Transport Phenomena in Biological Systems
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Lecture - 18
Pseudo Steady State Approximation - continued

Welcome back. In the previous class, we looked at the concept of pseudo steady state approximation and we said that it is going to help us reduce the mathematical complexity significantly .

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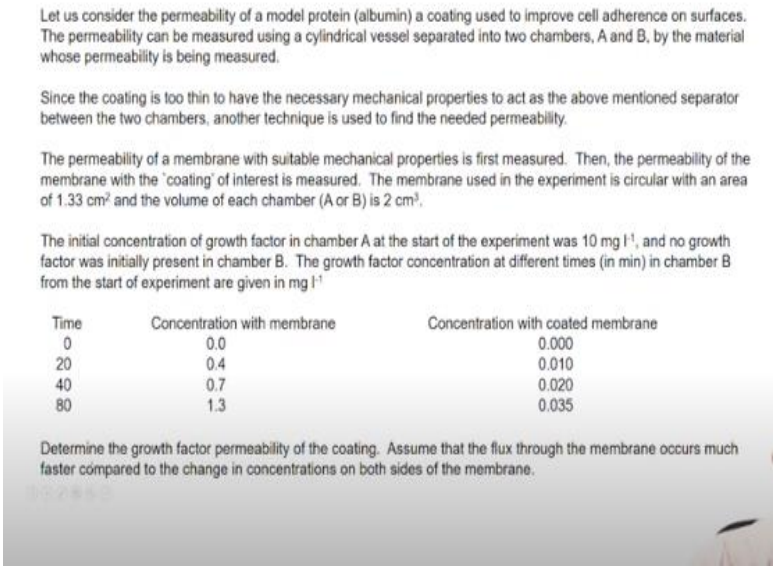

It would reduce the amount of effort that is needed in the mathematics especially brought on by the partial differential equation, the time variation and the space variation coming in. If we can avoid the effort we might as well . And this helps us avoid it. And I was going to illustrate better by using this particular problem, which is directly related to our kind of work.

Let me read it again for you for completeness. Let us consider the permeability of a model protein albumin through a coating used to improve the cell adherence on surfaces. The permeability can be measured using a cylindrical vessel separated into two chambers A and B, by the material whose permeability is being measured. Since the coating is too thin to have the necessary mechanical properties to act as the above mentioned separator between the two chambers, another technique is used to find the needed permeability. The permeability of the membrane with suitable mechanical

properties is first measured. Then the permeability of the membrane with the coating of interest is measured.

The membrane used in the experiment is circular with an area of 1.33 cm^2 and the volume of each chamber being 2 cm^3. The data for the concentration of the albumin, the model protein in B at various times from the start of the experiment is given here. And determine the growth factor permeability of the coating.

And you are also asked to assume that the flux through the membrane occurs much faster compared to the change in concentrations on both sides of the membrane. So, let us see how to go about doing this.

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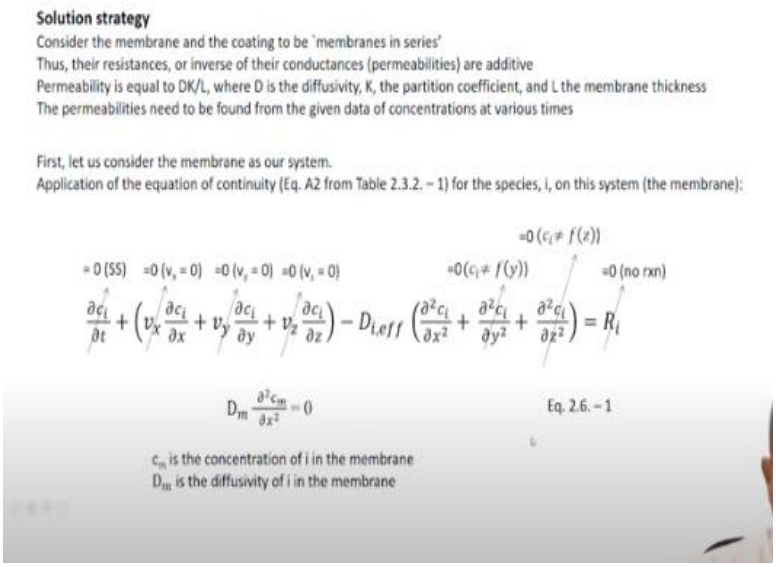

The solution strategy is going to be something like this. Consider the membrane and the coating to be membranes in series. You have first a membrane, and then you coat a thin layer on it. And it is quite easy to see from your experience, that these are membranes in series, their resistances are in series. Thus, the resistances are the inverse of their conductance.

The conductance is equivalent to the permeability right, you know that are additive. The inverse of the permeabilities are additive. The permeability as you have already seen when we did the initial steady state diffusion and so on so forth is the product of **diffusivity and the partition coefficient divided by the length of the membrane or the thickness of the membrane.**

And the permeabilities need to be found from the given data of concentrations in B at various times. Right, so this is what it is. To do this, first let us consider the membrane as a system. This is the framework and then we are still with the solution strategy. Let us consider the membrane as our system. If we apply the equation of continuity A2, c, D_{AB} are constants from 2.3.2-1.

Let us first consider the membrane as our system. Application of the equation of continuity (Eq. A2 from Table 2.3.2-1) for A on this system of interest (the membrane) yields

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

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

Thus, we get

$$D_m \frac{\partial^2 c_m}{\partial x^2} = 0 \qquad (2.6\text{-}1)$$

where the subscript m implies the membrane, c_m is the concentration of A in the membrane and D_m is the diffusivity of A in the membrane.

I hope you have it handy. Please take it and see what it is. We are going to apply this on the membrane. We have chosen the membrane as our system or the separator as our system. So this is the equation A2 from table 2.3.2-1 . And as usual, we are going to see which of the terms remain.

This goes out by the pseudo steady state assumption. It is the membrane that we are considering. Our interest is in the variation of the concentrations in the two solutions rate. And those concentrations vary much slower compared to the diffusion, which is already given in the problem. And therefore by pseudo steady state, we can try this to be zero.

Whether it is actually, whether it is actually at steady state or not, it does not matter. Also you know by now that there is since there is no convective motion of the fluid or there is no bulk fluid motion, the v_x, v_y, v_z which correspond to the fluid velocities are can be set to 0. Then this is a one dimensional case, we consider that as x and therefore,

the concentration does not depend on y. Therefore, that the derivative is 0. The concentration does not depend on z. The first derivative is 0 and therefore, the second derivative is 0. And of course, there is no reaction that is happening. So this is the equation that we get for the balance of the species i on the membrane, . This is a big blessing, right. We do not have the partial differential equation anymore.

Now since well coming from here, I am going to call $D_{i\ effective}$ as D_m the diffusivity through the membrane or species.

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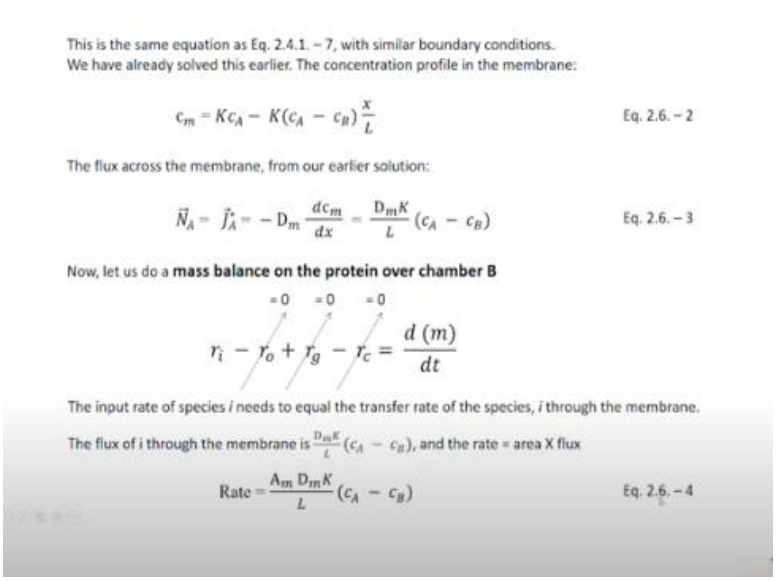

And of course, you know that since x is the only variable here you can write the partial differential equation as a total differential equation. So this equation is the same as equation 2.4.1-7 with very similar boundary conditions and we have already solved this earlier. You can go back and look at this thing. We considered this when we looked at the steady state diffusion through the membrane a few lectures ago.

We had earlier seen (Eq. 2.4.1-7) the solution of the above DE to be

$$c_m = Kc_A - K(c_A - c_B)\frac{x}{L} \qquad (2.6\text{-}2)$$

and the flux

$$\vec{N}_A = \vec{J}_A^* = -D_m \frac{dc_m}{dx} = \frac{D_m K}{L}(c_A - c_B) \qquad (2.6\text{-}3)$$

We already solved this, so I am not going to solve it earlier you go back and look. That will be good practice for you to solve it. The concentration profile in the membrane

would be c_m at any point x equals $Kc_A – K(c_A - c_B)$ (x/L), where x is the distance along the membrane from this side to this side. Equation 2.6-2.

The flux across the membrane also we had derived earlier was diffusive flux N_A equals j_A*. And that we can get from Fick's first law as shown above in 2.6-3.

Now let us do a mass balance on the protein over chamber B. This is the solution strategy. We are still in the solution. How do we actually get the permeability of the coating which does not have enough mechanical properties using the data that we have, which is the variation of the species in the chamber B. So let us do a mass balance on the protein over chamber B. How do you decide on this will come with various with practice.

You do more and more problems, then you will see this is going to come out of this and so on and so forth. There is no easy way of knowing this beforehand. But once you get into it, it is quite straightforward. It is not a big deal at all. So this is the standard material balance equation. There is no generation of B, generation of the species in chamber B. There is no output of the species from chamber B.

There is no consumption. There is only input through the membrane. And of course B accumulates in the chamber. The input rate of the species i into the chamber needs to be equal to the transfer rate of the species through the membrane because that is the only route inside.

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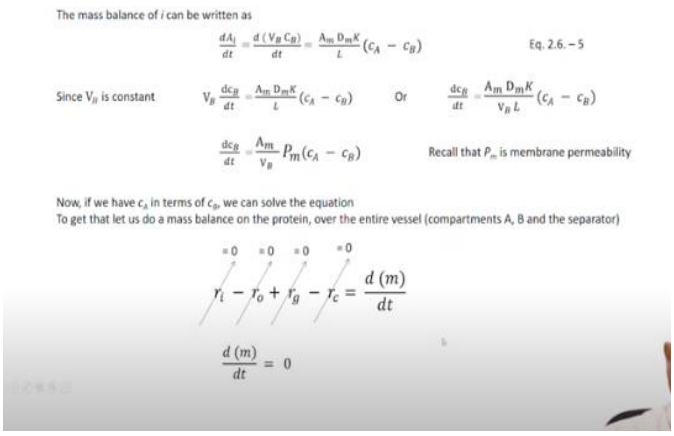

The mass balance of i can be written as

$\frac{dA_i}{dt} = \frac{d(V_B C_B)}{dt} = \frac{A_m D_m K}{L}(C_A - C_B)$ Equation 2.6-5.

Now since V_B is a constant okay here, you can take it out of the derivative.

$\frac{dA_i}{dt} = V_B \frac{d(C_B)}{dt} = \frac{A_m D_m K}{L}(C_A - C_B)$

Take V_B to the other side,

$\frac{d(C_B)}{dt} = \frac{A_m D_m K}{V_B L}(C_A - C_B)$

You realize that (D_m K /L) is nothing but the permeability of the membrane. Therefore, the right hand side of this becomes

$\frac{d(C_B)}{dt} = \frac{A_m P_m}{V_B}(C_A - C_B)$

Now if we have c_A, the other concentration of the other chamber in terms of c_B, we can solve this equation. Here we have c_A and c_B two variables. You know as c_B changes, c_A needs to change. It is a material in chamber A that is moving to B. So the concentration in A would change, it will reduce. So we have two variables here. If we can find the relationship between these two variables, we have solved this particular equation.

So to do that, let us do a mass balance on the protein over the entire vessel containing A, B and the membrane. So the compartments A, B and the separator, which is the membrane with or without the coating. So this is the material balance expression, this entire vessel by the way. And therefore, you get there is no input, there is no output, there is no generation, there is no consumption.

And the accumulation over the entire thing has to be equal to zero. That is the relationship that we get. Kind of an intuitive relationship. But this is a formal way of doing it so that we are absolutely clear. And we have it in the mathematical form that would become useful for the solution. When each compartment and the membrane are explicitly expressed, this is where the usefulness comes. . See this is mass rate of change in the chamber A. This is the mass rate of change of the species in chamber B.

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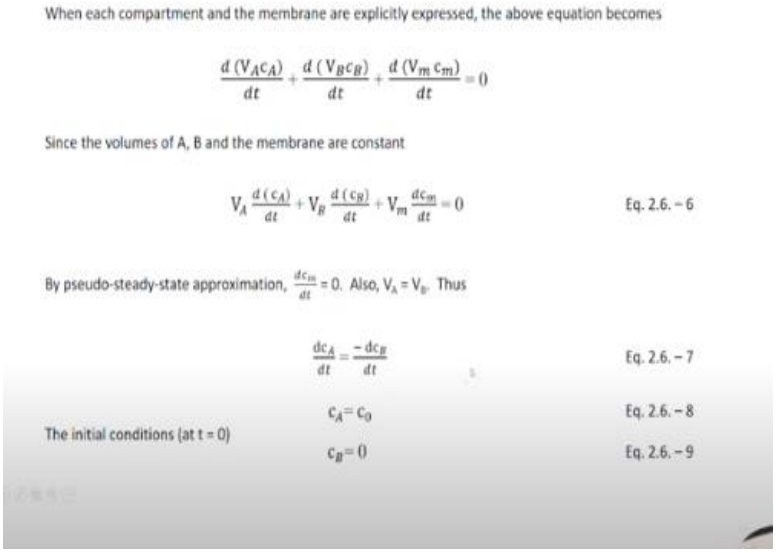

When each compartment and the membrane are explicitly expressed, the above equation becomes

$$\frac{d(V_A c_A)}{dt} + \frac{d(V_B c_B)}{dt} + \frac{d(V_m c_m)}{dt} = 0$$

Since the volumes of A, B and the membrane are constant

$$V_A \frac{d(c_A)}{dt} + V_B \frac{d(c_B)}{dt} + V_m \frac{dc_m}{dt} = 0 \qquad \text{Eq. 2.6.-6}$$

By pseudo-steady-state approximation, $\frac{dc_m}{dt} = 0$. Also, $V_A = V_B$. Thus

$$\frac{dc_A}{dt} = \frac{-dc_B}{dt} \qquad \text{Eq. 2.6.-7}$$

The initial conditions (at t = 0)

$$c_A = c_0 \qquad \text{Eq. 2.6.-8}$$

$$c_B = 0 \qquad \text{Eq. 2.6.-9}$$

This is the mass rate of change of species in the membrane. All those three put together must equal 0. The volumes V_A and V_B are constant as well as the membrane are constant. Therefore they can be taken out of the derivative.

Since the volumes are constant

$$V_A \frac{d(c_A)}{dt} + V_B \frac{d(c_B)}{dt} + \frac{V_m}{K} \frac{dc_m}{dt} = 0 \qquad (2.6\text{-}6)$$

Now we have a beautiful pseudo steady state approximation PSSA and by that the $\frac{dc_m}{dt}$ is 0 and it is at steady state. The concentration at any point in the membrane cannot change with time. Therefore, that is 0. And also we know that both A and B have equal volumes. So $V_A = V_B$. And therefore this equation becomes this thing goes away.

By pseudo steady state approximation, $\frac{dc_m}{dt} = 0$. Also, we know that $V_A = V_B$. Thus

$$\frac{dc_A}{dt} = \frac{-dc_B}{dt} \qquad (2.6\text{-}7)$$

Using the initial conditions (at $t = 0$)

$$c_A = c_o \qquad (2.6\text{-}8)$$

$$c_B = 0 \qquad (2.6\text{-}9)$$

V_A and V_B get cancelled out because they are equal. This is what happens at t equals 0.

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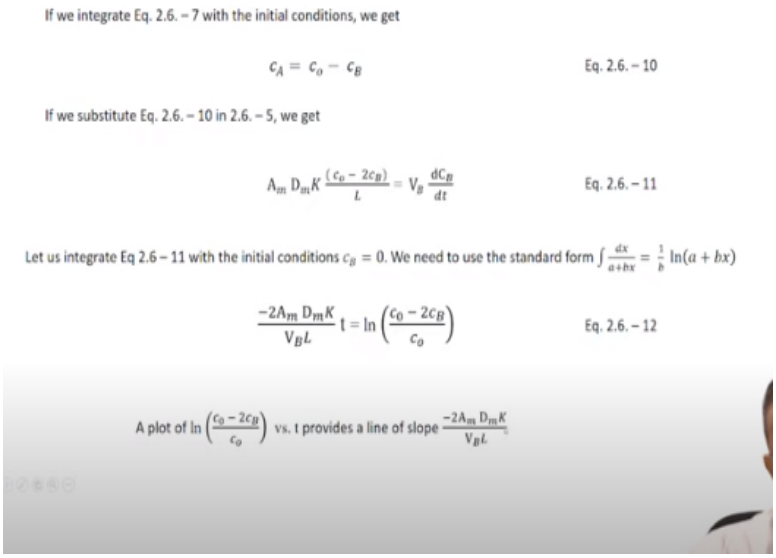

So now if we use this and integrate the differential equation 2.6-7 with the initial conditions given at t = 0(2.6-8,2.6-9), we get we will get $\mathbf{c_A = c_0 - c_B}$. Straightforward, I will let you solve that. That is a very straightforward thing. It is good practice for you. We will call this equation 2.6-10.

$\mathbf{c_A = c_0 - c_B}$ **2.6-10**

If we substitute this in equation in 2.6-5. What is 2.6-5? It is this , this written in terms of permeability and so on so forth. We can consider this is 2.6-5. Yeah, this is what it is. $c_A = c_0 - c_B$. Therefore, we will have this in terms of **the only variable c_B** and so you can solve it.

$$\frac{A_m D_m K}{L}(C_0 - C_B - C_B) = V_B \frac{d(C_B)}{dt}$$

$$\mathbf{\frac{A_m D_m K}{L}(C_0 - 2C_B) = V_B \frac{d(C_B)}{dt}} \qquad \mathbf{2.6\text{-}11}$$

Now if we integrate 2.6-11 with the initial conditions $c_B = 0$ to final condition $c_{B=} c_B$ and time =0 to t, then we could get the solution and for integration note that this equation is of the standard form , $\int \frac{dx}{a+bx} = \frac{1}{b}\ln(a + bx)$

$$\mathbf{\frac{A_m D_m K}{L}(C_0 - 2C_B) = V_B \frac{d(C_B)}{dt}}$$

Rearranging, $\frac{A_m D_m K dt}{L V_B} = \frac{d(C_B)}{(C_0 - 2C_B)}$

Solution after integration : $-2\ \frac{A_m D_m K}{L V_B} t = \ln(\frac{C_0 - 2C_B}{c_0})$ **2.6-12**

This you know from standard mathematical tables, integral tables. This is what comes about. One, you could probably write down the steps and check. We will call the solution as 2.6-12, . Now look at this form, . What do we have? We have concentration variation in c_B as function of time . So that is what we have here. We have c_B and t .

So this is of the form that we can directly manipulate with the given data to get the permeability (D_m K/L) . So that is what we have come down to. So let me show this and then just quickly the view. So a plot of y = mx + c can be related to equation 2.6-12 . Here y = $\ln(\frac{C_0 - 2C_B}{c_0})$, m= $-2\ \frac{A_m D_m K}{L V_B}$, x = t . Thus a plot $\ln(\frac{C_0 - 2C_B}{c_0})$ of vs t gives a slope of $-2\ \frac{A_m D_m K}{L V_B}$.

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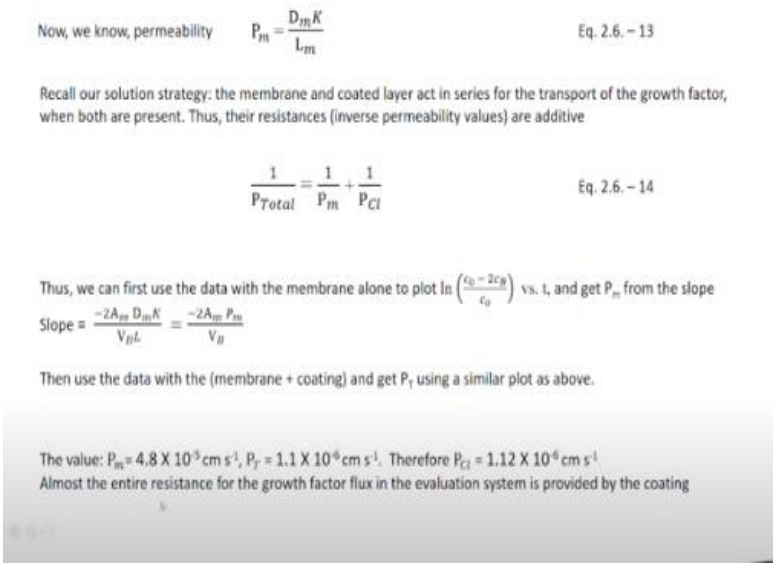

Now, recall that the permeability P is defined as (Section 2.4.1) $\frac{DK}{L}$. Thus

$$P_m = \frac{D_m K}{L_m} \tag{2.6-13}$$

and let us say that P_{cl} is permeability of the coated layer. Since the membrane and coated layer act in series for the transport of the growth factor, when both are present, their resistances (inverse permeability values) are additive

$$\frac{1}{P_{\text{Total}}} = \frac{1}{P_m} + \frac{1}{P_{cl}} \tag{2.6-14}$$

And we are interested in the permeability of the coating layer P_{cl}. And therefore, if we use the first set of data with the membrane alone and plot $\ln(\frac{C_0 - 2C_B}{c_0})$ versus t from the slope we will get P_m through the relation, $-2\ \frac{A_m D_m K}{L V_B} = -2\ \frac{A_m P_m}{V_B}$. And then when we use the data with the membrane plus coating, we would get P_{Total} through $-2\ \frac{A_T P_T}{V_B}$. And from these two, we can get P of the coating layer, $P_{cl,}$ (2.6-14).

The value: $P_m = 4.8 \times 10^{-5}$ cm s^{-1}, $P_T = 1.1 \times 10^{-6}$ cm s^{-1}. Therefore $P_{cl} = 1.12 \times 10^{-6}$ cm s^{-1}. (Almost the entire resistance for the growth factor flux in the evaluation system is provided by the coating).

So this is the strategy here. Let me quickly tell you what we did on an overall basis. We just used material balances and so on so forth in a fashion that will give us a solution. We had first considered the membrane as a system, wrote the balance, the equation of continuity and got some useful expressions for what happens in the membrane. And then we did a mass balance on the protein over the chamber B alone.

And then we did a balance on the overall chamber that was yeah overall chamber and we got useful expressions for our particular situation. And we found that if we plot $\ln(\frac{C_0 - 2C_B}{c_0})$ vs t, this will give us the slope which contains the permeability and therefore, we can back out the permeability from this. And by using the two sets of data separately, we would first get the permeability of the membrane from the slope of the line that we just mentioned.

And then the second set of data would give us P total, P_T. And from those two data values, we could get the slope values and therefore the permeability values, we can back out the coating layer permeability. Why do you not stop here, go through the solution, use a spreadsheet or a graph sheet or something like that. Do this problem, .

Actually work out the various numbers, their plot and get the slopes and that would be a very good learning. I have given you the solution because it is not very straightforward. And therefore I thought I would give you the entire solution. But let me, I will ask you to stop the video here. Go back and do that whatever time it takes. It might take half an hour, one hour whatever it is. And then come back and check your values.

Please go ahead and do that. Only if you do that, will you really learn. Otherwise it is just looking through a set of video, the learning through the set of lectures, the learning will not be appropriate. Learning is what you give yourself . This is just information to guide you, into you learning for your own. The learning is always done by you. I can only show you the way.

Go ahead to please pause, hopefully you did that. You could check your values. The permeability of the membrane, hopefully around this should be fine. There would be slight variation in your graphs and so on so forth. That does not matter. P_m is $4.8*10^{-5}$ cm/s. The total permeability is $1.1*10^{-6}$ cm/s. And therefore, the permeability of the coating layer is $1.12 *10^{-6}$ cm/s. Almost the entire resistance for the growth factor flux in the evaluation system is provided by the coating. Why because the total permeability is 10^{-6}. The membrane permeability it allows everything to pass through 10^{-5} an order of magnitude less almost half an order of magnitude less.

And the coating layer is 10^{-6}. Therefore, this is the one that is providing the biggest resistance or less transport in this case. And the entire resistance to the growth factor flux is residing in the coating layer, that is it for this class. When we begin in the next class I will summarize what we have done in this chapter. That completes the chapter on mass flux.
I will summarize what we have done in this chapter and then move on. See you then.