CHAPTER III

THEORY

3.1 Basic Equations

The general material balance equations for growth, substrate utilization and product formation can be written as follows:

Growth:

Cell mass = Cell + Cells - Cells - Cell
accumulation   growth   in   out   death

$$dX/dt = \mu X + FX_o/V - FX/V - \gamma X \tag{3.1}$$

Substrate Utilization:

Substrate = Substrate + Substrate - Substrate - Maintenance - Substrate
accumulation   consumed   feed   removal   requirement   consumed
   for product
   formation

$$dS/dt = -\mu X/Y_{x/s} + FS_o/V - FS/V - mX - \upsilon X/Y_{p/s} \tag{3.2}$$

Product Formation:

Product = Product + Product - Product - Product
accumulation   synthesis   feed   removal   destruction

$$dP/dt = \upsilon X + FPo/V - FP/V - KP \tag{3.3}$$

The above equations are applicable for both steady and unsteady state fermentation.

3.2 Batch Fermentation

For simplicity, it is based on the following assumptions:

1. At the exponential growth phase,

$$\mu \gg \gamma \; ; \tag{3.4}$$

2. At the product formation phase,

$$\upsilon \gg K \; ; \tag{3.5}$$

3. At the substrate consumption phase

$$mX \ll \mu X/Y_{x/s} \; ; \; \upsilon X/Y_{p/s} = 0 \tag{3.6}$$

$$\upsilon X/Y_{p/s} = 0$$

Since for the batch process, the feed rate F=0, equation (3.1), (3.2) and (3.3) can be rearranged using of assumptions (3.4), (3.5) and (3.6), and can be expressed as :

$$\mu = (1/X) \, (dX/dt) \tag{3.7}$$

$$\mu X/Y_{x/s} = (1/X) \, (dS/dt) = \upsilon_s \tag{3.8}$$

$$\upsilon \qquad = (1/X) \, (dP/dt) \tag{3.9}$$

Where υ_s denotes the specific substrate consumption rate, the production yield from carbon source, $Y_{p/s}$, can be calculated from

$$Y_{p/s} = \upsilon/\upsilon_s \tag{3.10}$$

3.3 Single-stage Continuous Fermentation

In addition to the assumptions (3.4), (3.5) and (3.6), it can be assumed that

1. Substrate is free from strain at initial condition, i.e.,

$$X_o = 0 \tag{3.11}$$

2. None of the product is fed to the fermentor, i.e.,

$$P_o = 0 \tag{3.12}$$

With assumptions (3.4)-(3.6) and (3.11)-(3.12), equation (3.1) can be simplified as shown ;

$$-FX/V + \mu X = dX/dt \tag{3.13}$$

For steady state, $dX/dt = 0$, equation (3.13) becomes

$$\mu = F/V \tag{3.14}$$

Let D denotes the dilution rate defined by the ratio between the flow rate of the substrate to the culture volume, i.e.,

$$D = F/V \tag{3.15}$$

At steady state, it can be seen that the specific growth rate is exactly equal to the dilution rate.

From equation (3.2), using assumptions (3.4) - (3.6) and (3.11) - (3.12), it can be obtained at steady state, i.e., $dS/dt = 0$

$$D(S_o - S) = \mu X / Y_{X/s} \tag{3.16}$$

Where D is defined in equation (3.15). Recalling from equation (3.15) that $\mu = D$, equation (3.16) becomes

$$X = Y_{X/s}(S_o - S) \tag{3.17}$$

Similarly, from equation (3.3) it can be obtained at steady state

$$\upsilon = DP/X \tag{3.18}$$

3.4 Single-stage Continuous Fermentation with Cell Recycling

If the outlet flow from microfiltration is αF and the outlet flow from fermentor is $(1+\alpha)F$. So that, equations for this system can be written as follows:

Cell accumulation	=	Cells growth	+	Cells in	+	Cells recycle	-	Cells out	-	Cell death

$$dX/dt = \mu X + (F/V)X_0 + \alpha(F/V)CX - (1+\alpha)(F/V)X - \gamma X \tag{3.19}$$

Substrate accumulation	=	Substrate consumed	+	Substrate feed	-	Substrate removal	-	Maintenance requirement	-	Substrate consumed for product formation

$$dS/dt = -\mu X / Y_{X/s} + FS_0/V - \alpha FS/V - (1+\alpha)FS/V - mX \tag{3.20}$$

$$- \upsilon X / Y_{p/s}$$

Product = Product + Product - Product - Product
accumulation formation in out destruction

$$dP/dt = \upsilon X + FP_O/V - FP/V - KP \qquad (3.21)$$

3.5 Control of Biomass Concentration in A Continuous Fermentation.

From Figure 3.1 and the general materail balance equations (equations (3.1), (3.2) and (3.3)), material balance for this system can be written as follows:

Cell = Cell + Cell - Cell - Cell $\qquad$ (3.22)
accumulation growth in out death

$$dX/dt = \mu X + FX_o/V - BFX/V - \gamma X$$

Substrate = Substrate + Substrate - Substrate - Maintenance - Substrate
accumulation consumed feed removal requirement consumed
for product
formation

$$dS/dt = -\mu X/Y_{x/s} + FS_o/V - FS/V - mX - \upsilon X/Y_{p/s} \qquad (3.23)$$

Product = Product + Product - Product - Product
accumulation synthesis feed removal destruction

$$dP/dt = \upsilon X + FPo/V - FP/V - KP \qquad (3.24)$$

Equations (3.22), (3.23), and (3.24) can be rearranged using assumptions (3.4), (3.5), and (3.6) and can be expressed as:

$$dX/dt = (\mu - BD)X \qquad (3.25)$$

$$P/dt = \upsilon X - DP \qquad (3.26)$$

$$dS/dt = D(S_o - S) - \mu X/Y_{x/s} \tag{3.27}$$

At steady state equations (3.25), (3.26) and (3.27) can be simplified

$$\mu = BD \tag{3.28}$$

$$\upsilon = DP/X \tag{3.29}$$

$$Y_{x/s} = \mu X/D(S_o - S) \tag{3.30}$$
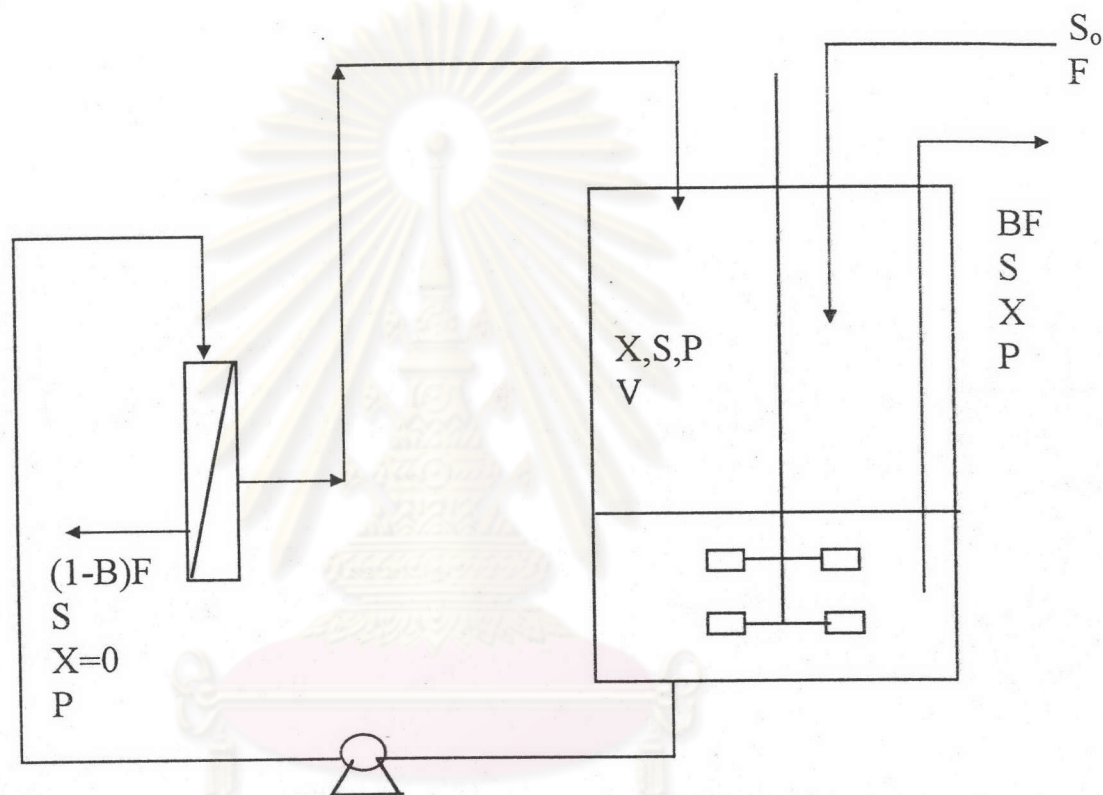
Where B= Bleed ratio

Figure 3.1 Schematic diagram of CSTR with cell recycling.

3.6 Cross Flow Filtration

At present, a separation process with membrane is interesting and is widely used in industry. Membranes is an energy-efficient, economical separation method used to concentrate chemicals and biologicals at a high degree of purity. Comparing the energy value in separation process, separation process with membrane used lower energy than other processes.

Microfiltration (MF) separate particle or colloid by using pore size of membrane approximately 0.05 to 10 micron at pressure 1-5 bar. Application of microfiltration was used in separation cells and wine process.

A typical MF operation is a pressure-driven process in which low-MW solutes and water pass through the filter and high-MW solutes are retained on the membrane surface. Therefore, a concentration gradient build up between the surface of the membrane and the bulk fluid. This gradient results in concentration polarization. As a result of concentration polarization, solute diffuses back from the membrane surface to the solution. (Figure 3.2) At steady state, the mass balance equation of solute concentration can be written as follows:

$$JC - D_e \, dC/dx = JC_p \qquad\qquad (3.31)$$

Where D_e is the effective diffusivity of solute in liquid film (cm^2/s), J is the volumetric

filtration flux of liquid (cm^3/cm^2 s), and C is the concentration of solute (mol/cm^3
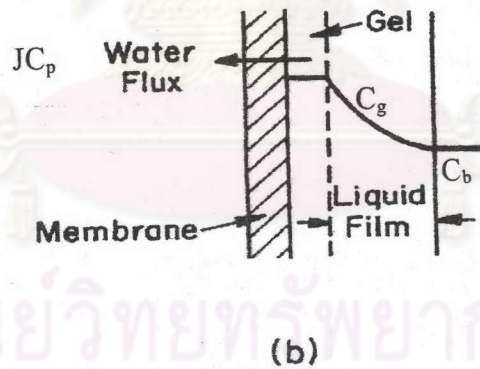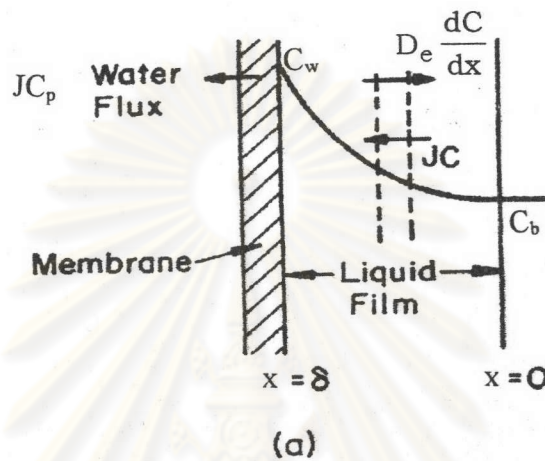
liquid).

Figure 3.2 Solute transfer in a MF membrane: (a) without gel formation;

(b) with gel formation.

Integration of eq.3.31 with the boundary conditions of $C = C_b$ at x = 0 and

$C_w = C$ at x = δ yields

$$J = D_e/\delta \ln C_w/C_b \tag{3.32}$$

or

$$J = k \ln C_w/C_b \tag{3.33}$$

Where $k = D_e/\delta$ is the mass transfer coefficient and δ is film thickness.

The mass transfer coefficient is a function of fluid and solute properties and flow conditions and is correlated with Re (Reynolds number) and Sc (Schmidt number).

$$Sh = dk/D_e = aRe^a Sc^b \tag{3.34}$$

where $Re = dv\rho/\beta$, $Sc = \beta/\rho D_e$, and $Sh = kd/D_e$, where Sh is the sherwood number. The value of a is 1/3 according to the boundary layer theory; b is approximately 0.5 for laminar flow and 1.0 for turbulent flow. That is,

$k \propto v^{0.5}$ for laminar and $k \propto v$ for turbulent flow.

$$J = k \ln C_g/C_b \tag{3.35}$$

Gel formation depends on the nature and concentration of the solute, pH, and pressure. One gel is formed, C_g becomes constant, and liquid flux decreases logarithmically with increasing solute concentration in the bulk liquid. The gel layer causes hydraulic resistance against flow and acts somewhat like a second membrane. Figure 3.2 depicts the variation of liquid flux with the logarithm of solute concentration in the absence and presence of gel formation.
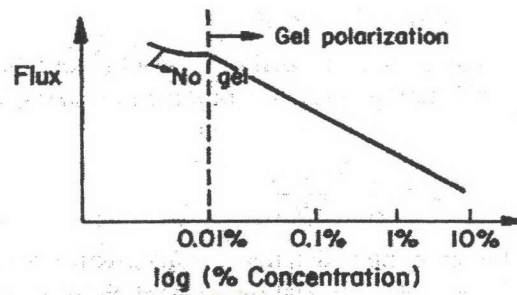
Figure 3.3 Variation of flux with solute concentration.

Gel formation can be partially eliminated by cross-flow filtration, where pressure is not applied directly perpendicular to the membrane, but parallel to the membrane surface. That is, fluid flows parallel to the membrane surface and passes through the membrane, leaving solutes in a liquid phase above the membrane. Mechanical agitation or vibration of the membrane surface can also be used to alleviate gel formation.

Schematic of cross-flow filtration is shown in Fig 3.4 The pressure drop driving fluid flow is

$$\Delta p = p_i - p_o \tag{3.36}$$

For laminar flow, using the Hagen- Poiseuille equation, we can derive the following:

$$p_i - p_o = \Delta p = \frac{C_1 \beta L V}{d^2} = \frac{C_2 \beta L Q}{d^4} \tag{3.37}$$

where L is the length of the tube, β is fluid viscosity, Q is the volumetric flow rate of the liquid, and d is diameter of the tube.

For turbulent flow, the following equation is used for ΔP :

$$p_i - p_o = -\Delta p = \frac{C_3 \beta LV}{d} = \frac{C_4 fLQ^2}{d^5} \tag{3.38}$$

where f is the Fanning friction, which is a function of Re. For cross-flow filtration, turbulent flow is desired.

The average transmembrane pressure drop is

$$\Delta p_m = \frac{p_i + p_o}{2} - p_f \tag{3.39}$$

Where p_f is the filtrate pressure, which is usually near atmospheric.

Assuming that $p_f = p_{atm}$ or p_f is zero gauge pressure, we can relate Δp_m to Δp.

$$\Delta p_m = p_i - \frac{1}{2}\Delta p \tag{3.40}$$

High inlet pressure and low fluid velocities need to be used to obtain high Δp_m.
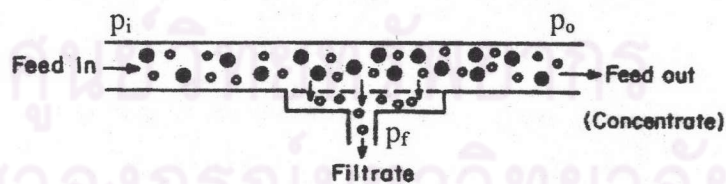

Figure 3.4 Schematic of cross-flow filtration

The filtration flux (J), as a function of transmembrane pressure drop, is given by

$$J = \frac{\Delta p_m}{R_g + R_m} \tag{3.41}$$

Where R_g and R_m are gel and membrane resistance, respectively. R_m is constant and R_g varies with the solute concentration and the tangential velocity across the membrane, which can retard or eliminate gel formation. Also, the filtration flux is a function if fluid velocity, as described by equations.(3.40) and (3.41). Usually, there is an optimal fluid velocity range maximizing the filtration rate. At low velocities, the mass transfer coefficient is low, resulting in high gel resistance and low filtrate flux. At high fluid velocities, Δp is high, resulting in low Δp_m and therefore low permeation flux. Also, there is an optimal values of Δp_m resulting in maximum flux. This is because of a pressure limitation on p_i. That is, the maximum value of Δp_m is p_i, and p_i is limited by the physical properties of the membrane. With modern membranes, specially the new ceramic membranes, it may be possible to push p_i to very high levels. Therefore, at low Δp_m values, flux increases with Δp_m. However, at high Δp_m, gel formation takes place, and gel resistance increases with increasing Δp_m, resulting in a constant filtration flux.

From over all equations, Permeation flux of solution depend on four parameter.

1. Pressure (From equations (3.39), (3.40), and (3.41)).

Permeation flux is proportional with pressure in system that it is continuous increasing. Until, gel layer formed on the surface membrane that it increased total filtration resistance and film resistance too. So, permeation flux is maximum and constant when it comparing with pressure.

2. Recirculation velocity (From equations (3.34), (3.35), and (3.39)).

The mass transfer coefficient increased that it is proportional with recirculation velocity (Equation (3.39) and (3.40)). Furthermore, Increasing of recirculation velocity is add to shear value on the surface membrane. So, gel thickness and gel resistance is decreased. But the average driving force(Δp_m) will decrease with increasing recirculation velocity.

3. Temperature.

The mass transfer coefficient increase with temperature which also results in the increase of permeation flux.

4. Concentration of solute.(C_b)

The permeate flux decrease with the solute concentration .

3.7 Membrane Rejection.

The rejection coefficient of a microfiltration is defined as

$$R = \frac{C_b - C_p}{C_b} = 1 - \frac{C_p}{C_b} \tag{3.42}$$

where C_p is the concentration of the solute in the filtrate. When $C_p = 0$, only water passes though the filter and $R = 1$, which is complete solute rejection. If $C_p = C_b$, complete solute transfer to the filtrate takes place and $R = 0$ (no rejection). Usually, the rejection coefficient is between 0 and 1 that is closer to 1 (that is, $R \approx$ 0.95 or 0.98). The value of R is a measure if the selectivity if the membrane for certain solutes. Selective separation if various compounds can be achieved using membranes with the right molecular-weight cutoff.