Bioreactor Design and Analysis
Prof. Dr. Smita Srivastava
Department of Biotechnology
Indian Institute of Technology - Madras

Lecture – 24
Heterogenous Reactions in Bioreactors – Part I

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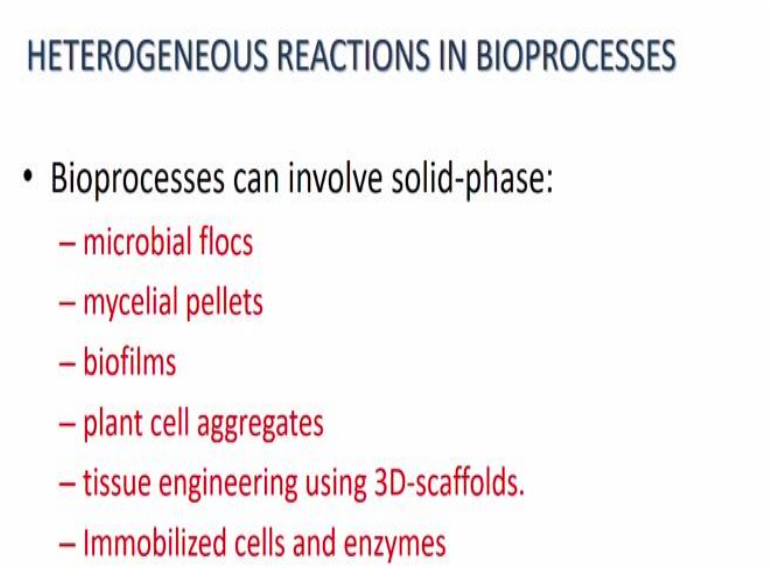

So now let us talk about heterogeneous reactions in bioprocesses. We have just discussed about the different types of fluid behaviors and under different conditions. So, we now have some idea that the fermentation at high cell density do not continue to behave as Newtonian, but they can start deviating from ideality and behave like non-Newtonian fluids. Now this may further lead to heterogeneous reactions in bioprocesses. Now what does this mean?

Now this can be involved in fermentations where there are either high cell densities or flocculation is happening or there are immobilized cells, structures where there can be mass transfer limitations. So now bioprocesses which involve for example solid phase where microbial flocs or mycelial pellets might be getting formed or in your wastewater treatment plants where biofilms are required.

Or like plant cell fermentations where plant cells tend to aggregate and they form a small aggregate size. Then tissue engineering on 3D-scaffolds where the tissue starts growing on a solid 3D structure or immobilized systems like immobilized cells or immobilized enzymes where heterogeneous reactions can happen.

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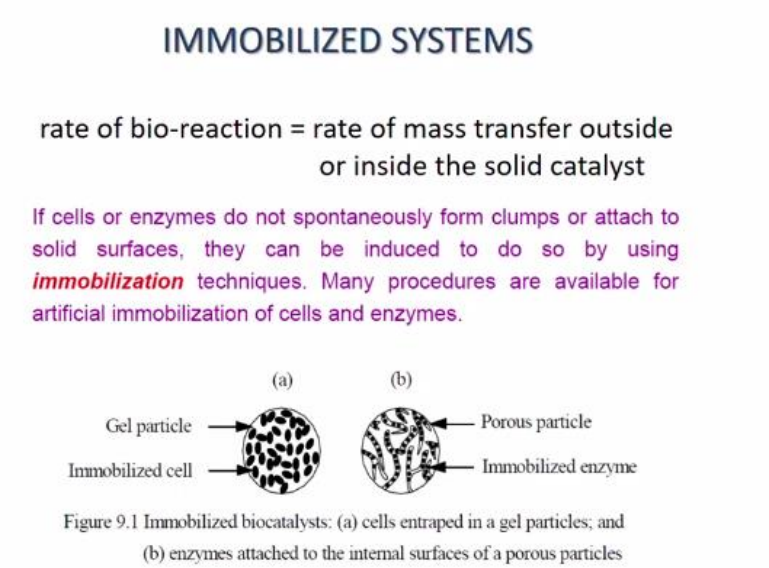

Now let us take an example of immobilized systems and let us try to characterize the mass transfer process in these immobilized structures. Now rate of bioreaction we know in an immobilized system would be dependent on the rate of mass transfer outside or inside the solid catalyst for the substrate. If cells or enzymes they do not spontaneously form clumps or attach to solid surface, they can be induced to do so by using immobilization techniques.

Many procedures for immobilization are available for artificial immobilization for cells and enzymes. Let us take an example as shown in the figure on the slide you can see figure a where a gel particle has immobilized cells embedded in it and the figure b shows a porous structure a porous particle where the cells have settled in the pores or the enzymes have settled inside the pores of the solid structure.

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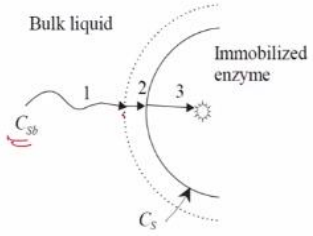

Schematic diagram of the path of the substrate to the reaction site in an immobilized enzyme.

1. Transfer from the bulk liquid to the surface of the boundary layer
2. Diffusion through the boundary layer
3. Diffusion to the active site inside the inert support

Step 1&2 form external mass transfer resistance
Step 3 forms internal mass transfer resistance

In both these cases, the substrate has to diffuse in from the bulk liquid and reach the reaction center or the enzyme for the reaction to happen. Let us assume as shown on the picture here that the substrate concentration in the bulk is denoted as C sb, so the path which it has to take to reach to the immobilized enzyme before the reaction can take place will involve step 1 which means movement from the bulk to the surface. This surface is nothing but the film.

So, as we had studied earlier, this is an immobilized enzyme suspended in a liquid. So, there will be a solid liquid boundary. So, this shows the boundary layer the dotted line till the surface of the immobilized enzyme. So, first it has to reach to the from the bulk to the surface of the boundary layer and then it has to cross the boundary layer and reach the surface of the enzyme and from the surface it has to diffuse in to reach the enzyme.

So, this is nothing but a diagram of the path of the substrate to the reaction site. So, as I said earlier step 1 it is the transfer of the substrate from the bulk liquid to the surface of the boundary layer. Step 2 is the diffusion through the boundary layer and step 3 will be diffusion of the substrate to the active site inside the inert support where the enzyme has been immobilized.

So now please note step 1 and step 2 here they come under external mass transfer resistance. So, they will give external mass transfer resistance. Step 3 will have to face internal mass transfer resistance.

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3.2.1. External Mass-Transfer Resistance

If an enzyme is immobilized on the surface of an insoluble particle, the path is only composed of the first and second steps, external mass-transfer resistance. The rate of mass transfer is proportional to the driving force, the concentration difference, as

$$N_S = k_S A (C_{Sb} - C_S) \qquad (3.1)$$

where C_{Sb} and C_S are substrate concentration in the bulk of the solution and at the immobilized enzyme surface, respectively . The term k_S is the mass-transfer coefficient (length/time) and A is the surface area of one immobilized enzyme particle.

So now let us characterize the external and the internal mass transfer. So, if we have to characterize the external mass transfer resistance let us assume a case. So, let us assume the enzyme has been immobilized on a surface of a solid particle. The path then would only compose of the first and the second step. So, the external mass transfer resistance would be coming into the picture.

The rate of the mass transfer we know is proportional to the driving force. What will be the driving force here? The concentration difference. This concentration difference is the concentration difference between the bulk and the surface of the immobilized particle. So, your rate; of mass transfer because there is a solid liquid boundary, so depending on the thickness of the boundary let us assume the resistance is 1 by k s.

Because it is a solid liquid boundary so we will denote the mass transfer coefficient with a subscript s as shown here in equation 3.1. So, here as we have done earlier your rate of mass transfer of substrates can be defined as k s A is the surface area of the film which is the particle and then C sb is the bulk substrate concentration and C s is the concentration at the surface of the immobilized particle where the enzyme has been coated.

Now C sb and C s are substrate concentrations in the bulk of the solution and at the immobilized enzyme surface respectively. So, the term k s is the mass transfer coefficient and A is the surface area of the immobilized enzyme particle.

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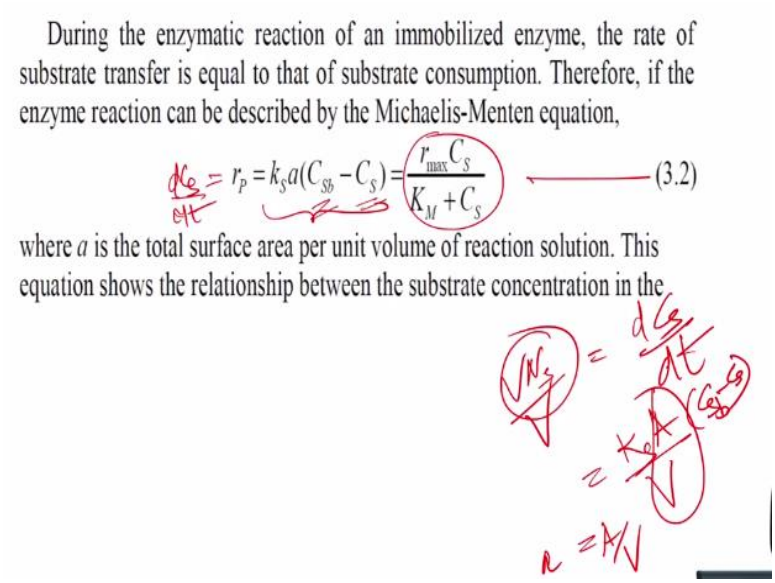
During the enzymatic reaction of an immobilized enzyme, the rate of substrate transfer is equal to that of substrate consumption. Therefore, if the enzyme reaction can be described by the Michaelis-Menten equation,

$$r_P = k_S a(C_{Sb} - C_S) = \frac{r_{max} C_S}{K_M + C_S} \quad \text{(3.2)}$$

where a is the total surface area per unit volume of reaction solution. This equation shows the relationship between the substrate concentration in the

So now rate of mass transfer of the substrate is what is equal to the rate of reaction. So rate of reaction let us assume is following Michaelis-Menten kinetics. So ds by dt or dC s by dt can be written as k s a C sb – C s and then we have used Michaelis-Menten model here where r max is the maximum rate of reaction, C s is the substrate concentration which has reached the enzymes K M is the Michaelis-Menten constant and small a is the total surface area per unit volume of the reaction.

So, because this is equal to dC s by dt initially it was mass transfer, this will become equal to dC s by dt because volume can be divided with the mass and this will become concentration of the substrate and the numerator volume will go to the RHS where we had k s a so that volume will come here and this will become C sb - C s. So now A by V here can be written as small a where V was the volume of the reaction and A was the surface area.

So, then this equation can be represented as shown here in equation 3.2. So small a is the total surface area per unit volume reaction solution or reaction volume and this equation then shows the relationship between the substrate concentration in the bulk of the solution and at the surface of the immobilized enzyme. So, we have now a relationship between C s and C sb.

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bulk of the solution and that at the surface of an immobilized enzyme. Eq. (3.2) can be expressed in dimensionless form as:

$$\frac{1-x_S}{N_{Da}} = \frac{\beta x_S}{1+\beta x_S} \tag{3.3}$$

where

$$x_S = \frac{C_S}{C_{Sb}}$$

$$N_{Da} = \frac{r_{max}}{k_S a C_{Sb}} \tag{3.4}$$

$$\beta = \frac{C_{Sb}}{K_M}$$

N_{Da} is known as *Damköhler number*, which is the ratio of the maximum reaction rate over the maximum mass-transfer rate. Depending upon the magnitude of N_{Da}, Eq. (3.2) can be simplified, as follows:

Now give it a dimensionless form, we will have the entire equation 3.2 divided by C sb. If we do that and substitute C s by C sb as x s then and also bring some constants together and further break them into some dimensionless entities which is called as Damkohler number which stands for the maximum reaction rate to the maximum mass transfer rate and beta which is given as the bulk substrate concentration to the Michaelis-Menten constant.

So, this dimensionless number which is called as Damkohler number it defines the ratio of the maximum reaction rate over the maximum mass transfer rate. So depending on the value of the Damkohler number, one can make out whether the system will be mass transfer limited or whether the system will be reaction rate limited. So, let us simplify this equation 3.3. So, after you substitute divide that 3.2 with C sb then we end up in equation 3.3. Now using 3.3 let us take some cases.

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

$$r_P = \frac{r_{max} C_{Sb}}{K_M + C_{Sb}} \qquad (3.5)$$

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

$$r_P = k_S a C_{Sb} \qquad (3.6)$$

To measure the extent which the reaction rate is lowered because of resistance to mass transfer, we can define the *effectiveness factor* of an immobilized enzyme, η, as

$$\eta = \frac{\text{actual reaction rate}}{\text{rate if not slowed by diffusion}} \qquad (3.7)$$

Let us take case one where the Damkohler number is found to be very small, very small Damkohler number if you go by the definition would mean what that the rate of mass transfer is very high than the rate of reaction. So the slowest step is the governing step. So which means that mass transfer is much greater than the reaction rate and therefore the overall reaction would be controlled by the enzyme reaction rate.

So, then reaction rate has given us in the form of Michaelis-Menten equation. So now because the mass transfer is taking place very fast, so there are no mass transfer limitations. So then what reaches the surface of the immobilized particle would be equal to the bulk concentration and then the bulk concentration of the substrate is what is participating in the enzymatic reaction so where the enzymatic reaction rate can then be given as equation 3.5**.**

Let us take the second case where the Damkohler number is found to be very high. In that case again, the reaction rate this means is much greater than the mass transfer rate and the overall reaction rate therefore is now being controlled by the rate of mass transfer. Now in this again if you see the rate of mass transfer, so the reaction rate is very fast. If the reaction rate is very fast and the rate of mass transfer so which means by the time as soon as it reaches it gets consumed in the reaction.

So, we can assume that on the surface the substrate concentration is nearly 0. So your maximum reaction rate or the reaction rate can then be given as k s a multiplied by C sb. Now this in terms of the bulk substrate concentration is a first order reaction. Now in order to

measure the extent with which the reaction rate is being lowered because of the resistance to mass transfer another term is defined which is called as effectiveness factor.

Now this effectiveness factor in immobilized systems the enzymes can be given as the actual reaction rate to the reaction rate if not diffusion limited.

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The actual reaction rate, according to the external mass-transfer limitation model, is as given in Eq. (3.2). The rate that would be obtained with no mass-transfer resistance at the interface is the same as Eq. (3.5) except that C_S is replaced by C_{Sb}. Therefore, the effectiveness factor is

$$\eta = \frac{\dfrac{r_{max} C_S}{K_M + C_S}}{\dfrac{r_{max} C_{Sb}}{K_M + C_{Sb}}} = \frac{\dfrac{\beta x_S}{1+\beta x_S}}{\dfrac{\beta}{1+\beta}} \qquad (3.8)$$

where the effectiveness factor is a function of x_S and β. If x_S is equal to 1, the concentration at the surface C_S is equal to the bulk concentration C_{Sb}. Substituting 1 for x_S in the preceding equation yields $\eta = 1$, which indicates that there is no mass-transfer limitation. On the other hand, if x_S approaches zero, η also approaches zero, which is the case when the rate of mass transfer is very slow compared to the reaction rate.

So, in immobilized enzyme systems which are following Michaelis-Menten this means what? That the efficiency factor if it is following Michaelis-Menten equation and in actual condition there is some substrate which reaches due to the diffusion limitations the resistance to the boundary layer, there is a substrate C s which is different from the bulk substrate concentration. So, your reaction rate was given as shown on the numerator.

This is the actual reaction rate. Now if the same system was not diffusion limited, so whatever was the bulk concentration would have reached the surface very fast mass transfer. So, in that case the reaction rate would have been as shown in the denominator where the substrate is then concentration is equal to C sb. Now we again use the dimensionless forms x s and beta and as shown here on the slide it will take this form.

So, your effectiveness factor has now become a function of x s and beta. Now if x s =1 which means what x s was what? The x s was C s by C sb. Now if x s = 1 which means C s = C sb, the concentration at the surface is equal to the bulk concentration. Now substituting 1 for x s in this equation, you will see the eta value becomes equal to 1 which means no mass transfer limitations.

On the other hand, if excess approaches 0 if it becomes very nearly 0, so then your eta value also becomes equal to 0. In this case this demonstrates that the rate of mass transfer is very slow as compared to the rate of reaction, the system is mass transfer limited.

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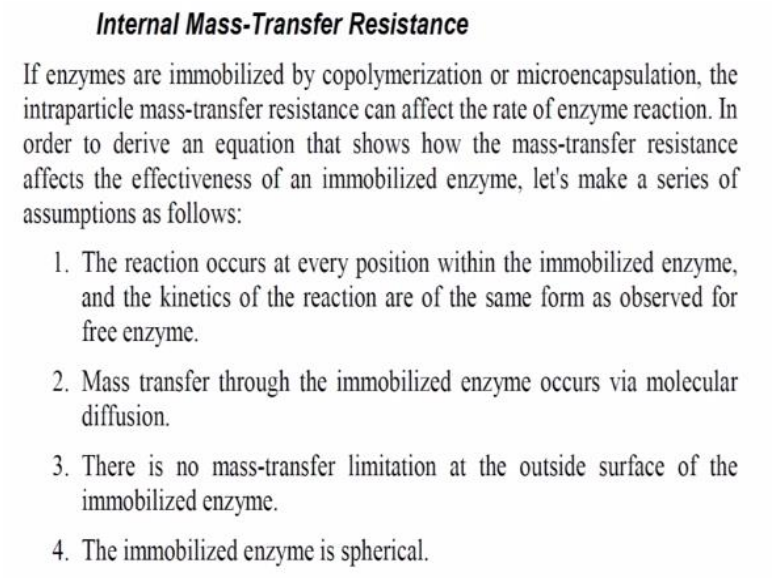

Now let us talk about internal mass transfer resistance. So if the enzymes are immobilized by copolymerization or by microencapsulation, then the intraparticle mass transfer resistance can affect the rate of enzymatic reaction. Now in order to now characterize this or derive an equation that can show how mass transfer resistance is affecting the effectiveness of this immobilized enzyme, then we start with few assumptions.

So, the reaction occurs, what are the assumptions? First, we will assume that the reaction occurs at every position in the immobilized enzyme and the kinetics of the reaction are of the same form as observed for the free enzyme. The second assumption mass transfer through the immobilized enzyme occurs via molecular diffusion. So, we are assuming that the mass transfer in this immobilized structure is only occurring through molecular diffusion process.

Third there is no mass transfer limitation at the outside surface of the immobilized enzyme and the fourth for ease we will assume that the immobilized particle is spherical in nature.

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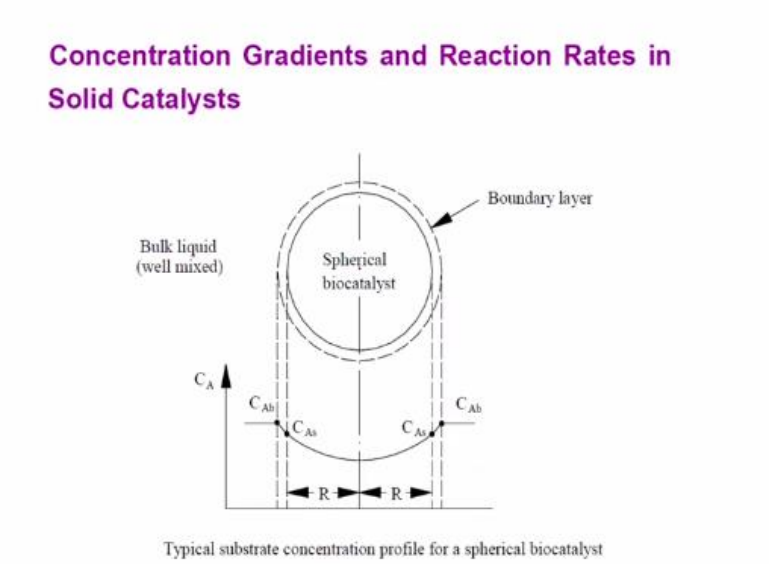

Typical substrate concentration profile for a spherical biocatalyst

So, if you see the picture on the slide there is a spherical biocatalyst inside which the enzyme has been immobilized. It is suspended in the bulk liquid and we will assume that there is no external mass transfer limitation. So the boundary layer is absent, but the photo shown here is an actual scenario where if you make a plot of the concentration of the substrate or any component in the medium versus the R which is the center of the spherical pellet is your origin.

So, what you can observe is that the concentration decreases wherever there is mass transfer limitation. So, from the bulk which is C Ab it goes down because of the solid-liquid boundary layer and then once it reaches the surface because of the intra mass transfer resistance is intraparticle the concentration further goes down diffusional limitations before it reaches the center of the spherical particle.

Now the spherical particle radii are given as capital R. So, this is the substrate concentration profile in a spherical biocatalyst expected in a immobilized system.

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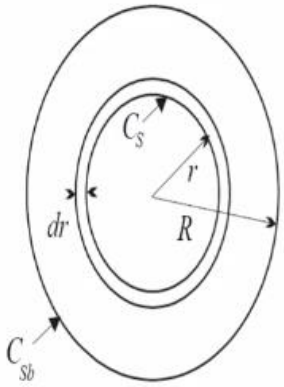

Shell balance for a substrate in an immobilized enzyme.

Now in order to find how the substrate concentration will change from the surface till the inner core. We need to bring the substrate concentration as a function of the radii of the pellet, so how do we do that? We will assume that it is a spherical particle and we will cut out a shell in this spherical particle and we will do a mass balance for the substrate across the shell.

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The model developed by these assumptions is known as the *distributed model*.

First we derive a differential equation which describes the relationship between the substrate concentration and the radial distance in an immobilized enzyme. The material balance for the spherical shell with thickness dr as shown in Figure 3.3 is

$$\text{Input} - \text{Output} + \text{Generation} = \text{Accumulation} \tag{3.9}$$

$$4\pi\left\{(r+dr)^2 D_S\left[\frac{dC_S}{dr}+\frac{d}{dr}\left(\frac{dC_S}{dr}\right)dr\right]-r^2 D_S\frac{dC_S}{dr}+(r^2 dr)r_S\right\}=4\pi r^2 dr\frac{dC_S}{dt} \tag{3.10}$$

where D_S is diffusivity of the substrate in an immobilization matrix.

For a steady-state condition, the change of substrate concentration, dC_S/dt, is equal to zero. After opening up the brackets and simplifying by eliminating all terms containing dr^2 or dr^3, we obtain the second order differential equation:

$$D_S\left(\frac{d^2C_S}{dr^2}+\frac{2}{r}\frac{dC_S}{dr}\right)+r_S=0 \tag{3.11}$$

Eq. (3.11) can be solved by substituting a suitable expression for r_S. Let's solve the equation first for the simple cases of zero-order and first-order reactions, and for the Michaelis-Menten equation.

Now the model which we will develop under these assumptions will be known as distributed model. Now because outside we assume there is no mass transfer limitation, so first we derive a differential equation which describes the relationship between the substrate with the radial distance in the immobilized enzyme. So, if we start doing the material balance for the substrate across the spherical shell.

Now this spherical shell we will assume has a thickness small dr and small r is the radii from the centre at which this shell has been cut of thickness dr and capital R is the radius of the pellet. And we can assume that C sb is the bulk substrate concentration at the surface and C s is the substrate concentration at the surface of the shell. So, if you use continuity equation which means do the material balance then input minus output plus generation or consumption will be equal to accumulation.

Now in case of a consumption this will become minus. Now because it is a substrate so there would be consumption and not generation. So, if you see the rate of input and the rate of output we know that it is following diffusion process, so here Fick's law of diffusion has been used and the rate of input and the rate output have been placed at the first two terms and the third term here defines your substrate consumption rate and on the RHS is your rate of substrate accumulation inside the shell of thickness dr.

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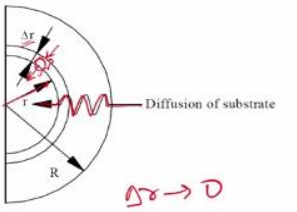
$$(D_{Ae}\frac{dC_A}{dr}4\pi r^2)|_{r+\Delta r} - (D_{Ae}\frac{dC_A}{dr}4\pi r^2)|_r - r_A 4\pi r^2 \Delta r = 0$$

$$\frac{(D_{Ae}\frac{dC_A}{dr}4\pi r^2)|_{r+\Delta r} - (D_{Ae}\frac{dC_A}{dr}4\pi r^2)|_r}{\Delta r} - r_A r^2 = 0$$

$$\frac{d}{dr}(D_{Ae}\frac{dC_A}{dr}r^2) - r_A r^2 = 0$$

$$D_{Ae}\frac{d}{dr}(\frac{dC_A}{dr}r^2) - r_A r^2 = 0$$

$$D_{Ae}(\frac{d^2C_A}{dr^2}r^2 + 2r\frac{dC_A}{dr}) - r_A r^2 = 0 \quad (1)$$



Now to understand this better let us take the half of this spherical shell. So, let us assume here the notations have been differed for the ease and understanding. Let us assume that this thickness is delta r, small r and as I said small r is the radii at which the shell has been kept and capital R is the actual radius of the pellet. So as shown here the substrate is diffusing inside this pellet to reach the core.

So now; with the Fick's law input as I am drawing here then output difference will be equal to the accumulation of the substrate in the shell. So, the rate at which it is coming inside is your first term. The second term which is again being defined by the Fick's law is the rate at

which the substrate is going out at a distance r and at a distance r + r it was coming in. And the third term is your reaction rate in this shell which is equal to the consumption rate of the substrate.

So now if you put the limit that delta r tends to 0, then putting this limit here you can bring it in the form of differential and it takes the form of equation given in the end. So, if you see this becomes equal to differential because you are putting the limits delta r tends to 0 and D Ae has been brought out of the bracket because this is the diffusivity constant assumed to be a constant C A and r are variables and r A is your reaction rate.

So, again when you take the differential of the entities in the bracket it will expand as shown here in the last equation. So now this equation 1 corresponds to equation 3.11 where r s here is the reaction rate can be any, can be zero order reaction, first order reaction kinetics, can have a Michaelis-Menten kinetics. So, what has happened this equation 1 here has been divided by r square completely.

So, if you divide the entire equation by r square this will become equal to your equation 3.11. So, now in order to solve 3.11, equation shown here, you can substitute a suitable expression for the reaction rate r s.

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Zero-order Kinetics: Let's assume that the rate of substrate consumption is constant (zero order) with respect to substrate concentration as

$$r_S = -k_0 \quad \text{if } C_S > 0$$
$$r_S = 0 \quad \text{otherwise} \qquad (3.12)$$

This is a good approximation when $K_M << C_S$ for Michaelis-Menten kinetics, in which case $k_0 = r_{max}$.

By substituting Eq. (3.12) into Eq. (3.11), we obtain

$$\frac{d^2C_S}{dr^2} + \frac{2}{r}\frac{dC_S}{dr} - \frac{k_0}{D_S} = 0 \quad \text{for } C_S > 0 \qquad (3.13)$$

The boundary conditions for the solution of the preceding equation are

$$\frac{dC_S}{dr} \to 0 \quad \text{as } r \to R_C \qquad (3.14)$$
$$C_S = C_{Sb} \quad \text{as } r = R$$

Now let us take some cases. Let us first assume a zero-order kinetics. So for a zero-order kinetics, the rate of substrate consumption is constant with respect to substrate concentration. So, your reaction rate let us assume is –k 0 where k 0 is your reaction constant rate constant

for any value C s greater than 0. And if the C s is not there, then obviously the rate of reaction is 0. So, if you remember your Michaelis-Menten kinetics which is your V= V max S upon S + K M.

In this this becomes this takes the form of a zero order-reaction if your K M value is very less than C s which means it has very high affinity for the substrate. Then in that case your k 0 will become equal to your maximum reaction rate which they have represented as r max. Now if we substitute this in your equation 3.11 in place of r s, then we place here as –k 0 and then you divide the entire equation by diffusivity constant D Ae here which is termed as D s here.

And this becomes your equation where your C s is being related to r. So, in order to solve this double differential equation, we make use of the boundary conditions. What are these boundary conditions? The change of substrate with r this will go to 0 when r becomes equal to some critical value. So, this is the maximum radii till which the substrate is being able to penetrate beyond which there is no substrate.

So obviously your dC s by dr the rate of change of substrate with the radii is nearly equal to 0 when your r tends to be the critical radius. Now at the surface where r is equal to capital R your substrate concentration is equal to the bulk substrate concentration because there are no external mass transfer resistances. So, this forms your boundary condition 2. So, the first one was dC s by dr tending to 0 at r is equal to R c and C s becoming equal to C sb at r is equals to capital R which is the radius of the pellet.

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If, $\alpha = r C_s$

$$\frac{d^2\alpha}{dr^2} = \frac{k_0}{D_S} r \qquad (3.15)$$

Integrating Eq. (3.15) twice with respect to r, we obtain

$$\alpha = \frac{1}{6}\frac{k_0}{D_S} r^3 + C_1 r + C_2$$

Therefore,

$$C_S = \frac{1}{6}\frac{k_0}{D_S} r^2 + C_1 + \frac{C_2}{r} \qquad (3.17)$$

Applying the boundary conditions (Eq. (3.14) on Eq. (3.17) yields

$$C_1 = C_{Sb} - \frac{1}{6}\frac{k_0}{D_S} R^2 - \frac{1}{3}\frac{k_0 R_C^3}{D_S R}$$

$$C_2 = \frac{1}{3}\frac{k_0}{D_S} R^3$$

So now in order to solve this differential equation given as 3.13 with the boundary conditions which we have numbered as 1 and 2 to solve this if you do a mathematical substitution of a quantity alpha which is a product of r and C s. And further use it you can reduce the earlier equation into a simple double differential form which you can integrate and then apply the boundary conditions to get the integration constant values.

And then come back to the original equation to find a relationship between C s and r. So, your equation 3.1 where C 1 and C 2 were integration constants, their value can be obtained using boundary conditions.

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Therefore, the solution of Eq. (3.13) is

$$\frac{C_S}{C_{Sb}} = \frac{k_0}{6 C_{Sb} D_S}\left[\left(r^2 - R^2\right) - 2R_c^3\left(\frac{1}{R} - \frac{1}{r}\right)\right] + 1 \qquad (3.20)$$

Eq. (3.20) is only valid when $C_S > 0$. The critical radius, below which C_S is zero, can be obtained by solving

$$\left(R_C^2 - R^2\right) - 2R_c^3\left(\frac{1}{R} - \frac{1}{R_C}\right) + \frac{6 C_{Sb} D_S}{k_0} = 0 \qquad (3.21)$$

$r = R_c$

$C_s = 0$

So, your solution for a zero-order kinetics is shown here in terms of your critical radii, your bulk substrate concentration and the radius of the pellet given the values of the reaction rate constant of zero-order kinetics and the diffusivity of the substrate through the pellet.

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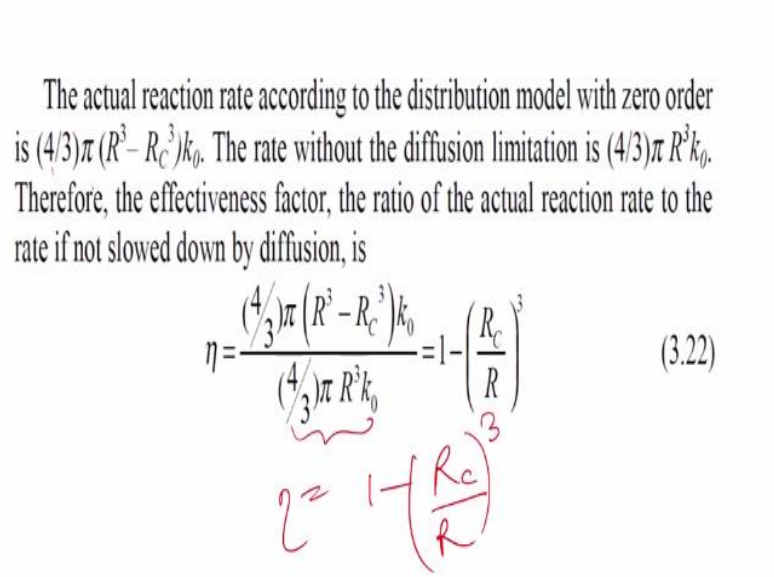

So now if we want to find out an expression for the efficiency factor for such a system, we can find out the actual reaction rate. So, what is the actual reaction rate? Now the actual rate here according to the distribution model with zero-order kinetics would be nothing but 4 by 3 pi R cube – R c cube which is the effective volume of the pellet because beyond R c there is no substrate getting inside.

So effective volume is R – R c 4 by 3 pi R cube is the total volume – 4 by 3 pi R c cube which is the solid pellet in which there is no substrate getting in. This volume multiplied by the reaction rate constant. So, this is your actual reaction rate the maximum rate possible with no diffusional limitations. So, there will be no diffusional limitations then your R c will become equal to 0.

So then in that case your reaction rate becomes 4 by 3 pi R cube into k0. So, then your eta which is your efficiency factor can be given as a function of the critical radii and the radius of the pellet. So, if we need to get an expression for that; critical radii in a zero-order kinetics immobilized system enzymatic system then we can find an expression by adding the boundary condition that when small r becomes equal to R c, your C s becomes equal to 0.

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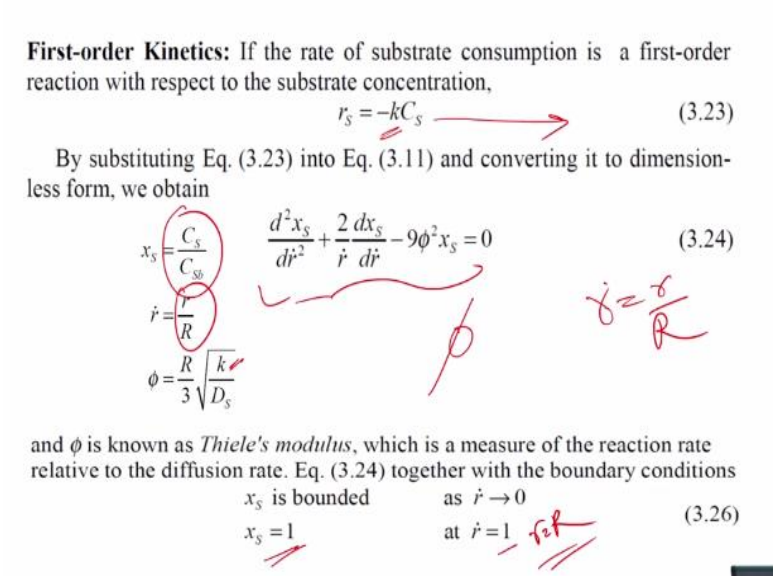

First-order Kinetics: If the rate of substrate consumption is a first-order reaction with respect to the substrate concentration,

$$r_S = -kC_S \qquad (3.23)$$

By substituting Eq. (3.23) into Eq. (3.11) and converting it to dimensionless form, we obtain

$$\frac{d^2x_S}{d\dot{r}^2} + \frac{2}{\dot{r}}\frac{dx_S}{d\dot{r}} - 9\phi^2 x_S = 0 \qquad (3.24)$$

$$x_S = \frac{C_S}{C_{Sb}}, \quad \dot{r} = \frac{r}{R}, \quad \phi = \frac{R}{3}\sqrt{\frac{k}{D_S}}$$

and ϕ is known as *Thiele's modulus*, which is a measure of the reaction rate relative to the diffusion rate. Eq. (3.24) together with the boundary conditions

$$x_S \text{ is bounded} \quad \text{as } \dot{r} \to 0$$
$$x_S = 1 \quad \text{at } \dot{r} = 1 \qquad (3.26)$$

So now let us take another case of a first order kinetics. So, if the rate of substrate consumption is a first-order reaction with respect to the substrate concentration, then in a first-order kinetics it can be demonstrated by equation shown here as 3.23 where k is your rate constant and C s is the substrate concentration. So your reaction rate is a function of substrate concentration.

Now putting this in the earlier equation double differential equation and using dimensionless entities which we did earlier as x s and r dot, r dot here is a dimensionless form for the radii where small r by capital R is your r dot and all the constants have been brought together in the form of Thiele's modulus which has been given as phi. Now this Thiele's modulus takes the form of r by 3 under root k by D s.

Now the physical significance of Thiele's modulus if you can understand from the arrangement of constants here it seems to be a measure of the reaction rate relative to the diffusion rate in the denominator. Now if the Thiele modulus is very less or very high, we can find out that whether reaction rate is high or whether diffusion rate is higher. So x s is bounded which means dC s by dr is nearly 0 when your r is 0.

So, we are assuming that it is able to reach till the inside. Your x s = 1 which means C s becomes equal to the substrate at the surface when your r is equal to capital R. So, it is saying that the substrate concentration is the bulk substrate concentration at the surface of the pellet. So, the boundary conditions have been framed in terms of the dimensionless entities.

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In order to convert Eq. (3. 24) to a form which can be easily solved, we set $\dot{\alpha} = \dot{r}x_S$, so that the differential equation becomes

$$\frac{d^2\dot{\alpha}}{d\dot{r}^2} - 9\phi^2\dot{\alpha} = 0 \qquad (3.27)$$

Now the general solution of this differential equation is

$$\dot{\alpha} = C_1 \cosh 3\phi\dot{r} + C_2 \sinh 3\phi\dot{r} \qquad (3.28)$$

or

$$x_S = \frac{1}{\dot{r}}\left(C_1 \cosh 3\phi\dot{r} + C_2 \sinh 3\phi\dot{r}\right) \qquad (3.29)$$

Since x_S must be bounded as $\dot{r}$ approaches zero according to the first boundary condition, we must choose $C_1 = 0$. The second boundary condition requires that $C_2 = 1/\sinh 3\phi$, leaving

$$x_S = \frac{\sinh 3\phi\dot{r}}{\dot{r}\sinh 3\phi} \qquad (3.30)$$

which shows how the substrate concentration changes as a function of the radial distance in an immobilized enzyme.

Now again, the same equation, the double differential equation to solve it we do the substitution in terms of alpha. So here the alpha dot becomes equal to r dot x s so that the double differential equation takes a simpler form for integration and we will again integrate twice to get the integration constants and using the boundary conditions we will solve for the integration constants.

So, when all this is done your x s is related to r, your x s was nothing but C s by C sb. So effectively your substrate concentration is being related and your r dot was r by R, so the C s is indirectly being related to your radii of the pellet. So, this equation 3.3 finally will show how your Cs will change with the radii of the pellet inside the pellet if the reaction kinetics is being governed by a first-order reaction rate kinetics.

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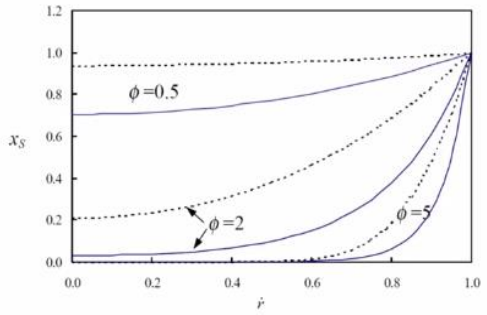

For a low value of Thiele's modulus ($\phi \leq 1$), the rate of the enzyme reaction is slow compared to the diffusion rate. Therefore, the substrate diffuses into the core of the particle, which results in a fairly flat concentration distribution throughout the radial location of a particle. On the other hand, for higher values of the modulus ($\phi \geq 5$), the reaction rate is faster than the diffusion rate, so most of the substrate is consumed near the particle surface. When $\phi = 5$, the substrate concentration at $\dot{r} \leq 0.6$ is nearly zero.

Now let us see how Thiele's modulus affects your profile of substrates versus the radii of the pellet or how does it affect the substrate profile inside the pellet. So, if x s versus r dot we have a plot here, there are different phi values given. So, for a very high value, higher the phi value you will see that r dot the range is from 0 to 1. It is a dimensionless entity, it is a fraction, r dot was small r by capital R, so it can change the form from 0 to 1, the range can be from 0 to 1.

So, when r dot = 1 which means at the surface, so when Thiele's modulus is very high, and what was this modulus? Thiele's modulus was a ratio of the mass transfer to the diffusion rate so which means mass transfer rate is higher than the diffusion rate. So, if mass transfer rate is higher than the diffusion rate, the reaction rate is faster than the diffusion rate. So, most of the substrate will be consumed near the particle surface.

Similarly, if the Thiele's modulus value is low, then this would mean that the rate of enzyme reaction is slower in comparison to the diffusion rate.