Ministry of Higher Education and
Scientific Research
University of Technology
Chemical Engineering Department

Biochemical engineering
Third Year

م.تغريد لطفي

$$r_p = k_3 \frac{C_S C_{E_0}}{\frac{k_2}{k_1} + C_S}$$

$\frac{k_2}{k_1} = K_m$ = Michaelis constant.

$k_3 = k_r$ = For the slow step of production.

$$\therefore \boxed{r_p = \frac{k_r \cdot C_S \cdot C_{E_0}}{K_m + C_S}} \quad \text{M.M.E}$$

The initial rate, given by

$$\boxed{r_{p_0} = \frac{k_r C_{S_0} C_{E_0}}{K_m + C_{S_0}}}$$

it is proportional to C_{S_0}

1- For low values of C_{S_0} ($C_{S_0} \ll K_m$)

$$\therefore r_{p_0} = \frac{k_r C_{S_0} C_{E_0}}{K_m}$$

2- The maximum initial rate is obtained for

$C_{S_0} >> K_m$ K_m is very low value.

$$r_{p_0 max} = \frac{k_r \cdot C_{S_0} C_{E_0}}{C_{S_0}}$$

$$\therefore r_{p_o\,max} = K_r \cdot C_{E_o} = V_{max}$$

V_{max} = is the maximum rate.

sub in eq M-M-E

$$\therefore \boxed{r_p = \frac{V_{max} \cdot C_s}{K_m + C_s}}$$

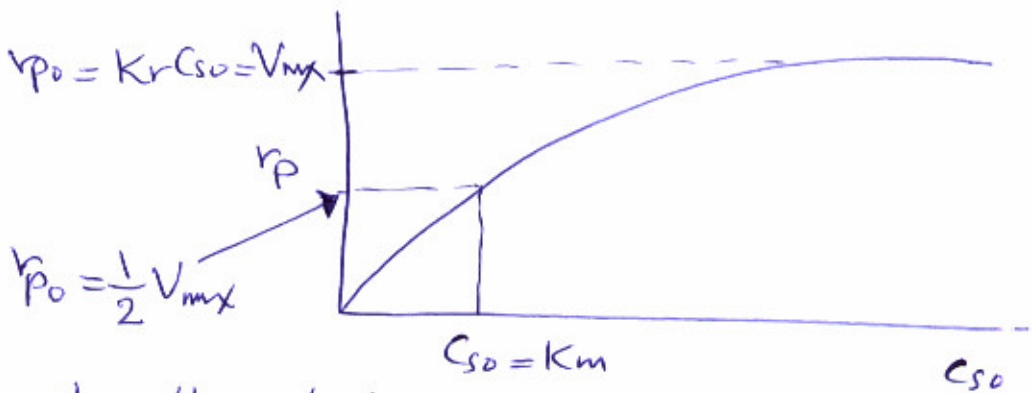
هذا المعادلة

3- $C_{so} = K_m$

$$r_{p_o} = \frac{V_{max} \cdot C_{so}}{C_{so} + C_{so}}$$

$$r_{p_o} = \frac{V_{max} - C_{so}}{2 C_{so}}$$

$$\therefore \boxed{r_{p_o} = \frac{1}{2} V_{max}.}$$



This fig show the initial rate plot showing interpretation of $r_{p_{o\,max}}$ interms of rate parameters, at constant C_{E_o}, T, pH

2- Briggs-Haldane Model

Briggs model is based upon the assumption that

1- After a short initial start up period, the concentration of the enzyme-substrate complex is in pseudo-steady state

2- For a constant volume batch reactor and other reactor type operated at constant (T & pH) without the assumption of (fast and slow step).

For material balance on S as free substrate, ES, E

$$S + E \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES$$

$$ES \xrightarrow{k_r} P + E$$

for substrate

$$r_S = -\frac{dC_S}{dt} = -k_1 C_S C_E + k_2 C_{ES} \quad \text{---- (1)}$$

$$r_{ES} = \frac{dC_{ES}}{dt} = k_1 C_E C_S - k_2 C_{ES} - k_r C_{ES} \quad \text{--- (2)}$$

$$C_{E_o} = C_E + C_{ES}$$

$$C_E = C_{E_o} - C_{ES} \quad \text{---------- (3)}$$

$$C_{S_o} = C_S + C_{ES} + C_P \quad \text{---------- (4)}$$

sub eq (3) into eq (1) بعد ترتيب معادلة ①

$$-\frac{dC_S}{dt} = k_2 C_{ES} - k_1 C_S (C_{E_o} - C_{ES})$$

sub eq ③ into eq ②

$$\frac{dC_{ES}}{dt} = k_1 C_S (C_{E_o} - C_{ES}) - k_2 C_{ES} - k_n C_{ES}$$

at $t = 0$ $\quad C_S = C_{S_o}$

$$C_{ES} = 0$$

$$\frac{dC_{ES}}{dt} = 0$$

$$\therefore \frac{dC_{ES}}{dt} = 0 = k_1 C_S (C_{E_o} - C_{ES}) - k_2 C_{ES} - k_n C_{ES}$$

$$0 = k_1 C_S (C_{E_o} - C_{ES}) - C_{ES} (k_2 + k_r)$$

$$0 = k_1 C_S C_{E_o} - k_1 C_S C_{ES} - C_{ES} (k_2 + k_r)$$

$$0 = k_1 C_S C_{E_o} - C_{ES} (k_1 C_S + (k_2 + k_r)$$

$$k_1 C_S C_{E_o} = C_{ES} (k_1 C_S + k_2 + k_r)$$

$$\therefore C_{ES} = \frac{K_1 C_S C_{E_0}}{K_1 C_S + K_2 + K_r} \quad \text{---} \quad (5)$$

The rate of production

$$ES \xrightarrow{K_r} P + E$$

$$r_p = K_r C_{ES} \quad \text{---} \quad (6)$$

sub eq (5) into eq (6).

$$r_p = K_r \frac{K_1 C_S C_{E_0}}{K_1 C_S + K_2 + K_r}$$

$$r_p = K_r \frac{K_1 C_S C_{E_0}}{K_1 \left(C_S + \frac{K_2}{K_1} + \frac{K_r}{K_1}\right)}$$

$$r_p = K_r \frac{C_S C_{E_0}}{C_S + \frac{K_2 + K_r}{K_1}}$$

$$K_m = \frac{K_2 + K_r}{K_1}$$

$$V_{max} = K_r C_{E_0}$$

$$\therefore \boxed{r_p = \frac{V_{max} \cdot C_S}{K_m + C_S}}$$

This is more general definition of the M.M.E Constant that given

$$K_m = -\frac{K_2}{K_1}$$

if $K_2 >> K_1$

$\therefore K_r =$ ثابت

$\therefore K_m = \frac{K_2}{K_1}$.

EVALUATION of KINETIC PARAMETERS

(K_m and V_{max})

The Michaelis - Menten equation can be rearranged to be expressed in linear form - This can be achieved in Three Ways :-

1- Langmuir Form

$$r_p = \frac{V_{max} \cdot C_s}{K_m + C_s}$$

$$\frac{1}{r_p} = \frac{K_m + C_s}{V_{max} \cdot C_s}$$

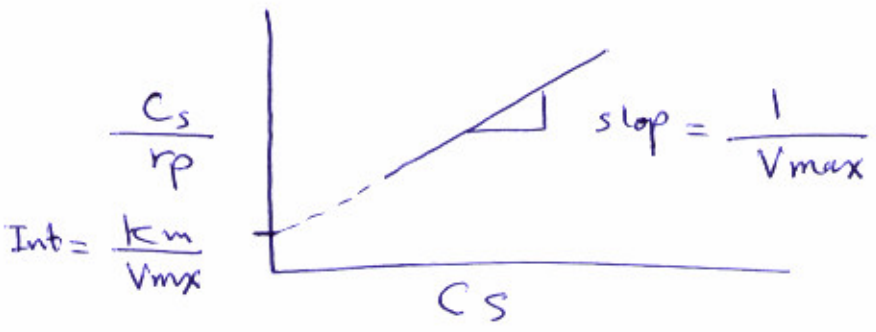
$$\frac{1}{r_p} = \frac{K_m}{V_{max} \cdot C_s} + \frac{C_s}{V_{max} \cdot C_s}$$

$$\left[\frac{1}{r_p} = \frac{K_m}{V_{max}} \cdot \frac{1}{C_s} + \frac{1}{V_{max}} \right] * C_s$$

$$\frac{C_s}{r_p} = \frac{K_m}{V_{max}} + \frac{C_s}{V_{max}}$$

$$\frac{C_s}{r_p} = \frac{K_m}{V_{max}} + \frac{1}{V_{max}} \cdot C_s$$

This is Langmuir form



Langmuir plot

plot $\frac{C_s}{r_p}$ Vs C_s The slop = $\frac{1}{V_{max}}$.

Int = $\frac{K_m}{V_{max}}$.

2- Lineweaver – Burk plot

$$r_p = \frac{V_{max} \cdot C_s}{K_m + C_s}$$

$$\frac{1}{r_p} = \frac{K_m + C_s}{V_{max} \cdot C_s}$$

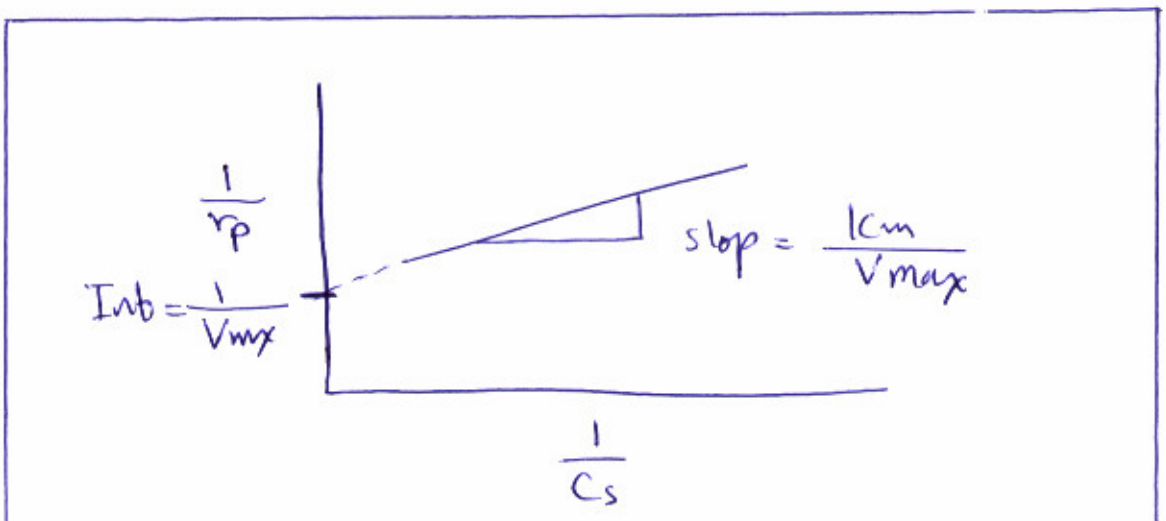
$$\frac{1}{r_p} = \frac{K_m}{V_{max}} \cdot \frac{1}{C_s} + \frac{C_s}{V_{max} \cdot C_s}$$

$$\boxed{\frac{1}{r_p} = \frac{K_m}{V_{max}} \cdot \frac{1}{C_s} + \frac{1}{V_{max}}}$$

This is Lineweaver–Burk form

plot $\frac{1}{r_p}$ Vs $\frac{1}{C_s}$

$$\text{Slop} = \frac{K_m}{V_{max}} \quad , \quad \text{Int} = \frac{1}{V_{max}}$$



The Lineweaver – Burk plot.

3- Eadie-Hofstee plot

$$r_p = \frac{V_{max} \cdot C_s}{K_m + C_s}$$

$$\left[r_p (K_m + C_s) = V_{max} \cdot C_s \right] \div C_s$$

$$\frac{r_p (K_m + C_s)}{C_s} = \frac{V_{max} \cdot \cancel{C_s}}{\cancel{C_s}}$$

$$\frac{r_p K_m}{C_s} + \frac{r_p \cdot \cancel{C_s}}{\cancel{C_s}} = V_{max}$$

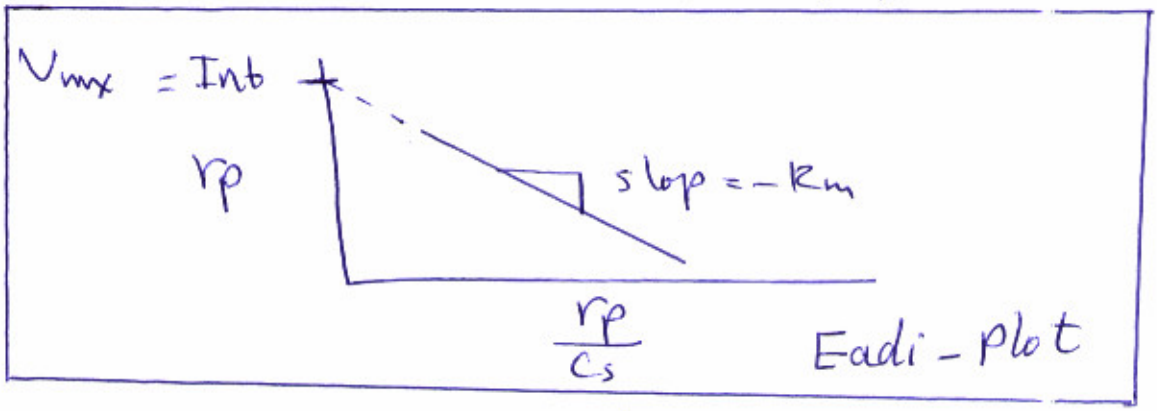
$$\frac{r_p \cdot K_m}{C_s} + r_p = V_{max}$$

$$r_p = V_{max} - K_m \frac{r_p}{C_s}$$

Eadie-Hofstee form

plot r_p Vs $\frac{r_p}{C_S}$ slop $= -K_m$

Int $= V_{max}$



Mode of Bioreactor Operation

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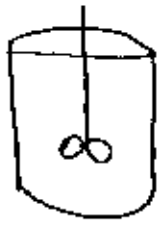
1- Batch Reactor

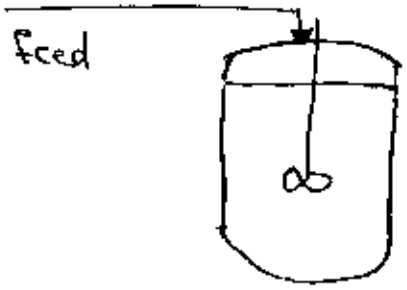
Reactor has neither feed nor product stream.



Batch mode.

2- Semi- Batch Reactor.

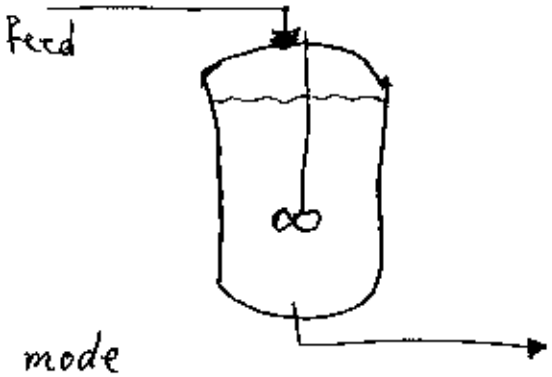
Feed is introduced either continuasly or intermittently while there is no continuous product removaL.



Semi-Batch reactor.

3- Continuous Reactor

Nutrients and organisms are fed and the liquid and gaseous product or effluent are removed continuously



Continuous mode

ENZYME REACTOR with SIMPLE KINETICS

1- Batch or Steady-State plug-flow Reactor

The simplest reactor configuration for any enzyme reaction is the batch mode. A batch enzyme reactor is normally equipped with an agitator to mix the reactant, and the pH of the reactant is maintained by employing either a buffer solution or a pH controller. The composition are uniform at all time.

Enzyme reaction is initiated at $t = 0$

The reaction mechanism can be represented by the Michaelies-Menten equation.

م. نقم أنيس

$$-\frac{dC_s}{dt} = \frac{V_{max} \cdot C_s}{K_m + C_s}$$

$$\left[-(K_m + C_s) \cdot dC_s = V_{max} \cdot C_s \cdot dt\right] \div C_s$$

$$-\left(\frac{K_m + C_s}{C_s}\right) \cdot dC_s = V_{max} \cdot dt$$

$$-\left(\frac{K_m}{C_s} + 1\right) \cdot dC_s = V_{max} \cdot dt$$

$$-\left[\left(K_m \cdot \frac{dC_s}{C_s} + dC_s\right]\right. = V_{max} \cdot dt$$

$$-\left[K_m \int_{C_{s0}}^{C_s} \frac{dC_s}{C_s} + \int_{C_{s0}}^{C_s} dC_s\right] = V_{max} \cdot \int_0^t dt$$

$$K_m \ln \frac{C_{so}}{C_s} + (C_{so} - C_s) = V_{max} \cdot t \quad \text{--- (1)}$$

This equation shows how C_s with respect to t

In plug-flow enzyme reactor (or tubular-flow enzyme reactor). The substrate enters one end of a cylindrical tube which is packed with immobilized enzyme and the product stream leaves at the other end.

* The equation above can also be applied to an ideal steady-state plug flow reactor.
* The plug flow reactor is operated in continuous mode

Rearranging the above equation

$$K_m \ln \frac{C_{so}}{C_s} + (C_{so} - C_s) = V_{max} \cdot t$$

$$K_m + \frac{(C_{so} - C_s)}{\ln \frac{C_{so}}{C_s}} = V_{max} - \frac{t}{\ln \frac{C_{so}}{C_s}}$$

$$\frac{(C_{so} - C_s)}{\ln \frac{C_{so}}{C_s}} = -K_m + V_{max} \cdot \frac{t}{\ln \frac{C_{so}}{C_s}} \quad \text{--- (2)}$$

t = is the residence time in continuous mode

Plot this equation (2) and find K_m & V_{max}

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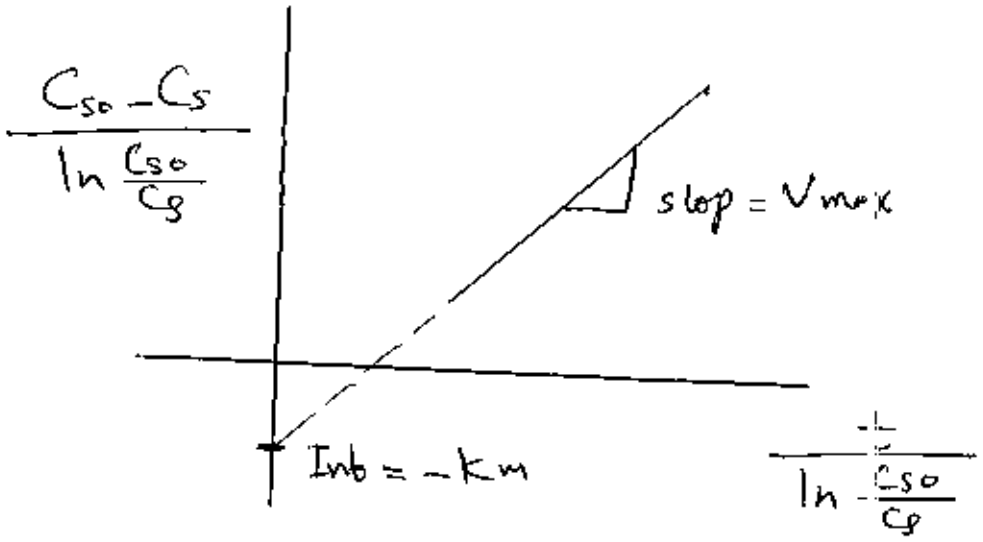

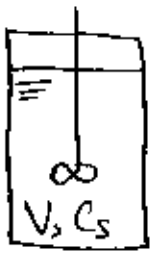

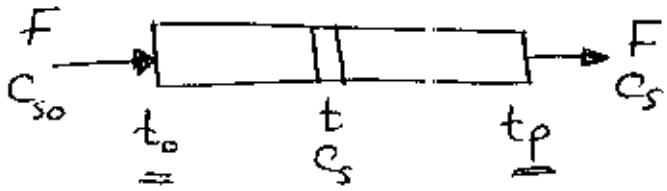

at $t = 0$ $\quad C_s = C_{so}$

a- batch stirred tank reactor

b- plug-flow reactor

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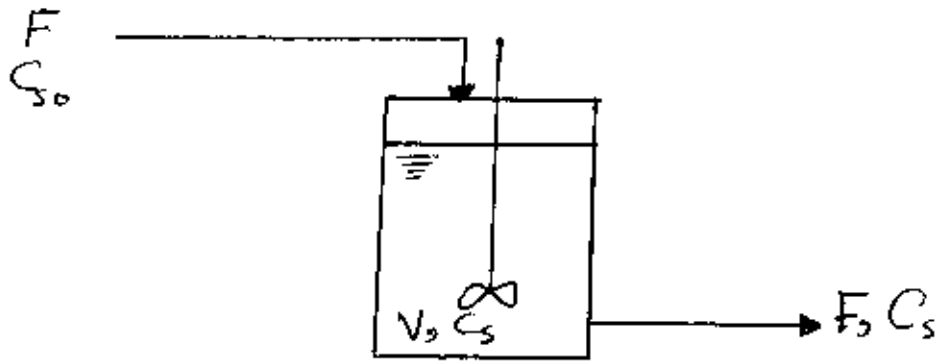
2- Continuous Stirred-Tank Reactor



CSTR

A continuous stirred-tank reactor is an ideal reactor which is based on the assumption that the reactor contents are well mixed. Therefore the concentration of the various components of the outlet stream are assumed to be the same as the concentration of these component in the reactor.

The Substrate Balance of CSTR is

$$F \cdot C_{so} - F \cdot C_s + V \cdot r_s = V \frac{dC_s}{dt}$$

Where

F = is the flow rate.

V = is the volume of the reactor.

r_s = is the rate of substrate consumption for the enzyme reaction

$\frac{dC_s}{dt}$ = is the change of the substrate concentration in the reactor.

when the flow rate is $= 0$

$$r_S = \frac{dC_S}{dt}$$ which is batch operation.

For steady-state CSTR the substrate concentration of the reactor should be constant.

$$\therefore \frac{dC_S}{dt} = 0$$

$$\left[F C_{S0} - F C_S + V r_S = 0 \right] \div V$$

$$\frac{F}{V} C_{S0} - \frac{F}{V} C_S + r_S = 0$$

$$\frac{F}{V} = \frac{1}{\tau}$$

$$\frac{C_{S0}}{\tau} - \frac{C_S}{\tau} + r_S = 0$$

$$\frac{(C_{S0} - C_S)}{\tau} + r_S = 0$$

$$\frac{(C_{S0} - C_S)}{\tau} = -r_S$$

The M.M.E is

$$r = \frac{dC_P}{dt} = -\frac{dC_S}{dt} = \frac{V_{max} \cdot C_S}{K_m + C_S}$$ { V_{max} is the max rate }

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$$\left[\frac{V_{max} \cdot C_s}{K_m + C_s} = \frac{(C_{so} - C_s)}{\tau}\right] \div (C_{so} - C_s)$$

$$\frac{1}{\tau} = D = \text{Dilution rate}.$$

$$D = \frac{V_{max} \cdot C_s}{(K_m + C_s)(C_{so} - C_s)}.$$

In biochemical engineering it is common to use the dilution rate rather than residence time.

$$\left[D = \frac{1}{\tau} = \frac{V_{max} \cdot C_s}{(K_m + C_s)(C_{so} - C_s)}\right] * \tau(K_m + C_s)$$

$$(K_m + C_s) = \frac{\tau \cdot V_{max} \cdot C_s}{(C_{so} - C_s)}$$

$$\boxed{C_s = -K_m + V_{max} \cdot \frac{\tau \cdot C_s}{(C_{so} - C_s)}}$$

K_m & V_{max} can also be estimated by running a series of steady-state CSTR runs with various flow rates and plotting C_s Vs $\frac{\tau \cdot C_s}{(C_{so} - C_s)}$

slop = V_{max}

Int = $-K_m$

م. نهى أديب

INHIBITION of ENZYME REACTION

م. نغم أديب

Inhibitor = Is a substance which can combine with enzyme to alter their catalytic activities.

It can decrease the rate of reaction either :--

a- Competitively.

b- non competitively.

c- partially competitively.

Competitive Inhibition

Both the inhibitor and substrate compete for the active site of an enzyme. The formation of (EI) complex reduce the amount of enzyme available for interaction with the substrate, as a result, the rate of reaction decreases.

The mechanism of competitive inhibition

$$E + S \underset{K_2}{\overset{K_1}{\rightleftharpoons}} ES$$

$$E + I \underset{K_4}{\overset{K_3}{\rightleftharpoons}} EI$$

$$ES \xrightarrow{K_5} E + P \quad \text{slow step}$$

$$r_p = K_s C_{ES}$$

The enzyme balance

$$C_{E_o} = C_E + C_{ES} + C_{EI} \quad \text{---- (2)}$$

from the two equilibrium reactions

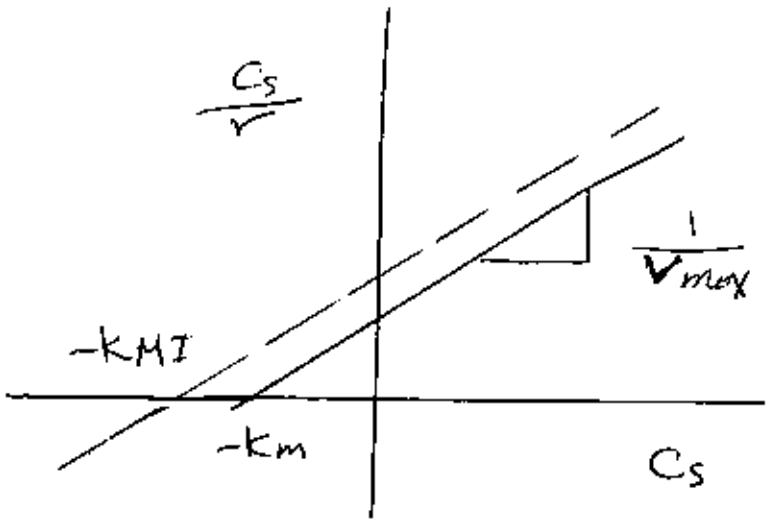
$$\frac{C_E C_S}{C_{ES}} = \frac{k_2}{k_1} = K_s \quad \text{---- (3)}$$

$$\frac{C_E C_I}{C_{EI}} = \frac{k_4}{k_3} = K_I \quad \text{---- (4)}$$

Combining the preceding four equations to eliminate C_E, C_{ES}, C_{EI} yeilds

$$\boxed{r_p = \frac{V_{max} \cdot C_s}{C_s - K_{MI}}} \quad \text{---- (5)}$$

If $K_{MI} > K_s$ the reaction rate decreases. a Large amount of substrate is required to reach the maximum reaction rate. The graphical consequences of competitive inhibition are shown in Fig. below



The effect of inhibitors as seen in the Langmuir plot

$$r_p = \frac{V_{max} \cdot C_s}{C_s - K_{MI}}$$

$$\frac{1}{r_p} = \frac{C_s - K_{MI}}{V_{max} \cdot C_s}$$

$$\left[\frac{1}{r_p} = \frac{1}{V_{max}} - \frac{K_{MI}}{V_{max} \cdot C_s} \right] * C_s$$

$$\frac{C_s}{r_p} = \frac{C_s}{V_{max}} - \frac{K_{MI}}{V_{max}}$$

Immobilized Enzyme

Since most enzymes are soluble in water (protein). Therefore it is very difficult to separate the enzyme for reuse in a batch process. Enzymes can be immobilized on the surface of or inside of an insoluble matrix either by.

a- Chemical method.

b- physical method.

c- immobilized in their soluble forms by retaining them with a semipermeable membrane.

The main advantage of immobilized enzyme :—

Can be easily separabed from the reaction solution and Can be easily retained in a continuous-flow rate.

EFFECT of MASS-TRANSFER RESISTANCE

The immobilization of enzymes may introduce a new problem which is absent in free soluble enzymes. Thiy are :—

a- The mass transfer resistance due to the large parbical size of immobilization enzyme.

b- The inclusion of enzymes in polymeric matrix.

We follow the hypothetical path of the substrate in the fig. below, it can be devided into 3 steps.

1- Transfer from the bulk liquid to a relatively unmixed Liquid Layer surrounding the immobilized enzyme.

2- Diffusion through the relatively unmixed liquid layer.

3- Diffusion from the surface of the particle to the active site of the enzyme in an inert support.

step (1 & 2) external mass transfer.

step (3) internal mass transfer.

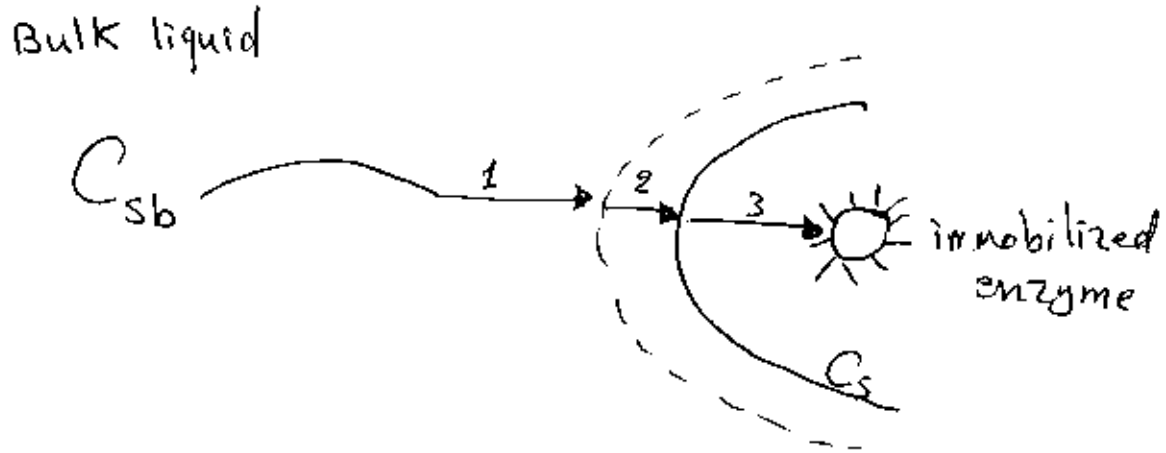


Fig schematic diagram of the path of the substrate to the reaction site in an immobilized enzyme.

م. نقرادي

External Mass-Transfer Resistance

The enzyme is immobilized on the surface of an insoluble particle, the rate of mass transfer is proportional to the driving force (the concentration difference). as

$$N_S = K_s \cdot A \, (C_{sb} - C_s) \quad ---(1)$$

where

N_s = The rate of mass transfer.

K_s = mass transfer coefficient (Length/time).

A = Surface area of one immobilized enzyme particle.

C_{sb} = Substrate concentration in the bulk of the solution.

C_s = Substrate concentration at the immobilized enzyme surface.

During the enzymatic reaction of an immobilized enzyme.

rate of substrate transfer = rate of substrate consumption

The M.M.E is

$$r_p = \frac{V_{max} \cdot C_s}{K_m + C_s} \quad --- (2)$$

$$\therefore \boxed{K_s \cdot a \cdot (C_{sb} - C_s) = \frac{V_{max} \cdot C_s}{K_m + C_s}} \quad --- (3)$$

a is the total surface area per unit volume

equation ③ shows

The relationship between the substrate concentration in the bulk of the solution and that at the surface of an immobilized enzyme.

equation ③ can be expressed in dimensionless form as:-

$$\frac{1 - x_s}{N_{Da}} = \frac{\beta x_s}{1 + \beta x_s} \quad ---④$$

where:-

$$x_s = \frac{C_s}{C_{sb}}$$

$$N_{Da} = \frac{V_{max.}}{K_s \cdot a \cdot C_{sb}}$$

$$\beta = \frac{C_{sb}}{K_m}$$

N_{Da} = is Damköhler number.

N_{Da} = is the ratio of the maximum reaction rate over the maximum mass transfer rate.

Depending upon the magnitude of N_{Da} equation ④ can be simplified as follows =——

1- If $N_{Da} \ll 1$ the mass transfer rate is much greater than the reaction rate and the over all reaction is controlled by the enzyme reaction.

$$r_p = \frac{V_{max} \cdot C_{sb}}{K_m + C_{sb}} \qquad (5)$$

2- If $N_{Da} \gg 1$ the reaction rate is much greater than the mass transfer and the over all reaction is controlled by the rate of mass transfer that is the first-order reaction.

$$r_p = K_s \cdot a \cdot C_{sb} \qquad (6)$$

The effectiveness factor of an immobilized enzyme (η) as

$$\eta = \frac{\text{actual reaction rate}}{\text{rate if not slowed by diffusion}}$$

the effectiveness factor calculated to measure the extent which the reaction rate is lowered because of resistance to mass transfer.

$$\eta = \frac{\dfrac{V_{max} - C_s}{K_m + C_s}}{\dfrac{V_{max} - C_{sb}}{K_m + C_{sb}}}$$

$$\boxed{\eta = \frac{\dfrac{\beta x_s}{1 + \beta x_s}}{\dfrac{\beta}{1+\beta}}} \quad \text{---} \quad (7)$$

η = is a function of x_s & β

$X_s = \dfrac{C_s}{C_{sb}}$ if $X_s = 1$ $\therefore C_s = C_{sb}$

C_s = concentration at the surface.

C_b = bulk concentration.

if $X_s = 1$ sub in eq (7)

$\therefore \eta = 1$ it mean that is no mass transfer.

if $x_s = 0$ sub in eq (7)

$\eta = 0$ it mean that the rate of mass transfer is very slow compared to the reaction rate.

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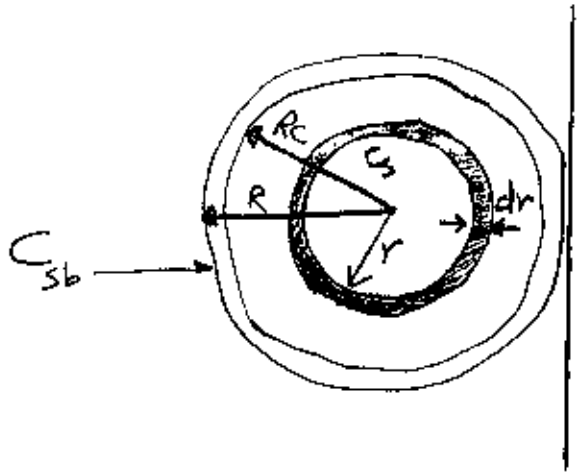
Internal Mass-Transfer Resistance.



Shell balance of a substrate in a immobilized enzyme.

Make a series of assumption as follows to derive an equation that shows how the mass transfer resistance effects the effectiveness of an immobilized enzyme.

1- The reaction occurs at every posibion wibhin the immobilized enzyme, and the kinetics of the reaction are of the same form as observed for free enzyme.

2- Mass transfer bhrough bhe immobilized enzyme occurs via molecular diffusion.

3- There is no mass transfer limitiation at the outside surface of bhe immobilized enzyme.

4- The immobilized enzyme is spherical.

The model developed by these assumption is known as the Distributed Model

FERMENTER

Classical Growth Curve (Biocell Growth)

A small quantity of live biocells are added to a nutrient solution maintained to correct conditions (T & pH). The cell will grow - Unicellular organisms will divide as they grow. The cell take in nutrients from the surrounding, they release metabolic and product. During this process the substrate is converted into a single product or several products.

There are five stages during the cell growth process.

1- Lag phase : A period of time when the change of cell number is zero.

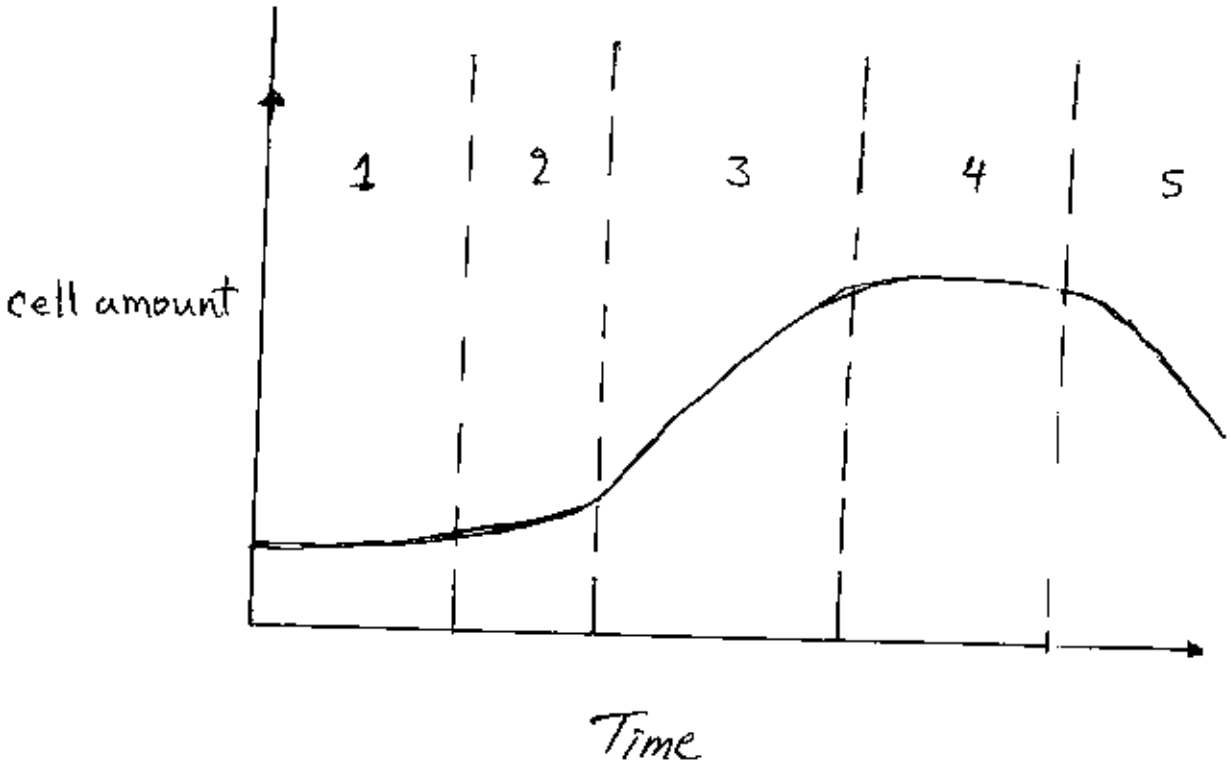
2- Accelerated growth phase = The cell number start to increase and the division rate increase to reach a maximum.

3- Exponential growth phase = The cell number increase exponentially as the cells start to divide. The growth rate is increasing during this phase.

4- Stationary phase = The cell population will reach a maximum value and will not increase any farther.

5- Death phase = After nutrients available for the cell are depleted, cells will start to die and the number of viable cells will decrease.

The fig below show these five stages.

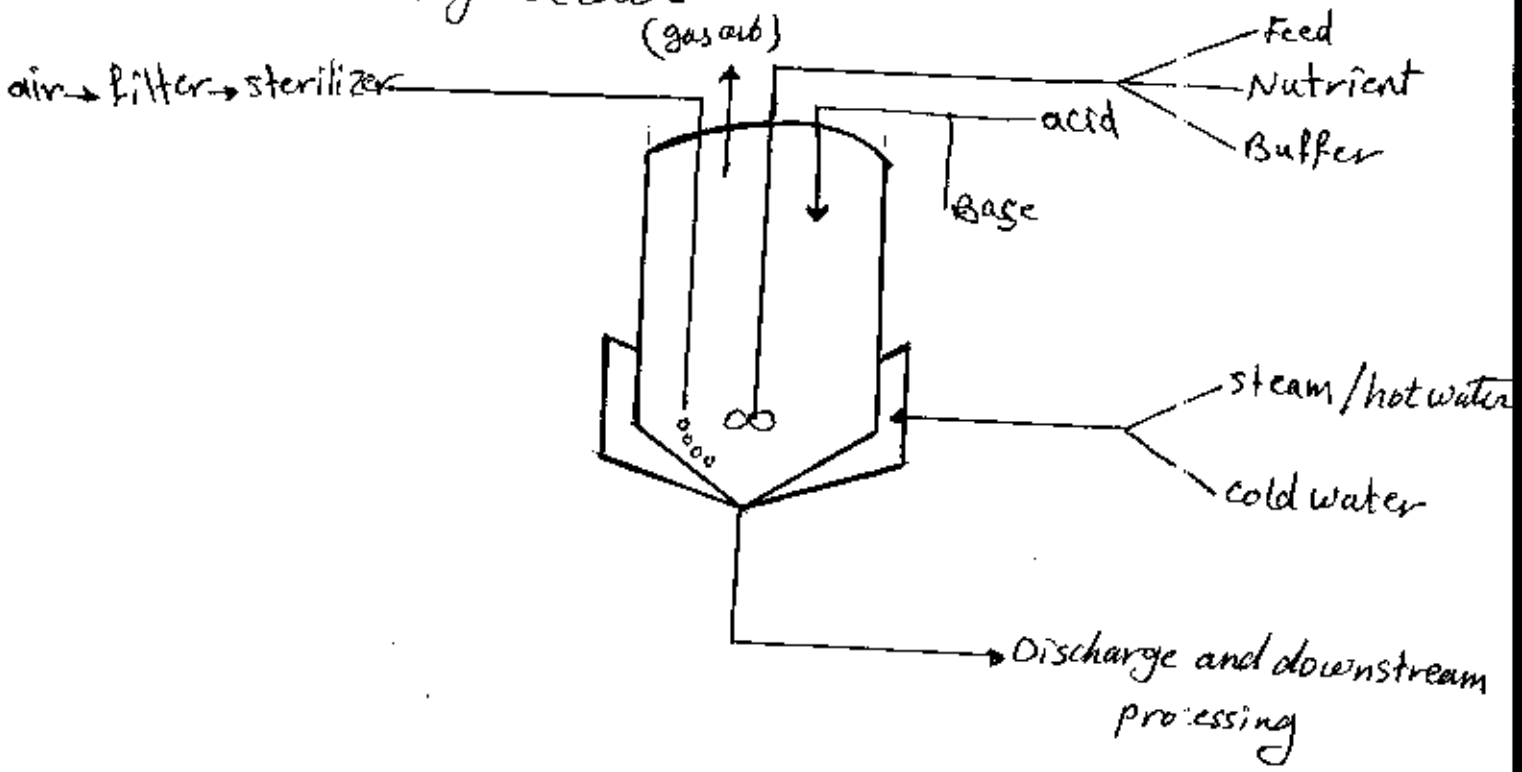


Various stages during cell growth.

Fermentors

A fermentor is generally a cylindrical stirred reactor where fermentation is carried out.

A typical agitated fermentor with the process control system is shown in fig- below.



typical Fermentor jacketted agitated vessel

$$\frac{\text{Fermenter hight}}{\text{Fermenter diameter}} = 1.2 - 1.5$$

$$\frac{\text{Impeller diameter}}{\text{bank diameter}} = 0.3 - 0.5$$

Fermentor may have both jacket and coils to achive the desired heat transfer area. They are made of stainless steel.

It is generally operated a- Batch. مغذى
b- Semi Batch.

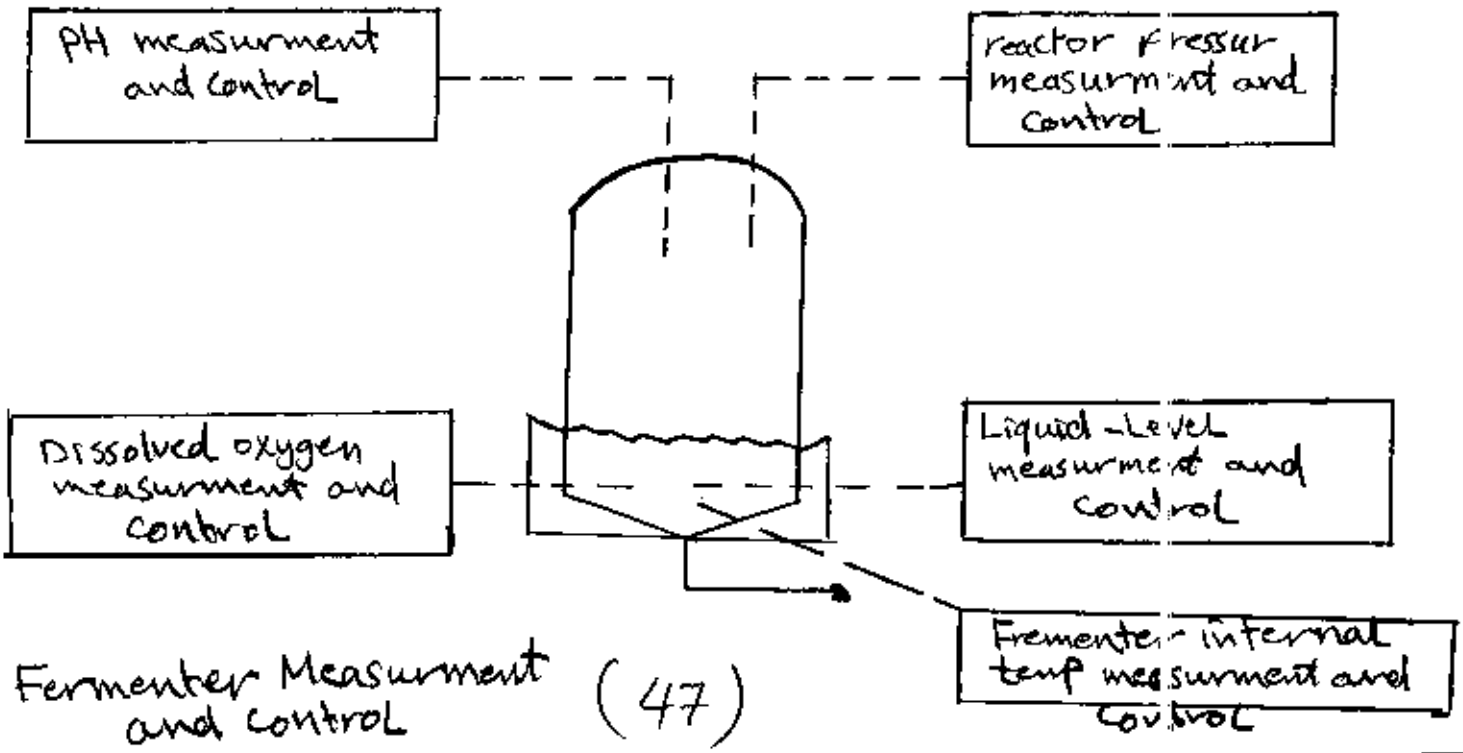
The continuous operation requires continuous sterelization of the feed and nutrients, and continuous downstream processing.

Air is continuously introduced in aerobic fermentor through a sparger located inside the vessel and mechanical agitation distributed the air uniformly.

Air is filtered and purified befor it is introduced inside the vessel.

Buffer and feed tanks are located above the main vessel and the various liquid are added in a preprogrammed manner.

Fermentors are highly instrumented and controlled.



Fermenter Measurment and control

Fermenters can be classified depending upon the nature of the growth microorganism.

1- Submerged Fermenter.

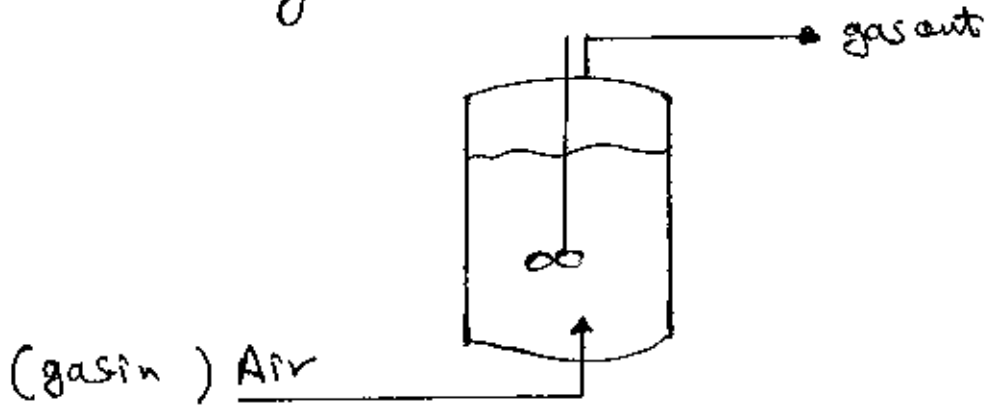
microorganisms remains submerged all the time inside the Liquid.

2- Surface Fermenter.

microorganisms adheres to the solid surface.

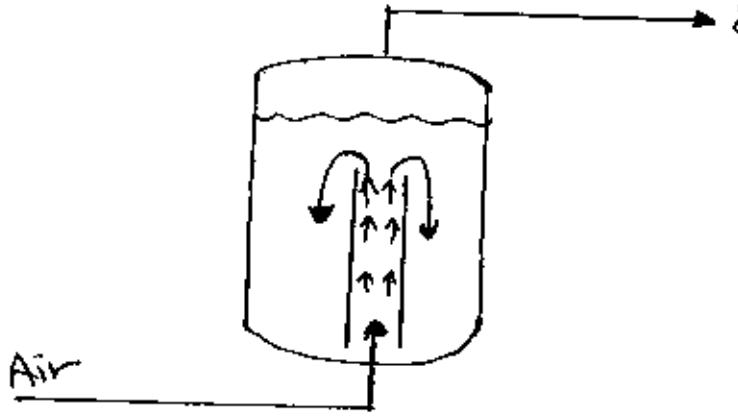
Type of Aerobic Fermentors Designs.

1- Mechanically stirred tank fermenter.



In mechanically stirred tank fermenter, air is introduced from the bottom through a sparging arrangement and the contents are agitated with the mechanical stirrers. Buffles are provided to prevent vortex formation and improving mixing.

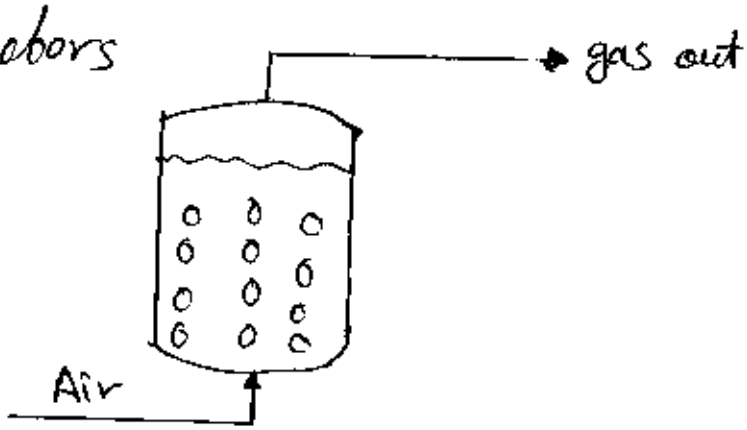
2- Air Lift Fermenters



Internal draft tube Fermenter.

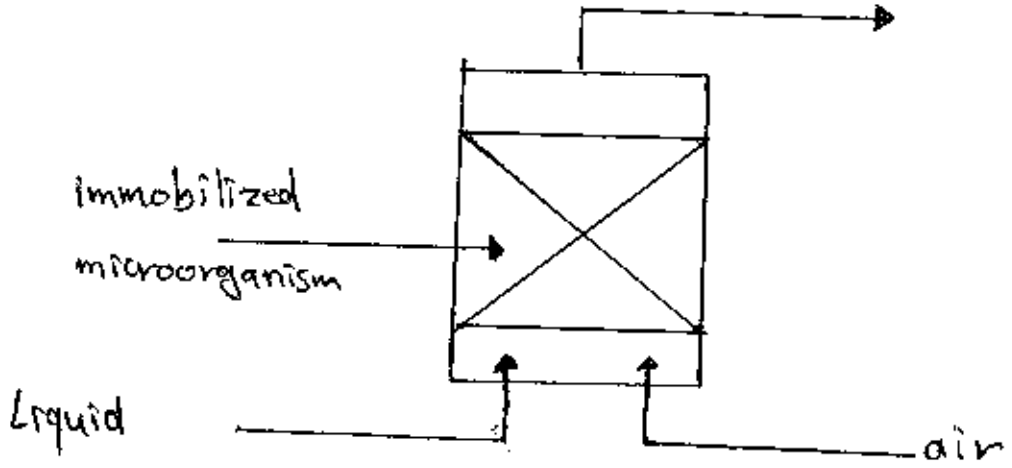
An inner draft tube is provided in the central section of a cylindrical reactor, which Leads to mixing of the liquid and gas. No mechanical agitation. The circulation of the liquid is due to the density difference between the mixed phase in the aerated tower and the liquid in the downcomer on the sides. Cell growth is found to be more uniform compared to mechanically agitated fermenter

3- Bubble Column reactors



Bubble column are slender tall columns with a gas distributor at the bottom without any mechanical agitation. The pressure at the bottom of the fermenter is high Leading to good oxygen dissolution

4- Packed bed or fixed bed bio reactor (fermenter) with attached biofilms.



Packed bed reactor (fermenter) are widely used with immobilized cells or enzymes. The biofilm is immobilized on inert support and packed inside the tube over which liquid and air is flow. The pressure drop is high because of low voidage.

5- Fluidized bed fermenter.

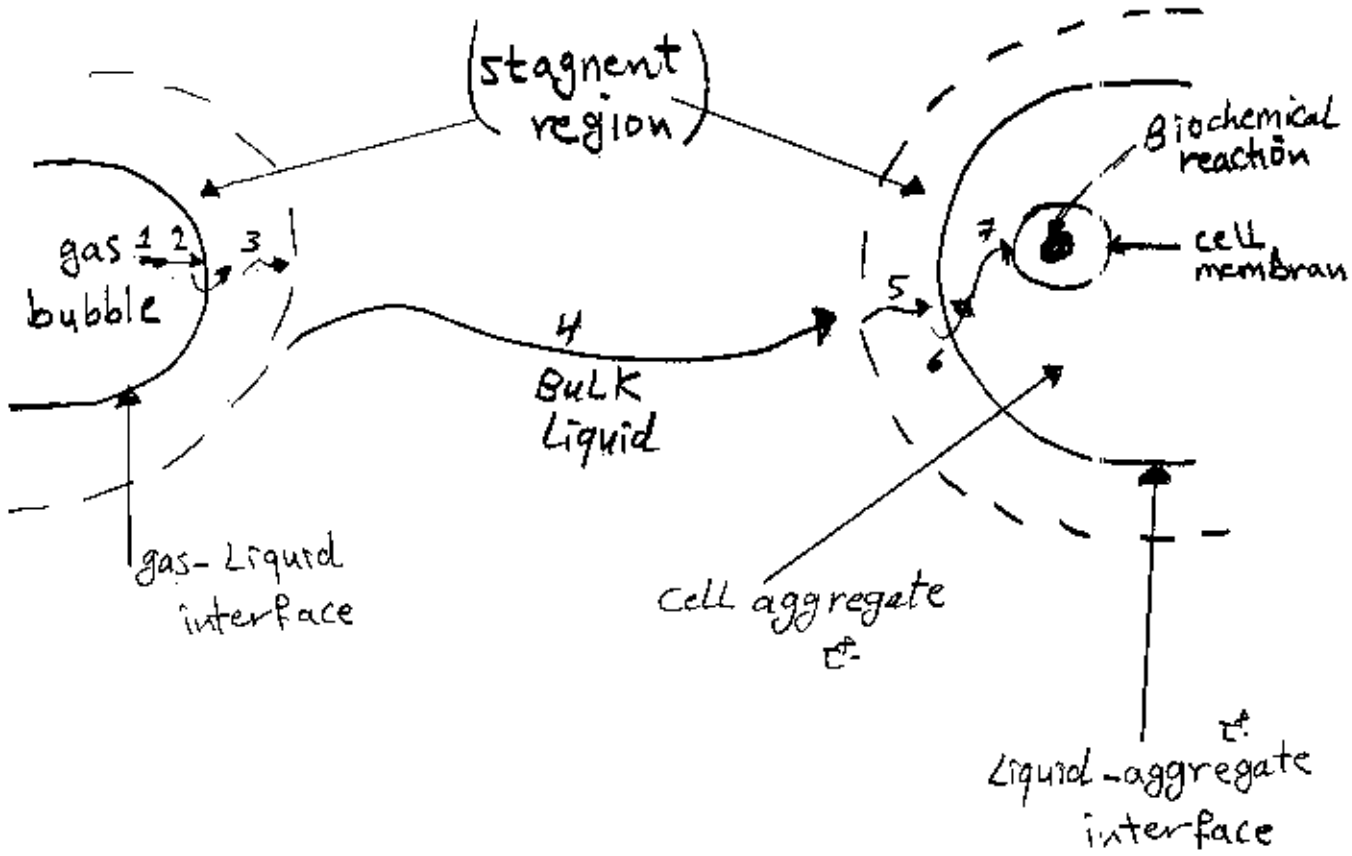
The fluid flow is high enough to keep the solids in suspended of fluidized state leading to good gas-liquid contact and mixing.

م. نغم ادريس

Mass Transfer in Aerobic Bioreactor (aerobic process and O_2 Through Gas-Liquid Interface).

In most fermentation processes, under aerobic conditions the supply of oxygen is a crucial factor. Oxygen is sparingly soluble in aqueous medium ($1.25 * 10^{-6}$ mole/cm³/atm) and it has to pass through a series of resistance in order to get consumed.

The various resistances that are possible in gas-sparged process are shown in fig. below.



schematic diagram of steps involved in transport of O_2 from gas bubble to inside a cell.

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1- Diffusion from bulk of the gas phase to gas- liquid interface.

2- Transport through gas- liquid interface.

3- Diffusion of the solut through the relatively unmixed liquid region adjacent to the bubble into the well unmixed bulk liquid.

4 - Transport of the solut through the bulk liquid to a second relativaly unmixed liquid region surrounding the cells.

5 - Transport through the second unmixed liquid region associated with the cell.

6- Diffusion transport into the cellular floc.

7- Transport across cell envelope and to intracellular reaction site.

$$Flux = J_{O_2} = K_L \cdot a \cdot \left(C^*_{O_2} - C_{L,O_2} \right) \quad \text{--- (1)}$$

where :-

J_{O_2} = The flux of O_2 transfer into the liquid $\left(\frac{\text{mole } O_2}{cm^2 \cdot sec}\right)$

K_L = Liquid side mass transfer coefficient.

$a = \frac{A}{V}$ = gas interfecial area per unit liquid volume.

$C^*_{O_2}$ = is the concentration of oxygen in the liquid phase in equilibrium with the gas phase concentration.

C_{L,O_2} = is the concentration of oxygen in the liquid phase.

$$\text{Maximum oxygen transfer rate} = K_L \cdot a \cdot C^*_{O_2} \quad \text{---(2)}$$

$$\text{oxygen utilization rate or maximum oxygen uptake rate} = \frac{x \cdot \mu_{max}}{Y_{O_2}} \quad \text{---(3)}$$

Where :—

x = is cell density (mass cell/unit culture volume).

μ_{max} = is maximum growth rate.

Y_{O_2} = Oxygen yeild factor.

Y_{O_2} = is moles of biomass formed per mole of oxygen consumed.

م. نغم أديب

equation (2) and (3) decide wether the supply of oxygen is sufficient for growth of the microbes -

$$\text{if } K_L \cdot a \cdot C^*_{O_2} \gg \frac{x \cdot \mu_{max}}{Y_{O_2}}$$

Is sufficient O_2 will be supplied to the microbial population since its consumption rate by the microbes for growth and sustenance will be lower than its supply and the process is (Biochemical Reaction Limited)

$$\text{If } K_L \cdot a \cdot C^*_{O_2} \ll \frac{x \cdot \mu_{max}}{Y_{O_2}}$$

In this case the rate of consumption of oxygen by the microbial population is faster than the rate a which it can be supplied and so the process is (Mass Transfer Limited)

For Intermediate conditions

$$\underbrace{K_L \cdot a \cdot (C^*_{O_2} - C_{L,O_2})}_{\text{absorption}} = \underbrace{\frac{x \cdot \mu}{Y_{O_2}}}_{\text{consumption}}$$

Definitions

C_x = Cell concentration, dry cell weight per unit vol. $\left(\frac{kg}{m^3}\right)$

C_N = Cell number density, number of cell per unit vol. (number of cells / m^3).

P = Cell density, wet cell weight per unit volume of cell mass, (kg/m^3).

$\frac{dC_x}{dt}$ = Change of dry cell concentration with time.

r_x = Growth rate of cells on a dry weight basis.

$\frac{dC_N}{dt}$ = Change of cell number density with time.

δ = Division rate of cells on a number basis

$$\delta = \frac{d \log_2 C_N}{dt}$$

* $\frac{dC_x}{dt} = r_x$ only for batch operations for continuous operation $\frac{dC_x}{dt} \neq r_x$.

because the change of cell concentration $\frac{dCx}{dt}$ may include the effect of input & output flowrates, cell recycling and other operating conditions of the fermenter while r_x is the actual growth rate of the cells.

* The growth rate based on the number of cells and that based on cell weight are not necessarily has the same responce to growth.

Division Rate

If all of cells in vessel at time $t=0$ ($C_N = C_{N_0}$) have divided once after a certain period of time, the cell population will have increased to ($C_{N_0} * 2$)

If Cells are divided $\underline{\underline{N}}$ times after the time $\underline{\underline{t}}$ the total number of cells will be :-

$$C_N = C_{N_0} * 2^N \quad \text{----} (1)$$

and the average division rate

$$\overline{\delta} = \frac{N}{t} \qquad \text{---} (2)$$

Exponential Growth phase

A bacterial culture under going balanced growth similar to a first-order ontic catalytic chemical reaction.

Therefore, the rate of cell population increase at any particular time is proportional to the number density (C_N) of bacteria present at that time.

$$r_N = \frac{dC_N}{dt} = \mu C_N \qquad \text{---} (6)$$

where:-

μ = Is constant, specific growth rate (hr^{-1}).

r_N = Growth rate, or growth per unit volume, based on cell number. (No. of cell / m^3. sec).

$\frac{dC_N}{dt}$ = Change of the cell number with time

$$\therefore \mu = \frac{1}{C_N} \cdot \frac{dC_N}{dt} = \frac{d \ln C_N}{dt} \qquad \text{---} (7)$$

From eq (1)

$$C_N = C_{N_0} * 2^N$$

$$\log C_N = \log C_{N_0} + \log 2^N$$

$$\log C_N = \log C_{N_0} + N \log 2$$

$$N = \frac{\log C_N}{\log 2} - \frac{\log C_{N_0}}{\log 2}$$

$$N = \log_2 C_N - \log_2 C_{N_0} \quad \text{---------} \quad (3)$$

sub eq 3 into eq 2

$$\bar{\delta} = \frac{1}{t}(\log_2 C_N - \log_2 C_{N_0}) \quad \text{---} \quad (4)$$

The division rate δ at time t is

$$\delta = \frac{d \log_2 CN}{dt} \quad \text{---} \quad (5)$$

Note $\bar{\delta} = \frac{1}{t}(\log_2 CN - \log_2 C_{N_0})$

$$\bar{\delta} t = \log_2 CN - \log_2 C_{N_0}$$

in derivation form

$$\delta \, dt = d \log_2 CN \Longrightarrow \delta = \frac{d \log_2 CN}{dt}$$

by integrabion

$$\int_0^t \delta \cdot dt = \int_{C_{N0}}^{C_N} d\log_2 C_N \Rightarrow \bar{\delta}\int_0^t dt = \int_{C_{N0}}^{C_N} d\log_2 C_N$$

$$\bar{\delta}\, t\Big|_0^t = \log_2 C_N \Big|_{C_{N0}}^{C_N}$$

$$\bar{\delta}\, t = \log_2 C_N - \log_2 C_{N0}$$

Comparing eq (5) & (7) show that

$$\mu = \frac{d\ln C_N}{dt} = \underbrace{\ln 2 * \frac{d\log_2 C_N}{dt}}_{\text{متوافق اللوغاريتمات}} = \delta \ln 2 \quad \text{---} (8)$$

If μ is constant with time during exponet growth period eq (6) can be integrated

$$\int_{C_{N0}}^{C_N} \frac{dC_N}{C_N} = \int_{t_0}^{t} \mu \cdot dt$$

$$\ln C_N \Big|_{C_{N0}}^{C_N} = \mu \cdot t \Big|_{t_0}^{t}$$

$$\ln C_N - \ln C_{N0} = \mu\,(t - t_0)$$

$$\ln \frac{C_N}{C_{N0}} = \mu(t - t_0) \quad \text{by exponenbial}$$

$$\frac{C_N}{C_{No}} = Exp[\mu (t - to)]$$

$$\therefore C_N = C_{No} \exp[\mu (t - to)] \quad \text{---} \quad (10)$$

C_{No} = Cell number concentration at twice t_o

t_d = The time required to double the population, then to find t_d

$$C_N = 2 C_{No} \text{ and } t_o = 0$$

$\therefore$ eq (10) become

$$2 C_{No} = C_{No} \exp[\mu (t_d - 0)]$$

$$\ln 2 = \ln \exp \mu . t_d$$

$$\therefore t_d = \frac{\ln 2}{\mu} = \frac{1}{\delta} \quad \text{---} \quad (11)$$

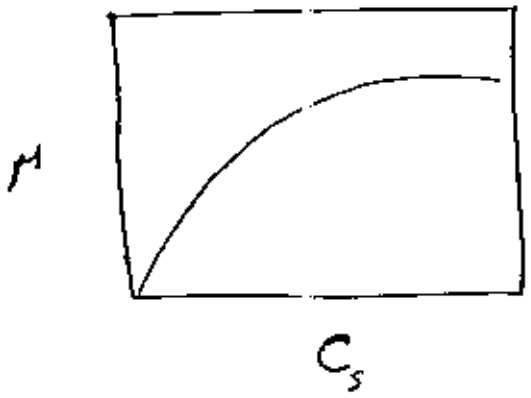
Factors Affecting The specific growth rate

1- Substrate concentration

one of the most widely employed expression for the effect of substrate concentration on μ is the Monod equation

$$\mu = \frac{\mu_{max} \cdot C_s}{K_s + C_s}$$

when $\mu = \frac{1}{2}\mu_{max}$ Then $C_s = K_s$



several other models:-

$$\mu = \frac{\mu_{max} \cdot C_s}{K_{I1} + C_s + (C_{I2} C_s)^2}$$

$$\mu = \mu_{max}\left[1 - \exp(-C_s/K_s)\right]$$

$$\mu = \frac{\mu_{max}}{1 + K_s C_s^{-\lambda}}$$

$$\mu = \frac{\mu_{max} C_s}{B C_N + C_s}$$

$$\mu = \mu_{max} \frac{C_1}{K_1 + C_1} - \frac{C_2}{K_2 + C_2}$$

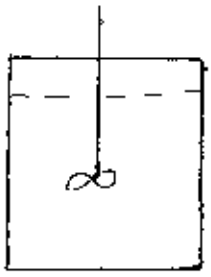
$$\mu = \frac{\mu_{max} - C_s}{K_s + C_s} - Ke$$

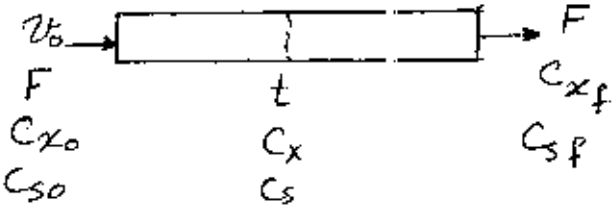
2- Product Concentration

$$\mu = \mu_{max} \left(\frac{C_s}{K_s + C_s} \right) \left(\frac{K_p}{K_p + C_p} \right)$$

$$\mu = \mu_{max} \left(\frac{C_s}{K_s + C_s} \right) \left(1 - \frac{C_p}{C_{pm}} \right)^n$$

Ideal Batch or Plug - Flow Fermenter





$C_x = C_{xo}$
$C_s = C_{so}$ } at $t = t_o$

$$\frac{dC_x}{dt} = r_x \quad \text{for batch and PFF.}$$

but $r_x = \mu . C_x$

$$\frac{dC_x}{dt} = r_x = \mu . C_x \quad ---(1)$$

$$\int_{C_{xo}}^{C_x} \frac{dC_x}{r_x} = \int_{C_{xo}}^{C_x} \frac{dC_x}{\mu C_x} = \int_{t_o}^{t} dt \quad ---(2)$$

sub. for $\mu = \frac{\mu_{max} . C_s}{K_s + C_s}$ into eq. 2

$$\int_{C_{xo}}^{C_x} \frac{dC_x}{\frac{\mu_{max} . C_s}{K_s + C_s} . C_x} = \int_{t_o}^{t} dt$$

$$\int_{C_{xo}}^{C_x} \frac{(K_s + C_s) . dC_x}{\mu_{max} C_s . C_x} = \int_{t_o}^{t} dt \quad ---(3)$$

لايمكن حل تكامل هذه الدالة لانه $C_x = f(C_s)$ لذا يجب أن نجد العلاقة الرابطة بين المتغيرين C_s , C_x

العلاقة الرابطة بين C_s , C_x هي

$$Y_{x/s} = \frac{\Delta C_x}{-\Delta C_s} = \frac{C_x - C_{x0}}{-(C_s - C_{s0})}$$

$Y_{x/s}$ give the relationship between the amount of cell mass produced (C_x) and the amount of a limiting substrate consumed (C_s)

$$Y_{x/s} = \frac{\Delta C_x}{-\Delta C_s} = \frac{C_x - C_{x0}}{-(C_s - C_{s0})} \quad \text{---} \quad (4)$$

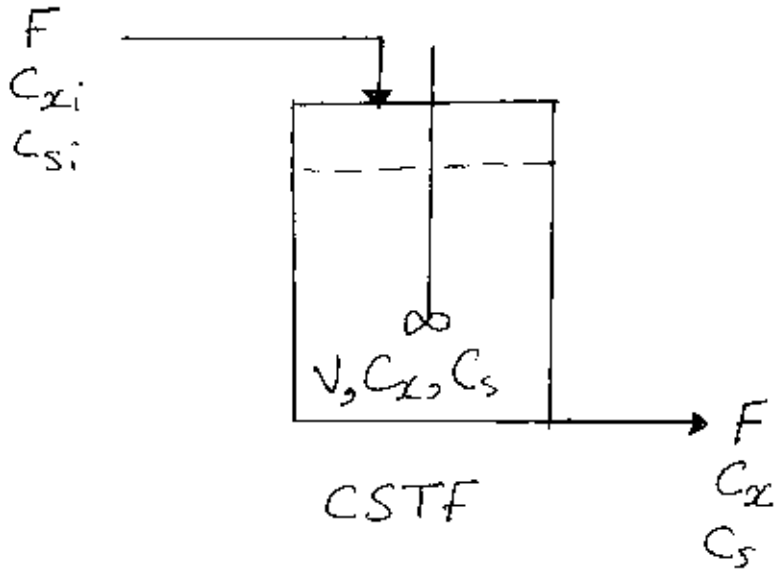
substitution of equation (4) into (3) and integration of the resultant equation gives a relationship which show how the concentration change with respect to time.

$$(t - t_0)\mu_{max} = \left[\frac{K_s Y_{x/s}}{C_{x0} + C_{s0} Y_{x/s}} + 1\right] \ln \frac{C_x}{C_{x0}} + \frac{K_s Y_{x/s}}{C_{x0} + C_{s0} Y_{x/s}} \ln \frac{C_s}{C}$$

--- (5)

م. نفم أديب

Ideal Continuous Fermenter - CSTF



Continuous culture system can be operated as Chemostat or as Turbiodostate.

In Chemostat the flow rate is set at a particular value and the rate of growth of the culture adjusts to this flow rate.

In a turbidostate the turbidity is set at a constant level by adjusting the flow rate.

M.B for Microorganisms in CSTF.

In - out + gen = Acc.

$$v_o C_{x_i} - v_o C_x + V r_x = V \frac{dC_x}{dt} \quad \text{---} \quad (6)$$

at steady state operation in a CSTF $\frac{dC_x}{dt} = 0$

{ يتم تنظيم نمو الكائن الحي داخل المفاعل بحيث كما يجب لأجل مقادرة الكائن الحي المفاعل مع تيار out flow }

$$V \cdot r_x = V_o (C_x - C_{xi})$$

$$\frac{V}{V_o} = \frac{(C_x - C_{xi})}{r_x}$$

$$\tau_m = \frac{V}{V_o} = \frac{(C_x - C_{xi})}{r_x} \quad \text{---} \quad (7)$$

τ_m = is residence time.

$C_{xi} = 0$ because the inlet stream is sterile

Optimum operater for CSTF

If the input stream is sterile $C_{xi} = 0$ and cell in CSTF are growing exponentially.

$$r_x = \mu . C_x$$

$$\therefore \tau_m = \frac{C_x - C_{xi}}{r_x} = \frac{C_x - 0}{\mu . C_x} = \frac{C_x}{\mu . C_x}$$

$$\therefore \tau_m = \frac{1}{\mu} = \frac{1}{D} \quad \text{---} \quad (8)$$

$$D = \frac{1}{\tau_m}$$

D = is Dilution rate

$\mu = D$ for CSTF & $C_{xi} = 0$, $r_x = \mu$

$$D = \mu = \frac{1}{\tau_m} = \frac{\mu . C_x}{K_s + C_x} \quad \text{----} \quad (9)$$

C_s can be calculated with a know τ_m & mond kinetic

$$C_s = \frac{K_s}{\tau_m \cdot \mu_{max}^{-1}} \quad \text{---} \quad (10)$$

$$Y_{x/s} = \frac{C_x - C_{xi}}{C_{si} - C_s} = \frac{C_x}{C_{si} - C_s}$$

$Y_{x/s}$ is constant

$$C_x = Y_{x/s} (C_{si} - C_s) \quad \text{---} \quad (11)$$

sub eq. (10) into eq. (11)

$$C_x = Y_{x/s} \left(C_{si} - \frac{K_s}{\tau_m \cdot \mu_{max}^{-1}} \right) \quad \text{---} \quad (12)$$

$$Y_{p/s} = \frac{C_p - C_{pi}}{C_{si} - C_s}$$

$$C_p = C_{pi} + Y_{p/s} \left(C_{si} - \frac{K_s}{\tau_m \cdot \mu_{max}^{-1}} \right)$$

م. نقم أديب

HEAT TRANSFER IN BIOLOGICAL REACTORS

In biological reactors, heat may be added or removed from a microbial fluid for the following resons :—

1- it is desired to sterilize a liquid reactor feed by heati in a batch or continuous - flow vessel.

2- if the heat generated in substrate conversion is in a dequate to maintain the desired temperature Level, heat must be added.

3- the conversion of substrate generates excess heat with respect to optimal reactor condition.

4- the water content of cell (sludge) is to be reduced by drying.

Method of Heat Transfer in Biological Reactors

1- Externally jacketed vessels.

2- Coils inserted in a Large vessels.

3- Flow through a heat exchanger.

4- Evaporation and condensation.

Heat can be transported from higher temperature to lower temperature, they are

1- Conduction (q) happens in a stagnant medium.

$$q = -\lambda \cdot A \cdot \frac{\Delta T}{\Delta X}$$

where

λ = thermal conductivity.

A = heat transfer area.

ΔT = temperature difference.

ΔX = film thickness.

2- Convection (q_h) happens in a following medium.

$$q_h = h \cdot A \cdot \Delta T$$

h = heat transfer coefficient.

A = heat transfer area.

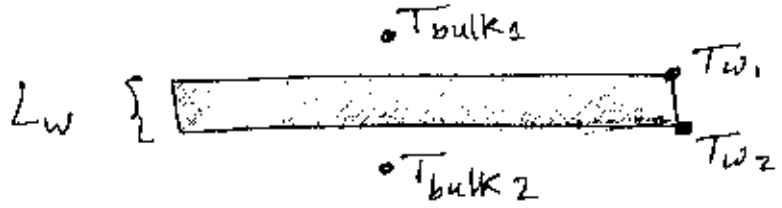
ΔT = Temperature difference.

3- Radiation is not important in bioreactor.

م. نغم أديب

Heat Transfer Correlations

For steady state heat transfer through a flat wall of thickness (L_w) separating the fermentation fluid at (T_{bulk_1}) from heating or cooling fluid at (T_{bulk_2})



$$h_{w_1}(T_{bulk_1} - T_{w_1}) = K_s\left(\frac{T_{w_1} - T_{w_2}}{L_w}\right) = h_{w_2}(T_{w_2} - T_{bulk_2})$$

$$= \text{K Cal} / \text{Cm}^2 \cdot \text{hr}$$

In term of an over all heat transfer

$$\text{heat flux} = \overline{h}\,(T_{bulk_1} - T_{bulk_2})$$

Rearrengement of the pervious equation yeild's

$$\frac{1}{\overline{h}} = \frac{1}{h_{w_1}} + \frac{1}{K_s} + \frac{1}{h_{w_2}}$$ for planar wall

$$\frac{1}{\overline{h}_o d_o} = \frac{1}{h_o d_o} + \frac{\ln(d_o/d_i)}{2K_s} + \frac{1}{h_i d_i}$$ For tube wall

STERILIZATION

Sterilization = is carried out to destroy the microbes present and make the fluid free from any contamination = (Cell).

Liquid and gas befor entering the bioreactor or fermenter are sterilized. Different sterilization techniques include.

1- UV or X-ray radiation.
2- Sonication.
3- filtration.
4- heating and chemical addition.

Mode of sterilization

1- Continuous sterilization.
2- Batch sterilization.

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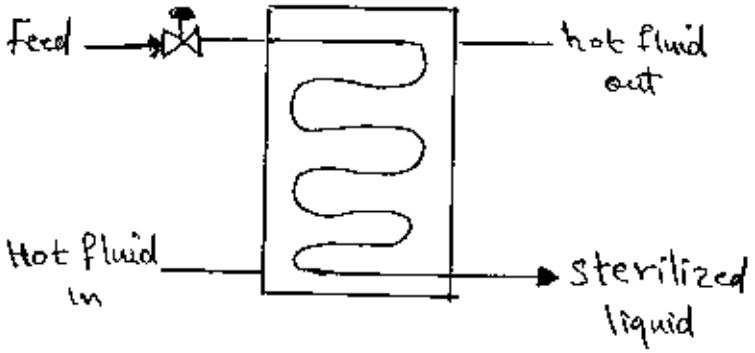
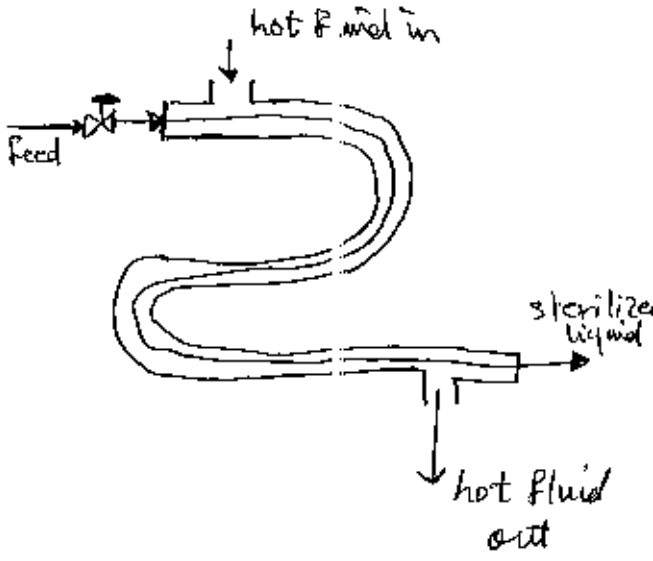
1- Continuous sterilization

Are of tubular design with high temperature and short residence time. The liquid flows through the tube at high velocity and the wall are heated by the heating fluid.



shell and tube



double pipe.

2- Batch sterilization.

In a batch sterilizer the liquid is feed in, the contents heated to the desired temperature and maintained for specified a mount of time, cooled and finally discharged from the vessel for further processing. The liquid is heated either by sparging live steam, electrical heating or through a heat exchanger.

منتظر أديب

WASTE WATER TREATMENT.

Waste water is obtained from various sources such as :—

a - wastewater from food industry.

b - wastewater from chemical and petrochemical industry.

c - Sewage.

The principal objective of wastewater treatment is to produce an effluent that can be discharged without causing serious environmental impacts. The contaminants in wastewater are removed by physical, chemical and biological methods.

These processes are carried out in a variety of combinations and grouped together to provide what is known as primary, secondary and tertiary process

1 - Primary process.

Primary treatment process remove only those pollutants that will either float or settle out by gravity. Variety of mechanical devices are used like screening, grinding and grit chambers. After preliminary treatment the wastewater still contains suspended organic solids that can be removed by sedimentation.

٣. نغم أديب

2- Secondary treatment.

The purpose of secondary treatment is to remove the suspended solids that did not settle out in the primary tanks. Biological treatment involves the use of microorganisms, they must be provided with enough oxygen, suitable temperature and other conditions. Microbes converting pollutants into carbon dioxide, water and energy for their growth and reproduction.

3- Final treatment

The purpose is to disinfect the liquid chlorination, ozonation and treatment with UV radiations are done in this step.

م. نغم ادريس

Ministry of Higher Education and
Scientific Research
University of Technology
Chemical Engineering Department

Biochemical engineering
Third Year

نغم اديب

CE 543-U **Biochemical Engineering** *Unit Operations Branch*

Units 2
Theoretical 2 hr/week
Tutorial 1 hr/week
Practical - hr/week

1. Definition, introduction: (2hrs)

2. Industrial micro organisms and methods of separation: (2hrs)

3. Micro organisms genetics: (4hrs)

4. Biotechnological methods of growths:
Liquid systems, batch and continuous cultures. Breaded cultures Solid Fermentation's (6hrs)

5. Single cells proteins:
Microorganisms used, treatment of waste, production of single cell protein. Diet value (3hrs)

6. Bakery yeast:
Dry and ready effective types. (3hrs)

7. Amino acids:
Clotamic acid. (1hr)

8. Organic acids:
Acetic acid. (1hr)

9. Enzymes: (1hr)

10. Antibiotics:
Microorganisms producing antibiotics, Penicillin (1hr)

11. Industrial Alcohol:
Alcoholic fermentation, microorganism used, production method. (1hr)

12. Animal cell cultivation: (2hrs)

13. Plant cell Cultivation: (1hr)

14. Environmental cleaning using biotechnology:
In the fields of water treatment. Organic Pollutants. Petroleum wastes. (2hrs)

References

1- Rajiv Dutta, "Fundamentals of Biochemical Engineering", India, 2007.

2- Nukesh Doble, "Biochemical Engineering", India, 2007

3- James E. Bailey, David F. ollis, "Biochemical Engineering Fundamentals", 2nd ed, 1986.

4- Ronald W. Missen; charles A. Mims; Bradley A. Saville (1999), INTRODUCTION TO CHEMICAL REACTION ENGINEERING AND KINETICS, 1st edition, John Wiley & Sons Inc., USA.

بسم الله الرحمن الرحيم

Defenitions

1- Biochemical Engineering :-

Is a branch with applies chemical engineering principles to biological systems to produce the desired product from raw materials.

2- Biotechnology :-

Is a commercial techniques that use living organisms, or substances from those organisms, to make or modify a product, including techniques used for improvment of the characteristics of economically important plant and animal and for the development of microorganisms to act on the environment.

For industrial applications of microorganisms, Bacteria and Fungi are especially important.

3- Bacteria :-

Are unicellular microscopic organisms. The typical diameter of the cell ranges from (0.5 .. 1) μm.

The length of bacterial cells vary greatly. Bacteria occur in a variety of shapes such as :-

a- Spherical.
b- cylindrical or rod shaped.
c- helically coiled.

Bacteria reproduce predominatly by a process know as binary fission.

Nutritional Requirements :

ALL biological systems, from microorganisms to man, share a set of nutritional requirements, which are:-

1- Sources of energy.

a- phototrophs :-

organisms which are capable of employing radiant energy.

b- Chemotrophs :-

organisms which obtain the energy for their activities and self-synthesis from chemical reactions that can occur in the dark.

2- Sources of carbon.

a- autotrophs :-

organisms which can use CO_2 or carbonates as a sole source of carbon.

b- hetrotrophs :-

Organisms which can not use CO_2 as a sole source of carbon but require, in addition to minerals, one or more organic substances, such as glucose or amino acids, as a sources of carbon.

3- Sources of nitrogen.

Atmospheric nitrogen, inorganic nitrogen compounds.

4- Sources of sulfur and phosphorus.

Organic or inorganic sulfur.

5- Sources of metallic elements.

Sodium, potassium, calcium, Znic, Copper and cobalt.

Physical Conditions.

Three major physical factors to be taken into consideration are

a- Temperature.

b- gaseous environment.

c- pH.

Depending on the temperature range over which they grow. Bacteria are called :-

a- psychrophiles optimum temperature (20-30) C°.

b- Mesophiles " " (30-40) C°.

c- Thermophiles " " (45-60) C°.

Depending to their response to oxygen.

a- Aerobic bacteria grow in the presence of free O_2.

b- Anaerobic bacteria grow in the absence of free O_2.

c- Facultatively anaerobic bacteria grow in either the absence or the presence of free O_2

d- Microaerophilic bacteria grow in the presence of minute quantities of free O_2.

For most bacteria the optimum pH for growth lies between (6.5 - 7.5).

Fungi: الفطريات

Fungi are plants devoid of chlorophyll and are therefore unable to synthesize their own food. They range in size and shape from single celled yeasts to multicellular mushrooms. Among them Yeasts and Molds are industrially important.

Yeasts:

Are generally unicellular organisms and their shape is spherical to ovoid. Their size is (1-5) μm in width and from (5-30) μm in length. The cell wall is quite thin in young cells but thickenes with age. Yeasts do not have chrorophyll, they depend on higher plants for their energy.

Molds:

Are filamentous fungi. Molds are used in the product of antibiotics, industrial chemicals, enzymes and food additives.

Cultivation:

Is the growth of microbial population in artificial environments.

Pure culture =

A culture that contains only one kind of microorganisms.

Mixed culture =

A culture that contains more than one kind of microorganisms -

Inoculation

Is the seeding of culture vessel with the microbial material (inoculum).

Enzymes =

Are biological catalysts that are protein molecules in nature -

They are produced by living cells (animals, plants and microorganisms) and are absolutely essential as catalysts in biochemical reactions. The catalytic ability of enzymes is due to its particular protein structure. A specific chemical reaction is catalyzed at a small portion of the surface of an enzyme, which is known as the "Active site".

Substrate :-

In biological reaction is equivalent to the term reactant in chemical reaction.

Differences Between Chemical Reaction and Enzyme Reactions :-

1- An enzyme catalyst is highly specific, and catalyzed only one or a small number of chemical reactions.

2- The rate of an enzyme-catalyzed reaction is usually much faster than that of the same reaction when directed by non biological catalysts.

3- Only a small amount of enzyme is required to produce a desired effect.

4- The reaction conditions (T, pH, P) for the enzyme reactions are very mild.

like P (pressure) ⟶ atmospheric.
and
T (temperature) ⟶ (25-40) C°.

5- Enzymes are comparatively sensitive or unstable molecules and require care in their use.

6- Enzymatic reactions do not form any by products which reduce the product cost.

Classification of Enzymes.

The enzymes can be classified into three major categories :-

1- Industrial enzymes.
2- Analytical enzymes.
3- Medical enzymes.

Factors Influencing The Rate of Reaction.

The important factors influencing the rate of reactions are :-

a- The concentration of the reactants.
b- Temperature. (T).
c- Pressure. (P).

لتفسير ظاهرة الاختلاف في سرعة التفاعلات
وجدت عدة نظريات لتفسير هذه الظاهرة.

The Theories

1- Collision Theory.

The reactants react to form product only if they are in Collision with each other and the parameters (C, T, P) definitely influence the collision of molecules.

It should also be noted that all collision do not effectively Lead to a reaction that.

i- not all colliding molecules possess sufficient energy between them to undergo a reaction

ii- not all collision bring right molecules in contact with each other.

2- Transition state.

According to the transition state theory, chemical reactions proceed via the formation of an unstable intermediate between reactants and produts. This unstable intermediate disintegreats to a more stable one and so must posse more free energy that stable compound.

Activation Energy

colliding molecules must posses a ~~ce~~ certain amount of energy to cross a potential barrier in order to the reaction take place.

The activation energy of a reaction can be calculated by the Arrhenius Equation.

$$K = K_0 \exp\left(\frac{-E}{RT}\right)$$

where :-

K = rate constant.

K_0 = Arrhenius constant.

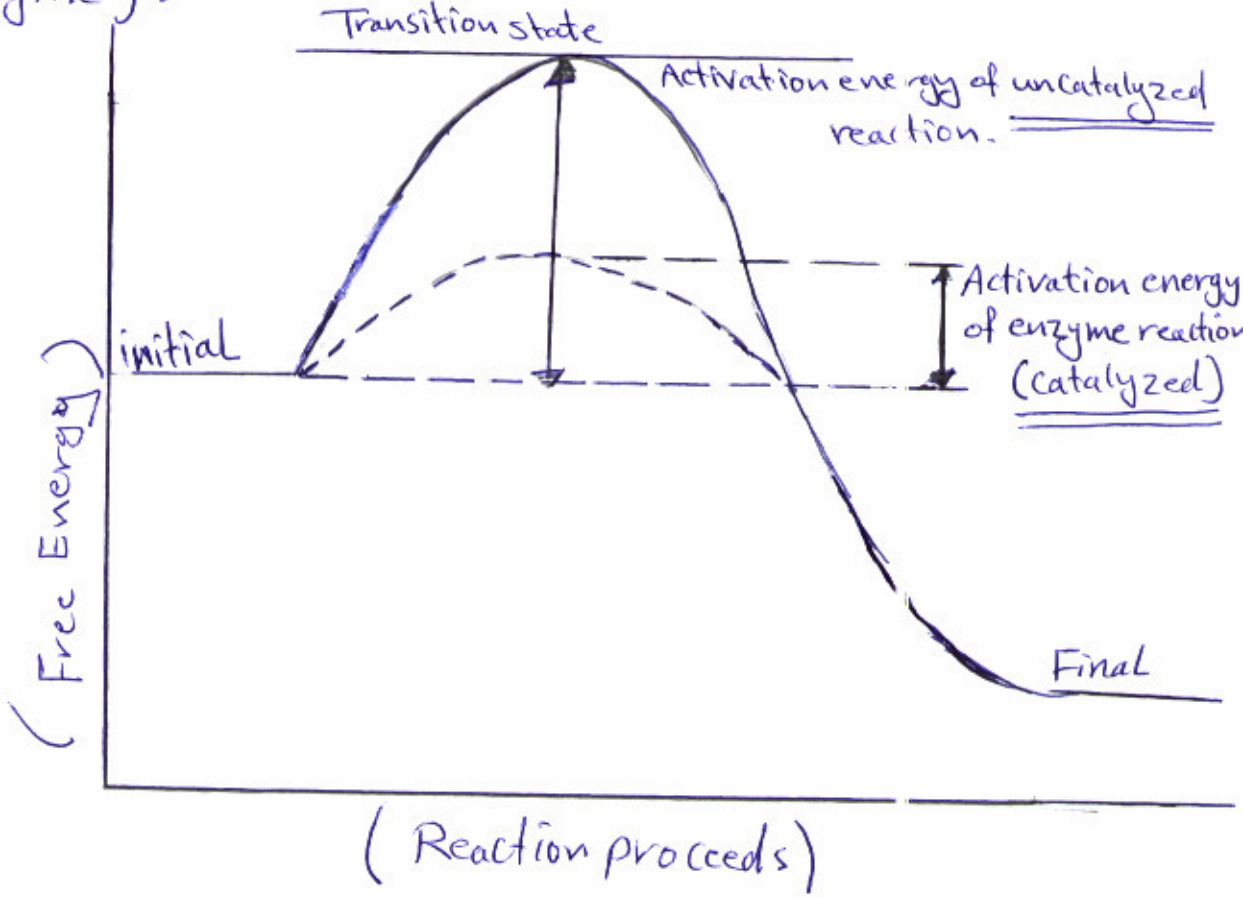
E = activation energy.

R = gas constant.

T = absolute temperature.

The Role of Catalysts (Enzyme).

Catalysts enhance the rate of reaction. The catalyst reduce the activation energy of the reaction. The catalyst binds to reactant and forms a different transition state complex than that of un catalyzed reaction; which is more stable and therefore requires less activation energy to cross the potential barrier for the reaction to proceed. The fig below show the role of catalysts (enzyme).



Free energy change for catalyzed and uncatalyzed reactions

Biochemical Reactors

Biochemical reactors are generally multiphase systems, handling air (in aerobic process), liquid and immobolized microorganism.

Biochemical reactors are made of

a- Stainless steel, have simple geometric shape.

b- minimum number of flanges and welds.

c- measuring and sampling nozzles.

d- no dead zone and minimum surface roughness.

ENZYME KINETICS

Simple enzyme Kinetics

$$S \xrightarrow{E} P$$

The substrate (S) is converted to product (P) with the help of an enzyme (E) in a biochemical reactor. The product concentration will increase and reach a maximum value, whereas the substrate concentration will decrease as shown in the fig. below.

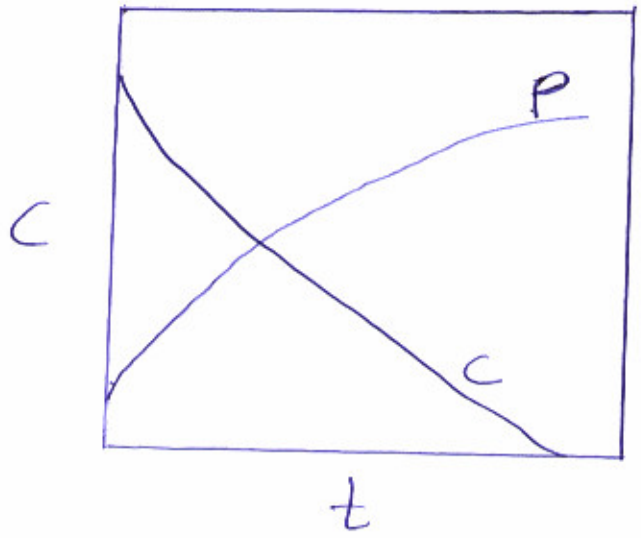


Fig. The change of substrate and product concentration with respect to time.

The rate of reaction can be expressed as follows :—

$$r_S = -\frac{dC_S}{dt}.$$

$$r_P = \frac{dC_P}{dt}.$$

where :—

C_S = substrate concentration change with time.

C_P = product concentration change with time.

The reaction rate equation can derived from the preceding mechanism based on the following assumptions :—

1- The total enzyme concentration stays constant during the reaction

that is $C_{E_o} = C_E + C_{ES}$

2- The amount of an enzyme is very small compared to the amount of substrate, beacause of

i- enzymes are very efficient.

ii- use a little enzyme as possible because of their costs.

3- The product concentration is so low that product inhibition may be considered negligible.

MODEL OF ENZYME KINETICS

1- Michaelies-Menten Model.

For a single substrate reaction catalyzed by an enzyme, there are Several Steps involved and they are as follows :-

1- Substrate binds to the enzyme at the active site to form an enzyme-substrate complex.

2- Formation of a transition state.

3- Enzyme - product complex.

4- Separation of products from the enzyme and freeing the active enzyme site. The active enzyme site is one again available for the reaction.

These steps can mathematically represented as below.

$$E + S \rightleftharpoons ES$$

$$ES \rightleftharpoons EP$$

$$EP \rightleftharpoons E + P$$

The second equation is ignored.

$$E + S \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES \quad \text{---} (1)$$

$$ES \longrightarrow P + E \quad \text{---} (2)$$

The michaelies _ Menten assumption -

The equation (2) is much slower than equation (1) and the slow step determines the rate, while the other is at equilibrium.

This is an assumption which is often employed in hetrogeneous catalytic reactions in chemical kinetics.

$$-\frac{dC_S}{dt} = k_1 C_S C_E - k_2 C_{ES} \quad \text{---- (3)}$$

$$\frac{dC_P}{dt} = k_3 C_{ES} \quad \text{---- (4)}$$

at steady-state

$$\frac{dC_S}{dt} = 0$$

∴ equation (3) become.

$$k_1 C_S C_E = k_2 C_{ES}$$

$$\therefore \boxed{C_{ES} = \frac{k_1}{k_2} C_S C_E} \quad \text{---- (5)}$$

The material balance for the total amount of enzyme.

$$C_{E_o} = C_E + C_{ES}$$

$$\therefore \boxed{C_E = C_{E_o} - C_{ES}} \quad \text{---- (6)}$$

sub eq (6) into eq (5)

$$C_{ES} = \frac{k_1}{k_2} C_S (C_{E_o} - C_{ES})$$

$$C_{ES} = \frac{k_1}{k_2} C_S C_{E_o} - \frac{k_1}{k_2} C_S C_{ES}$$

$$C_{ES} + \frac{k_1}{k_2} C_S C_{ES} = \frac{k_1}{k_2} C_S C_{E_0}$$

$$C_{ES}\left(1 + \frac{k_1}{k_2} C_S\right) = \frac{k_1}{k_2} C_S C_{E_0}$$

$$C_{ES} = \frac{\frac{k_1}{k_2} C_S C_{E_0}}{1 + \frac{k_1}{k_2} C_S}$$

$$C_{ES} = \frac{\frac{k_1 C_S C_{E_0}}{k_2}}{\frac{k_2 + k_1 C_S}{k_2}}$$

$$C_{ES} = \frac{k_1 C_S C_{E_0}}{k_2 + k_1 C_S}$$

$$C_{ES} = \frac{k_1 C_S C_{E_0}}{k_1\left(\frac{k_2}{k_1} + C_S\right)}$$

$$\boxed{C_{ES} = \frac{C_S C_{E_0}}{\frac{k_2}{k_1} + C_S}} \quad \text{---------} \quad (7)$$

From slow step eq (4)

$$r_p = k_3 C_{ES}$$

sub eq (7) into eq (4) and