Bioreactor Design and Analysis
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Lecture – 25
Heterogenous Reactions in Bioreactors – Part 2

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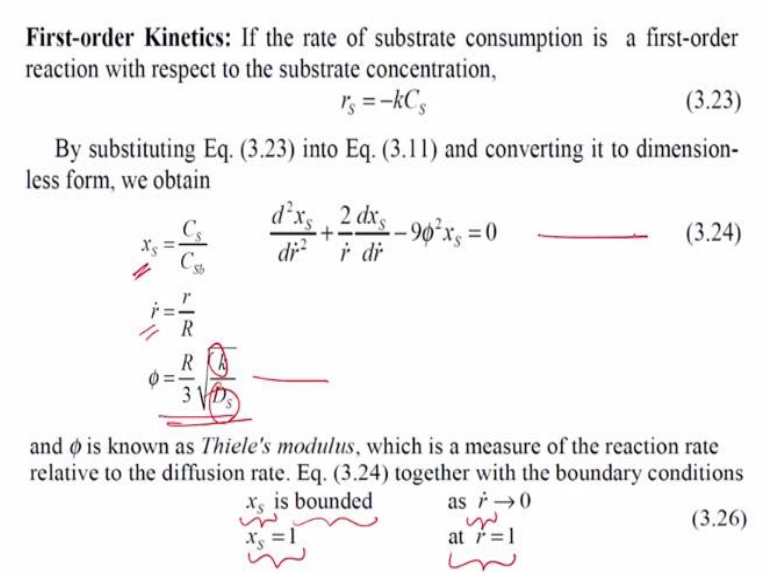

Welcome back students. In the last class, we were discussing about the internal and external mass transfer limitations in immobilized cell systems or immobilized enzyme systems. And while characterizing the internal mass transfer limitations in systems, we assumed different reaction kinetics in which we started with the zero-order kinetics and then today we are going to assume a first-order kinetics.

And see how does the efficiency factor or the substrate profile in the presence of diffusional limitations changes with the radius of the pellet. So, if you can see on the slide the first-order kinetics it will be a linear function of the substrate. So, because here the rate of reaction is in terms of the substrate, the sign is negative here for the rate constant and C s stands for the concentration of the substrate.

Now in the same double differential equation where we did a shell balance for the substrate diffusing in from the surface of the pellet till the inner core or of the immobilized system in the same equation where we were describing the net accumulation rate of the substrate.

There, if you see equation 3.24 it has been converted in dimensionless variables of x s shown here and r dot.

Now x s has been made a dimensionless variable or a ratio of C s to C sb where C sb stands for bulk substrate concentration. Your r dot is a ratio of small r to capital R where if you remember the capital R was the radius of the pellet or that immobilized shell and small r is the distance travelled by the substrate from the center and phi which is a club of constants here after rearrangement.

So, these constants include the rate constant, the reaction rate constant and the diffusivity with the radius of the pellet. Now phi stands for this constant which is called as Thiele's modulus. If you can see in this equation here which I am underlining, it is a measure of the reaction rate to the diffusion rate. So, again with the changing values of phi, phi being low or high we can determine whether the reaction rate is high or the diffusion rate is high.

Then the boundary conditions in terms of C s and r have been now changed in terms of the dimensionless variables x s and r dot. So as dC s by dr was 0 at r tending to 0, so x s is called again will be bounded at r dot nearly 0 and x s will become 1 which means when cs is equals to C sb at what point at the surface of the pellet which is r dot is equal to 1 where r is equal to capital R.

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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 in order to solve this differential equation 3.24 again like we did for zero-order kinetics, a substitution has been done in terms of alpha dot where alpha dot stands for r dot times x s

and then we simplify the double differential equation and then we integrate it twice to get x s in terms of r dot. Now as x s must be bounded when r dot approaches 0, so therefore C 1 has to be chosen as 0.

And using the second boundary condition we can determine the value of C 2 as 1 by sin h 3 phi. So, if C 2 is 1 by sin h 3 phi your x s then becomes a function of r dot as shown in the equation 3.3.

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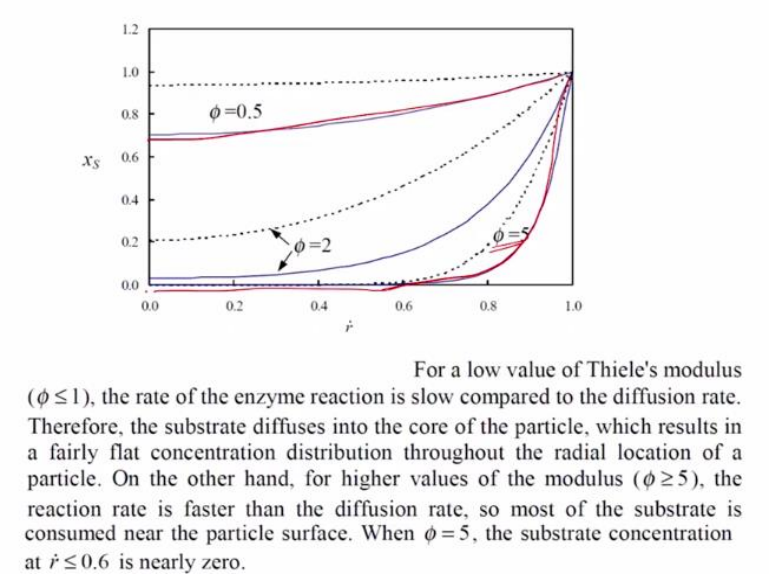

For a low value of Thiele's modulus ($\phi \leq 1$), the rate of the enzyme reaction is slow compared to the diffusion rate. Therefore, the substrate diffuses into the core of the particle, which results in a fairly flat concentration distribution throughout the radial location of a particle. On the 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.

So, if we make a plot between x s and r dot with varying value of Thiele's modulus, we can see how Thiele's modulus affects the substrate profile inside the pellet. So, if the Thiele's modulus is very low effectively meaning that the rate of enzymatic reaction is slow compared to the diffusion rate. Then the substrate would diffuse into the core of the particle which will result in fairly flat distribution as shown here by the blue line.

On the other hand, for higher values of modulus like let us take phi = 5 this would mean that the reaction rate is much faster than the diffusion rate. So, most of the substrate will get consumed in the reaction near the particle surface itself before it diffuses in and therefore you see a sharp decrease in the substrate profile as it moves inside.

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The actual reaction rate with the diffusion limitation would be equal to the rate of mass transfer at the surface of an immobilized enzyme, while the rate if not slowed down by pore diffusion is kC_{Sb}. Therefore,

$$\eta = \frac{\frac{A_P}{V_P} D_s \frac{C_{Sb}}{R} \left. \frac{dx_S}{d\dot{r}} \right|_{\dot{r}=1}}{kC_{Sb}} \qquad (3.31)$$

where A_p and V_p are the surface area and volume of an immobilized enzyme particle, respectively. Therefore, differentiating Eq. (3.30) with respect to $\dot{r}$ and substituting the resultant equation into Eq. (3.31) will yield

$$\eta = \frac{3\phi \coth 3\phi - 1}{3\phi^2} \qquad (3.32)$$

Now in order to find an expression for the efficiency factor in such a system, then efficiency factor if you remember it is the ratio of the actual reaction rate to the reaction rate without diffusional limitations. So, without diffusional limitation would mean that maximum mass transfer. So maximum mass transfer rate would be what? Will be k C sb because there is no diffusional limitation.

So, then whatever is at the surface should be able to reach to the inner core, so maximum rate would k Cs b. And the actual rate will be equal to the diffusional rate here at r dot =1. So we will be using the Fick's law of diffusion so for the entire pellet we will be calculating, so therefore the r dot value will be equal to 1. And we will multiply and divide the dC s by dr with C sb.

And r and then taking it in inside the differential function being a constant and converting it into a x s and r dot form. So, then outside we will have the C sb and r the diffusivity constant and your area of the particle and the volume of the particle. So, this would be your reaction rate. So, if we solve this, the expression for the efficiency factor comes in the form of Thiele's modulus.

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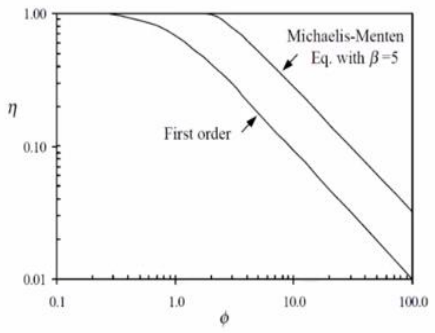

Figure 3.5 shows how Thiele's modulus affects the effectiveness factor for spherical immobilized particles. When $\phi \leq 1$, the effectiveness factor is nearly equal to one, which is the case when the rate of reaction is not slowed down by the diffusion. On the other hand, when $\phi \geq 1$, the effectiveness factor is inversely proportional to the Thiele's modulus.

And now if we try to visualize how Thiele's modulus can affect the efficiency of the immobilized system, then what we can find is that for different types of reaction kinetics. As the value of phi is less than 1, the effectiveness factor is nearly equal to 1 which is the case when the rate of reaction is not getting slowed by the diffusion process.

On the other hand, if the Thiele's modulus is becoming greater than 1, then the effectiveness factor is found to be inversely related to the Thiele's modulus. So as the Thiele's modulus will keep on getting increased the efficiency factor is going to go down.

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Michaelis-Menten Kinetics: If the rate of substrate consumption can be expressed by the Michaelis-Menten equation,

$$r_s = \frac{-r_{max} C_S}{K_M + C_S} \qquad (3.33)$$

By substituting Eq. (3.33) into Eq. (3.11) and changing it to dimensionless form, we obtain

$$\frac{d^2 x_S}{d\dot{r}^2} + \frac{2}{\dot{r}} \frac{dx_S}{d\dot{r}} - 9\phi^2 \frac{x_S}{1+\beta x_S} = 0 \qquad (3.34)$$

where β is C_{Sb}/K_M and Thiele's modulus (ϕ) is defined slightly differently from the first-order kinetics as

$$\phi = \frac{R}{3}\sqrt{\frac{r_{max}}{D_e K_M}} \qquad (3.35)$$

Eq. (3.34) cannot be solved analytically because it is a nonlinear differential equation. It can be solved by various numerical techniques. Again

Now if we take Michaelis-Menten enzyme kinetics or reaction kinetics in the enzyme system, we know that the reaction rate can be given as shown in equation 3.33 as Michaelis-Menten kinetics. So now substituting in place of the reaction rate here also furthers changing the C s

and the r in terms of the dimensionless variables x s and r dot, so we have Thiele's modulus and an extra constant called beta which is defined as C sb by K M, K M stands for the Michaelis-Menten constant.

So, if you do the rearrangement of the second-order differential equation and do all the substitutions bring all the constants together. then the Thiele's modulus in this case gets slightly changed in comparison to that with the first-order kinetics where now inside the square root you will find we have the Michaelis-Menten constant, the diffusivity and the maximum reaction rate.

Now this is a non-linear function in x s if you notice equation 3.34. It is a non-linear function in x s, so it cannot be solved analytically. So, we use various numerical techniques.

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$$\frac{dY}{d\dot{r}} = \frac{2}{\dot{r}}Y + 9\phi^2 \frac{x_S}{1+\beta x_S} = 0 \qquad (3.36)$$

$$\frac{dx_S}{d\dot{r}} = Y \qquad (3.37)$$

The boundary conditions for the preceding equations are

$$Y = 0 \quad \text{at } \dot{r} = \frac{R_C}{R}$$
$$x_S = 1 \quad \text{at } \dot{r} = 1 \qquad (3.38)$$

effectiveness factor when the reaction rate is expressed by the Michaelis-Menten equation can be calculated as

$$\eta = \frac{\frac{A_P}{V_P} D_S \frac{C_{Sb}}{R} \frac{dx_S}{d\dot{r}}\Big|_{\dot{r}=1}}{\frac{r_{max} C_{Sb}}{K_M + C_{Sb}}} \qquad (3.41)$$

And in order to simplify it, we again do a substitution converting dx s by dr dot as Y and then this is equation, the earlier equation 3.35 gets converted to a single differential equation form as shown in equation 3.36. And similarly, your boundary conditions can be changed in terms of Y with r dot where Y now becomes equal to 0 as x s was bounded. Let us assume that there is a critical radius r beyond which the substrate is not able to diffuse in, so it is bounded.

So, your r dot then in that case becomes R c which is the critical radius by the total radius of the pellet at the surface. And at xs = 1 which means at the surface where the substrate concentration is equal to the bulk concentration, this is happening at the surface. So, therefore

r dot value is 1. So, the boundary conditions remain the same it is just the change in the variables.

And in this case the effectiveness factor can be represented as the actual reaction rate and the reaction rate in the absence of any diffusional limitations. So, if there are no diffusional limitations the substrate which is available for reaction is your bulk substrate concentration. So, it has been substituted in the Michaelis-Menten equation for maximum reaction rate without diffusional limitations and the numerator is using Fick's law for the reaction rate.

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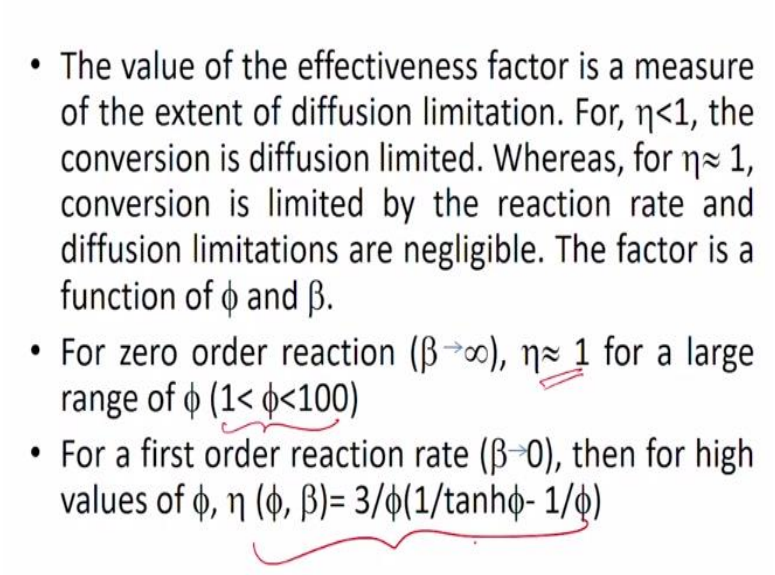

So as the value of the effectiveness factor is a measure of the extent of diffusional limitations let us see some cases. If the effectiveness factor is less than 1, this means that the conversion is diffusion limited. Whereas if effectiveness factor is nearly 1, this means the conversion is limited by the reaction rate and the diffusional limitations are negligible. And eta in turn is a factor of Thiele's modulus and the function beta in this case.

Now if we want to use this as a generalized equation and try to find the conditions for the zero order and the first-order reaction rate, so if you substitute the value of beta as very large value which means beta tending to infinity. So, beta was C sb by K M, is not it? And beta is very large which means the substrate is in x s, so it becomes a zero-order reaction. Then your efficiency factor is nearly equal to 1 for a wide range of Thiele's modulus.

Now if you remember to visualize this what was Thiele's modulus? The Thiele's modulus was maximum reaction rate to the diffusion rate. So, for a wide range of Thiele's modulus,

the reaction rate will be higher than the diffusional rate because the substrate is in x s, so your efficiency factor will be nearly equal to 1. And this range of phi is given as between 1 to 100**.** Now let us take the case for the first-order reaction rate.

So, for the first-order reaction rate beta tends to 0, so your beta was C sb by K M, so beta is tending to 0 here. For high values of phi, your eta can be given as a function of hyperbolic functions of phi and beta is a very small value.

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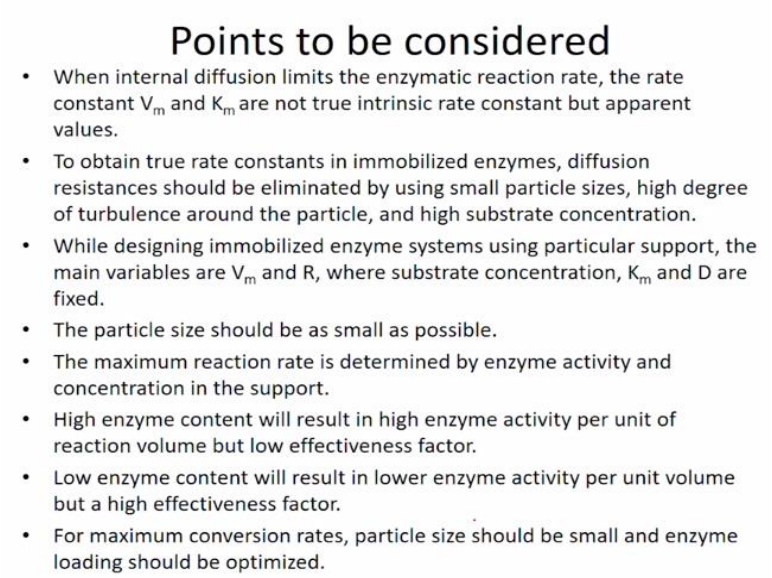

So now let us see how can we use all these information in a practical scenario? Now the points which we must keep in mind when we are designing immobilized systems for maximum efficiency because internal diffusion will limit the enzymatic reaction rate the constants V m and the K in such immobilized system they will not be the true intrinsic rate constants, but what we will measure through the experimental data would be the apparent values.

Now in order to obtain the true rate constants inside the immobilized systems, the diffusional limitations they should be eliminated by doing what all things? By using small particle size, having high degree of turbulence around the particles so that the boundary layers are reduced or having high substrate concentration. Now while designing immobilized enzyme systems using particular support, the main variables are the maximum reaction rate and the radius of the pellet.

Now maximum reaction rate would in turn be dependent on the concentration of the enzyme. Now when the substrate concentration K m which is the affinity of the enzyme towards the substrate and D stands for the diffusivity of the substrates., this we assume are fixed the given values because the substrate is given. So, the particle size is what which can be manipulated or designed and the second is the enzyme concentration which is being immobilized in the system.

So, the maximum reaction rate is determined by enzyme activity and the concentration inside the support. So high enzyme content will result in high enzyme activity per unit of the reaction volume. However, this will lead to low effectiveness factors because all the substrate will quickly get consumed near the surface, efficiency factor will reduce because whatever is present inside will be devoid of the substrate.

Whereas if there is low enzyme content it will result in lower enzyme activity per unit volume, however high efficiency factor. So, for maximum reaction rates what should one do? The particle size should be kept small and the enzyme loading should be optimized so that although the enzyme activity per unit volume is being optimized the size of the particle is being designed. So that all the substrate is able to reach and get converted with the enzymes present in the inner core.