Transport Phenomena in Biological Systems
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Lecture-11
Steady-state diffusion

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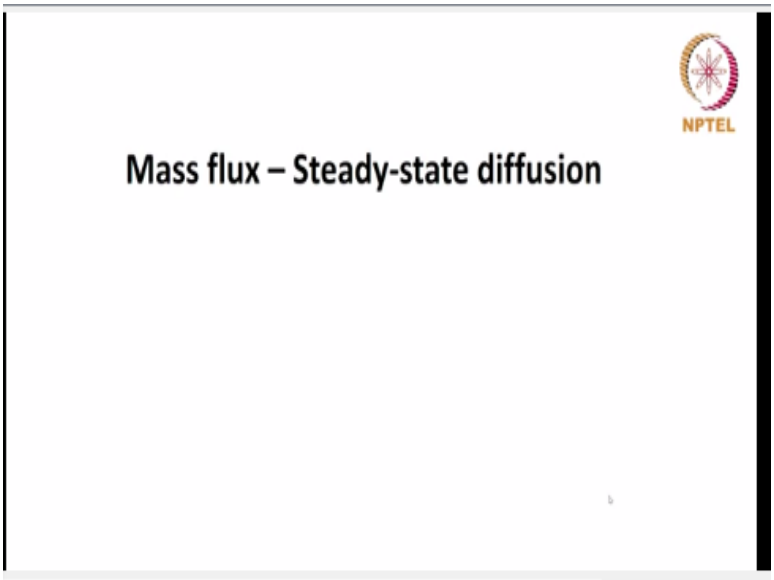

Welcome back today let us look at steady state diffusion, we are still in mass flux, we are in the middle of mass flux now, we look at steady state diffusion. The steady state diffusion aspect is so useful in many different situations of biological engineering interest. And that is the reason why we are looking at it separately.

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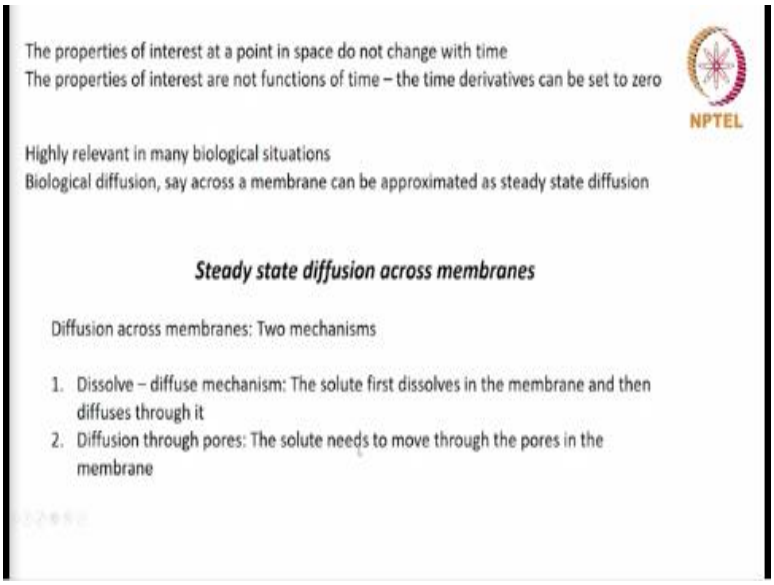

As you already know the properties of interest at a point in space do not change with time at steady state, that is the definition of steady state. And what it means is that the properties of interest are not functions of time, the time derivatives can be set to 0. It is highly relevant in many biological situations, biological diffusion, say across a membrane can easily be approximated as steady state diffusion in a wide variety of situations.

And that is what we are going to see here in this class in greater detail steady state diffusion across membranes. The diffusion across membranes can take place through 2 broad mechanisms. The first mechanism is called the dissolve diffuse mechanism, the species i first dissolves in the membrane and then diffuses through the membrane.

The second mechanism is diffusion through pores in the membrane there is no dissolution here, the species i just diffuses through the various pores in the membrane. The first case we are assuming that there are no pores in the membrane. The second case it is more realistic there could be pores or pores equivalent in the membranes. And this is the second mechanism, solute needs move through the pores in the membrane.

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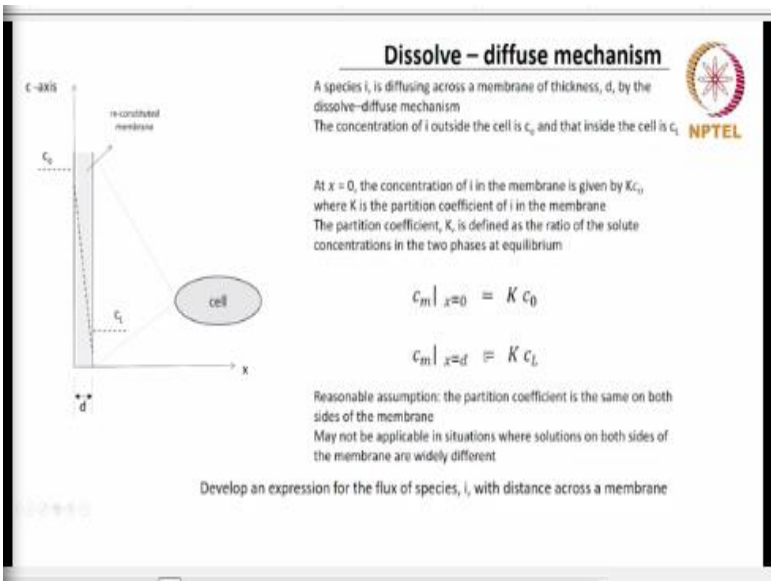

Let us look at dissolve diffuse mechanisms first and then I will give you some pointers to look at the diffusion through pores. Dissolve diffuse mechanism, to understand this let us say that we have a reconstituted membrane which does not have any proteins and so on just the lipid bilayer and that is what is indicated here. Consider the screenshot picture above. This is the x direction, we would look at one dimension first to understand it.

In other words if you have a cell like this and if you take a small part of the cell membrane even though it is curved it can be approximated to a straight membrane, that is what we have done here. We have blown up a small part of this here and considered as a straight membrane, you could do this.

And therefore, it can be approximated to a straight membrane, that straight membrane is placed here, re-consolidated membrane, this is the concentration axis, this is the distance axis. This is the thickness of the membrane d, from here this is the concentration c_0 in the liquid on this side of the membrane, this is a concentration of the species i in the liquid on the side of the membrane.

And there is a variation in the membrane concentrations here, we are going to look at this in some detail. Let us go through this again a species i is diffusing across the membrane of thickness d by the dissolve diffuse mechanism. The concentration of i outside the cell is c_0 and the concentration inside the cell is c_L of the species at $x = 0$.

The concentration of i in the membrane, remember the c_0 is a concentration in the extracellular space or outside the membrane. We are interested in the membrane; membrane is our system of interest. Therefore, we would like to know the concentrations on the membrane. At x = 0 the concentration of i in the membrane is given as some constant(K) times c_0. And the constant is nothing but the partition coefficient of i in the membrane. By definition, the partition coefficient is nothing but the ratio of the concentration of the species in the membrane divided by the concentration in the bulk at equilibrium, i.e. partition coefficient K is defined as the ratio of the solute concentrations in the 2 phases at equilibrium.

$$c_m|_{x=0} = Kc_0$$

$$c_m|_{x=d} = Kc_L$$

$\frac{K D_{i,\text{eff}}}{d}$ is defined as 'permeability' P of the solute i across the membrane.

Note that it is a product of the partition coefficient K and diffusivity $D_{i,\text{eff}}$. The dependence of permeability on both the above parameters indicates the dissolve (K)-diffuse ($D_{i,\text{eff}}$) mechanism. Nevertheless, permeability is not an intrinsic membrane property since it depends on the thickness of the membrane, d.

Also, note that

$$K = \frac{c_m|_{x=0}}{c_o}$$

and we have assumed that to be equal to

$$\frac{c_m|_{x=d}}{c_L}$$

If $K < 1$, $c_m|_{x=0} < c_o$ and $c_m|_{x=d} < c_L$.

So, c_m which is the concentration of i in the membrane at x = 0 is Kc_0, this is the way of converting this concentration into an equivalent to this concentration. And the concentration of i in the membrane at x = d which is here is Kc_L. And a reasonable assumption is that the partition coefficient is the same on both sides of the membrane. This usually holds in many cases when the liquids on both the sides are not very different.

If they are different of course the case would be different and you need to consider a different case. It is just a small extension you could always derive another equation for such a case, here we will consider both cases to be the same. This assumption may not be applicable in situations with the solutions on both sides of the membrane are widely different.

And our aim here should develop an expression for the flux of species i with the variation with distance across the membrane. As we develop an expression for the flux of species i with distance across the membrane. In other words we want to see how the flux changes with distance here, that is our interest. We want to gain insights into what is happening to the movement of the species i in the membrane.

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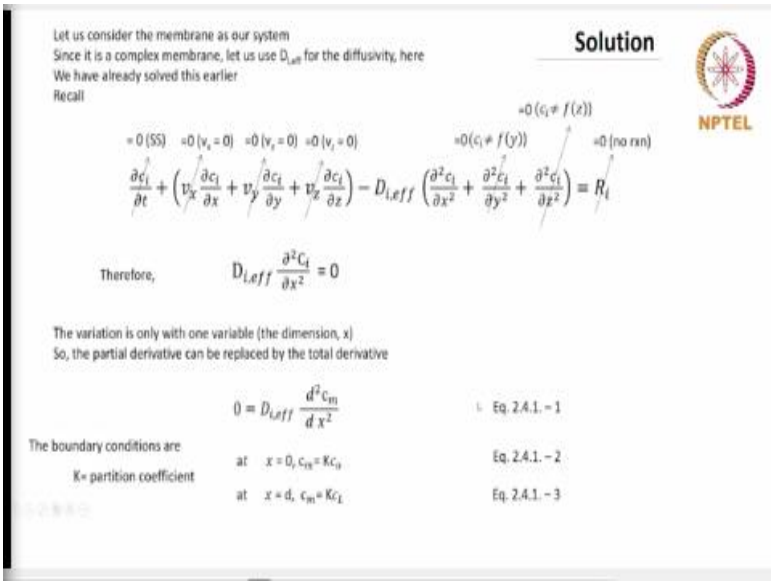

The solution is something like this we are going to use the conservation equation approach easier to use and there is no variation area, so that is fine. We are going to consider the membrane as a system therefore this is going to be our system. It is a complex membrane it could be a lipid bilayer membrane. Therefore, it uses $D_{i,eff}$ for the diffusivity D_i strictly speaking, as the diffusivity of species i in the multi component mixture.

$$\frac{\partial c_i}{\partial t} + \left(v_x \frac{\partial c_i}{\partial x} + v_y \frac{\partial c_i}{\partial y} + v_z \frac{\partial c_i}{\partial z}\right) - D_{i,eff}\left(\frac{\partial^2 c_i}{\partial x^2} + \frac{\partial^2 c_i}{\partial y^2} + \frac{\partial^2 c_i}{\partial z^2}\right) = R_i$$

For a binary system, it is defined as below.

$$\frac{\partial c_A}{\partial t} + \left(v_x \frac{\partial c_A}{\partial x} + v_y \frac{\partial c_A}{\partial y} + v_z \frac{\partial c_A}{\partial z} \right) - D_{AB} \left(\frac{\partial^2 c_A}{\partial x^2} + \frac{\partial^2 c_A}{\partial y^2} + \frac{\partial^2 c_A}{\partial z^2} \right) = R_A$$

$= 0$ (SS) $= 0$ ($v_x = 0$) $= 0$ ($v_y = 0$) $= 0$ ($v_z = 0$) $= 0$ ($c_A \neq f(y)$) $= 0$ ($c_A \neq f(z)$) $= 0$ (no *rxn*)

Hence

$$D_{AB} \frac{\partial^2 C_A}{\partial x^2} = 0$$

And therefore, there is huge $D_{i,eff}$ for the diffusivity and we have already solved this diffusivity of i through a membrane and it is nothing. To do this above equation, we cancelled out the irrelevant terms, this $\frac{\partial c_i}{\partial t}$ goes to 0 because of steady state conditions. There is no bulk velocity or momentum of liquid. And therefore v_x, v_y and v_z which are the velocities of the liquid go to 0. And here there is no variation in the y direction of concentration therefore this $\frac{\partial^2 c_i}{\partial y^2}$ gets to 0, here again there is no variation in the z direction therefore this $\frac{\partial^2 c_i}{\partial z^2}$ goes to 0 there is no reaction occurring, R_i is 0. And we got our final equation as $\mathbf{D_{i,eff}\frac{\partial^2 c_i}{\partial x^2} = 0}$ **, we already solved this. The variation is only in one dimension therefore one variable is good enough**.

And rather, we do not need the partial we can convert it into a total there is only one dimension here only a function of only one variable. Therefore the partial is converted to total easier to solve total differential equations compared to partial differential equations, you already know this, if not you can pick it up as a part of this course whatever is necessary, we are not doing a comprehensive math course here. But I am sure you have the basic calculus background otherwise this course is very difficult. This is mentioned in the prerequisites of the course itself, you need background in engineering mathematics to be able to do this course.

$$\mathbf{D_{i,eff}\frac{d^2 c_m}{dx^2} = 0} \qquad \text{2.4.1-1}$$

And you know that to solve any differential equation you need boundary conditions. This is the second order differential equations, so you need two boundary conditions with respect to space. Those at x = 0, the place where it enters the concentration in the membrane as Kc_0.

You need 2 concentrations of the species with respect to x, one we have x = 0, $c_m = Kc_0$. The other one we have at x = d, $c_m = Kc_L$, so those 2 become the boundary conditions. If we solve this equation differential equation subject to these boundary conditions.

The boundary conditions are:

At $$x = 0,\ c_m = Kc_o \qquad (2.4.1\text{-}2)$$

$$x = d,\ c_m = Kc_L \qquad (2.4.1\text{-}3)$$

where K is the partition coefficient defined as the ratio of the species concentration in the membrane to that in the bulk solution.

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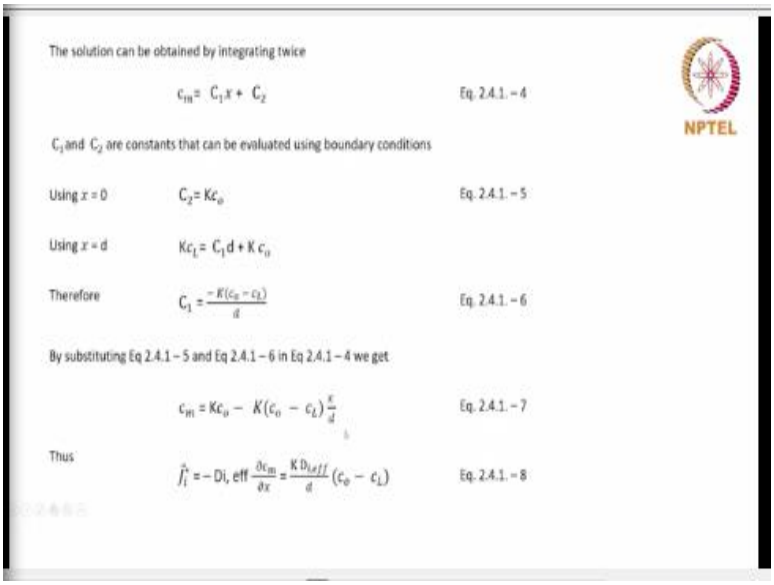

We just need to integrate it twice we get $\mathbf{C_m = C_1x + C_2}$. Here we have $\frac{d^2c_m}{dx^2} = 0$ which means $\frac{d}{dx}\frac{dc_m}{dx} = 0$. Therefore, $\frac{dc_m}{dx} = 0$ becomes a equation that you can solve, integrate it twice you get $c_m = C_1x + C_2$. C_1 and C_2 are the constants of integration. To find the constants of integration you need the boundary conditions.

If you substitute x = 0 you get $C_2 = C_m$ here at x = 0, C_m at x = 0 is Kc_0 therefore **$C_2 = Kc_0$**. Similarly using the other boundary condition you can get $Kc_L = C_1 d$ you are substituting x = d here, thus C_1 d added with C_2 (we have already know that C_2 is Kc_0) so you get this, $C_1 d + Kc_0$. And therefore, **C_1 becomes ($Kc_L - Kc_0$) divided by d** and that is written in this form here equation 2.4.1 - 6.

The solution obtained by integrating Eq. 2.4.1-1 twice with the realisation that the second derivative is zero, and hence, the first derivative is a constant is

$$c_m = C_1 x + C_2 \qquad (2.4.1\text{-}4)$$

where C_1 and C_2 are constants that can be evaluated using boundary conditions. At $x = 0$

$$C_2 = Kc_o \qquad (2.4.1\text{-}5)$$

At $x = d$

$$Kc_L = C_1 d + Kc_o$$

Therefore

$$C_1 = \frac{-K(c_o - c_L)}{d} \qquad (2.4.1\text{-}6)$$

Now, by substituting Eq. 2.4.1-5 and Eq. 2.4.1-6 in Eq. 2.4.1-4 we get

$$c_m = Kc_o - K(c_o - c_L)\frac{x}{d} \qquad (2.4.1\text{-}7)$$

So, we have C_2 and C_1, therefore we have solved the equation **$C_m = Kc_0 - k(c_0 - c_L)*(x/d)$.** So, we have a concentration profile of C in the membrane, C as a function of x(distance). Therefore the flux which is what we are looking at as a part of this problem is purely diffusive flux therefore $D_{i,eff} \frac{dc_m}{dx}$ we can get from this which turns out to be $(K/d)(c_0 - c_L) * D_{i,eff}$, this is your flux, that is equation 2.4.1 - 8.

Thus

$$\vec{J}_i^* = -D_{i,\text{eff}} \frac{\partial c_m}{\partial x} = \frac{K D_{i,\text{eff}}}{d}(c_o - c_L) \qquad (2.4.1\text{-}8)$$

So, what do we get here, **flux is a constant,** there is no variation with space(x) in the membrane of the flux, flux is a constant.

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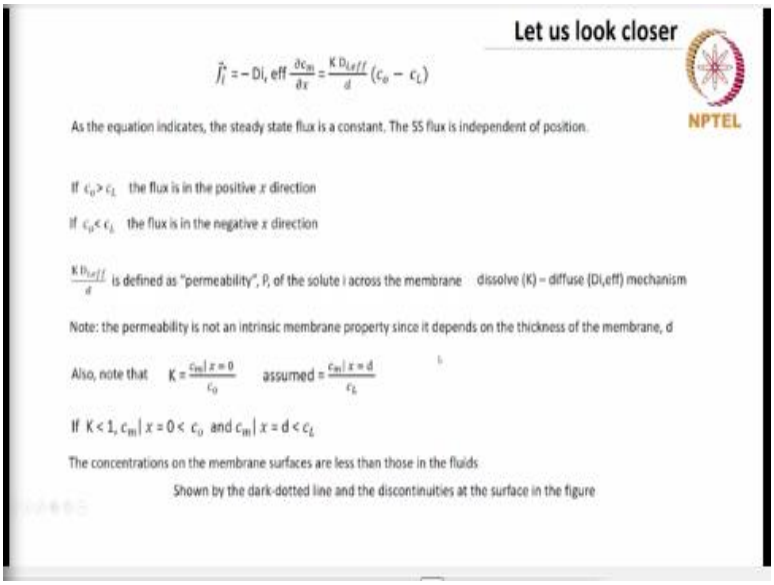

That is what we are going to see first when we look closer while doing an analysis. So, we need to draw some insights the flux is a constant across the membrane is a good insight. From here we got the equation that indicates the steady state flux is a constant there is no x term in the equation 2.4.1-8 **therefore the steady state flux is independent of position.** Also if c_0 is greater than c_L the flux is in the positive x direction as given by this expression here flux will be positive as long as c_0 is greater than c_L. If c_0 is less than c_L the flux will be the opposite direction, you get a negative of the flux which means the flux is in the opposite direction (flux is the vector). This group here K $D_{i,\text{eff}}$ by d is called or it is defined as the permeability of the membrane for the solute i in this case. So, permeability of the membrane to solute i, so it is K*($D_{i,\text{eff}}$ / d).

Since this is a steady state process, the flux is a constant, and as the equation indicates, it is independent of position.

If $c_o > c_L$ the flux is in the positive x direction.
If $c_o < c_L$ the flux is in the negative x direction.

See how nicely this is come about, K is nothing but the dissolution representation, $D_{i,eff}$ is nothing but the diffusivity representation. So, the dissolve diffuse mechanism comes about nicely in the way this is popping out. Also note that the permeability is dependent on the thickness of the membrane. And therefore it is not an intrinsic membrane property, if a membrane is thicker the permeability would be lesser. So, that is inversely proportional to the thickness, therefore it is not an intrinsic property. The permeability is a very useful property. Also note that this K, the partition coefficient is nothing but the concentration of i in the membrane at x = 0 divided by c_0. And we assumed that the constant, K is the same and therefore it can be equated to the other side also, the concentration in the membrane divided by c_L.

If K is less than 1 which can happen quite often the concentration in the membrane is at x = 0 is actually less than c_0, that is intuitive that is not against intuition. However, it also means that the concentration in the membrane on the other side at x = d is also less than the bulk concentration, that is counterintuitive when you do not think about it that way, right.

The concentrations on the membrane surfaces are less than that in the fluids, it is here intuitive, here it is actually not. And this is already shown to you but I did not point it out at that time. I had indicated at here in this figure(screenshot image 3), this is the concentration profile, the variation, the linear variation that we actually got, this is first indication and this could have been whatever.

Since I knew the answer I had indicated this, it is a linear variation. But here the point is here the concentration of C_m at x = 0 is less than c_0 which is fine. Here the concentration of C_m at x = d is actually less than c_L, this you kind of do not expect it is counterintuitive but it was actually true, this is the concentration axis right. So, there are these nice things that come out of analysis which

we looked closer and shown by the dark dotted line and the discontinuities at the surface in the figure as we just discussed.

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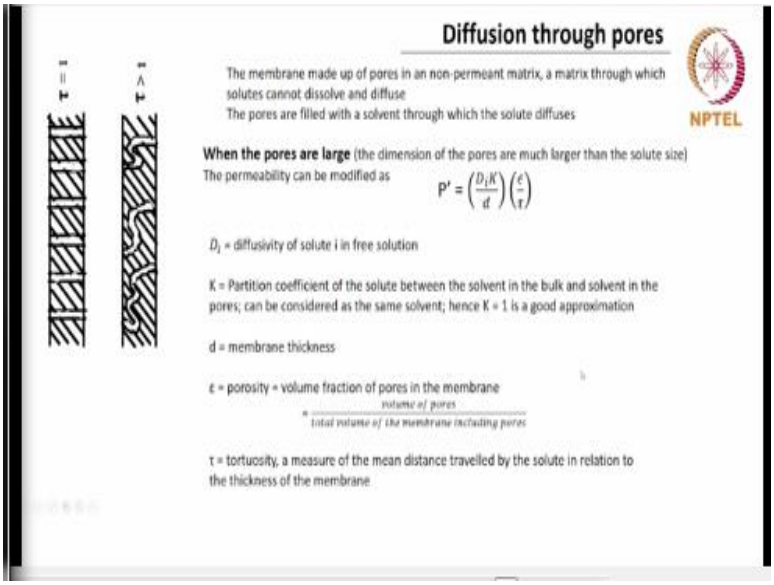

So, that is the dissolved diffuse mechanism. For the diffusion through pores, I am just going to point out to how to go about it. You can complete the information by looking at various books, the textbook. So, diffusion through pores for completeness, suppose this is the membrane you could have pores like this through which the solute diffuses and we are going to assume that it is not going to pass through the other parts of the membrane.

The pores could be straight if the pores are straight the tortuosity is supposed to be 1, the pores could be convoluted which means the tortuosity is greater than 1 tortuosity is nothing but the length of the pore divided by the thickness of the membrane. If it is straightforward then the length of the pore will be equal to the thickness of the membrane therefore the ratio is 1 tortuosity.

Here the length of the pore turns out to be greater than the thickness of the membrane therefore the tortuosity is greater than 1. So, to repeat the membrane is made up of pores in a non-permeant matrix, a matrix through which the solutes cannot dissolve and diffuse, the pores are filled with the solvent through which the solute diffuses when the pores are large. That is the first thing that

we are going to consider when the pores are large, dimension of the pores are much larger than the solute size, that is what we have mean.

The dimensions of the pores are much larger than the solute size and the permeability can be modified as this, this is good enough, P' becomes the D_i (K/ d) which is the actual permeability of the membrane. You just multiply it by something called an epsilon(ε) divided by the tortuosity(τ) you will be fine you will get the permeability of the membrane with pores to the species i this has been shown already**.**

For completeness Di is a diffusivity of solute, i in free solution, k is the partition coefficient, d is the membrane thickness, e**psilon (ε) is the porosity which is the volume fraction of pores in the membrane** i.e. volume of pores divided by the total volume of the membrane including pores. And **τ is the tortuosity, a measure of the mean distance travelled by the solute in relation to the thickness of the membrane**, this ratio is good enough.

So, this is fine for the situation when the pores are large, I have just mentioned it, I have not derived it, I am not going to derive it. I will give you a reference later where you can go and see how this turns out.

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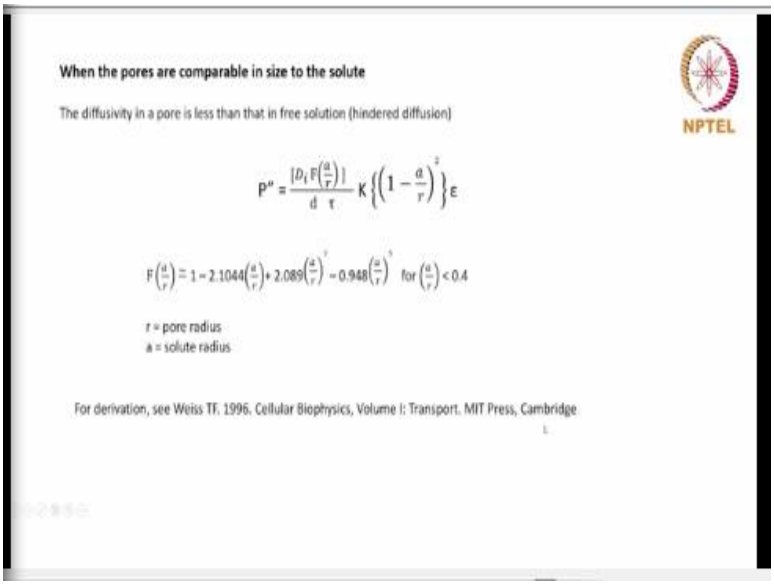

However, the more interesting situation is when the pores are comparable in size to that of the solute. Then the solute is not so free to move, so free to diffuse as in the case of a free solution. The diffusivity in a pore is less than that in free solution and this is called hindered diffusion. Here I am just going to give you the expression and I am going to give you a reference where this has been derived.

P" is the permeability of the membrane when the pores are comparable in size of the solute it is given as below. And the derivation of this is actually given in Weiss which is one of your reference books 1996 Cellular biophysics volume , Volume 1 transport. If you go to this book, you will get how this is derived. I do not want to derive this as a part of this course it is a little beyond what I envisioned as the scope of this course and therefore please go to this reference to get this.

$$\varepsilon = \text{Porosity} = \text{Volume fraction of pores in the membrane} = \frac{\text{Volume of pores}}{\text{Total volume of the membrane including pores}}$$

When the Pores are Comparable in Size to the Solute

When the pores become sufficiently small, the diffusivity in a pore is less than that in free solution. This process is sometimes referred to as hindered diffusion. We give the final expression for the modified permeability in such a case. The derivation can be found in other sources (e.g. Weiss 1996)

$$P'' = \frac{\left[D_i F\left(\frac{a}{r}\right)\right]}{d \quad \tau} K\left\{\left(1-\frac{a}{r}\right)^2\right\}\varepsilon$$

where $F\left(\frac{a}{r}\right) \simeq 1 - 2.1044\left(\frac{a}{r}\right) + 2.089\left(\frac{a}{r}\right)^3 - 0.948\left(\frac{a}{r}\right)^5$ for $\left(\frac{a}{r}\right) < 0.4$

r is pore radius and a is solute radius.

We will stop here, in this class we looked at the dissolve diffuse mechanism of diffusion of a species i through a membrane. And diffusion through pores of a species i through a membrane and got useful expressions for permeability. When we meet next we will continue the course further, see you in the next class.