} X}{6\, Y^M_{X/S} D_e}(R^2 - r_{cr}^2)$$

$$\left(\frac{r_{cr}}{R}\right)^2 = 1 - \frac{6\, D_e\, S_o\, Y^M_{X/S}}{\mu_{max}\, X\, R^2}$$

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Particle Effectiveness (cont.)

Equation 9.58 can be solved analytically for limiting cases:

Case 2, for $S_o >> K_S$

$$\eta = \frac{\frac{\mu_{max} X}{Y^M_{X/S}} \frac{4}{3}\pi (R^3 - r_{cr}^3)}{\frac{\mu_{max} X}{Y^M_{X/S}} \frac{4}{3}\pi R^3} = 1 - \left(\frac{r_{cr}}{R}\right)^3$$

or

$$\eta = 1 - \left(1 - \frac{6\, D_e\, S_o\, Y^M_{X/S}}{\mu_{max}\, X\, R^2}\right)^{\frac{3}{2}}$$

Bioreactors Using Immobilized Cells Figure 9.15

The single particle analysis for η can be used in the analysis of bioreactors having immobilized cells:

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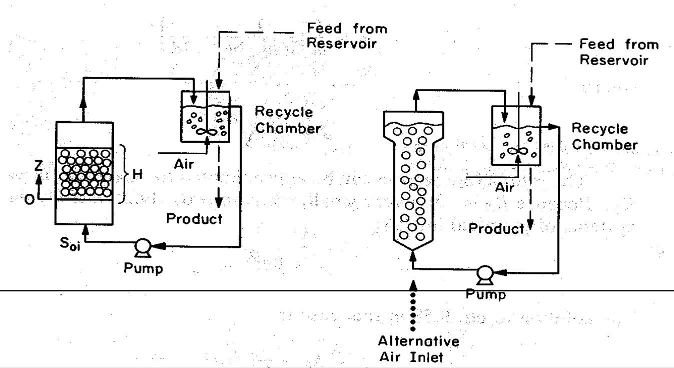
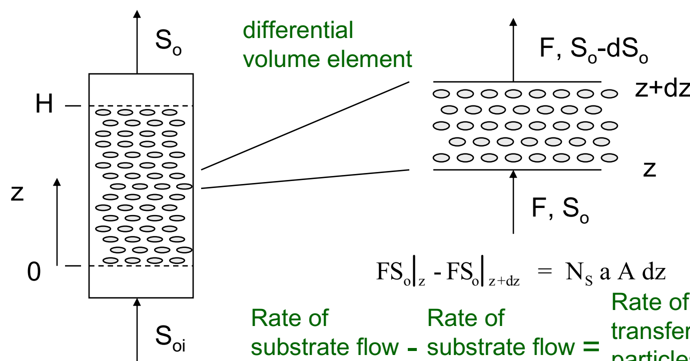
Consider a plug flow reactor filled with immobilized cell particles



Bioreactors Using Immobilized Cells (cont.)

A differential balance on a thin slice of particles within the reactor:



$$FS_o\big|_z - FS_o\big|_{z+dz} = N_S \, a \, A \, dz$$

Rate of substrate flow into element - Rate of substrate flow out of element = Rate of mass transfer into particles within element

Bioreactors Using Immobilized Cells (cont.)

Using the definition of η:

$$N_S A_P = \eta \left(\frac{\mu_{max} S_o X}{Y^M_{X/S} (K_S + S_o)} \right) V_P$$

$$-F \frac{dS_o}{dz} = \eta \left(\frac{\mu_{max} S_o X}{Y^M_{X/S} (K_S + S_o)} \right) \left(\frac{V_P}{A_P} \right) a A$$

where a = surface area of particle per unit volume of bed (cm^2 / cm^3 bed)

A = cross-sectional area of the bed (cm^2)

Bioreactors Using Immobilized Cells (cont.)

At z = 0, $S_o = S_{oi}$: integrating assuming η is constant

$$K_S \ln\left(\frac{S_{oi}}{S_o}\right) + (S_{oi} - S_o) = \eta \left(\frac{\mu_{max} V_P X a A}{Y^M_{X/S} F A_P}\right) H$$

for low substrate concentration ($S_{oi} << K_S$)

$$\ln\left(\frac{S_o}{S_{oi}}\right) = -\eta \left(\frac{\mu_{max} V_P X a A}{Y^M_{X/S} F A_P K_S}\right) H$$

note $\bar{x} = x\left(\frac{V_P}{A_P}\right)a$ (average cell mass conc. in the bed)