Mathematical Modelling and Stimulation of Chemical Engineering Process
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Lecture 23
Modelling transport phenomena problems - part 3

Hello everyone, in this class we are going to learn about a very sophisticated process, I mean it is a biomedical process (of course) known as extra corporeal membrane oxygenation. So, this process actually involves, I mean is actually done to critically ill patients who has almost very low levels of oxygen saturation or his or her lungs is not able to properly deoxygenate the blood as well as the alveolus, etcetera, the functioning of the lungs is severely damaged and as a result oxygen saturation is below the critical levels.

And these systems have become quite popular in the current area of this Covid 19 pandemic when we have several respiratory distresses happening due to this infection in the lungs and becomes very fatal.

So, extra corporeal membrane oxygenation is a very important, one of the very critical and a life saving critical equipment I would say in this way, where it operates or it acts as an artificial lungs to the patient and in the process it can be used to temporarily have a life support system till the normal lungs is either repaired or exchanged by some means or it is transplanted. So, this extra corporeal membrane oxygenator is a device that can help in oxygenation of the blood outside the human body.

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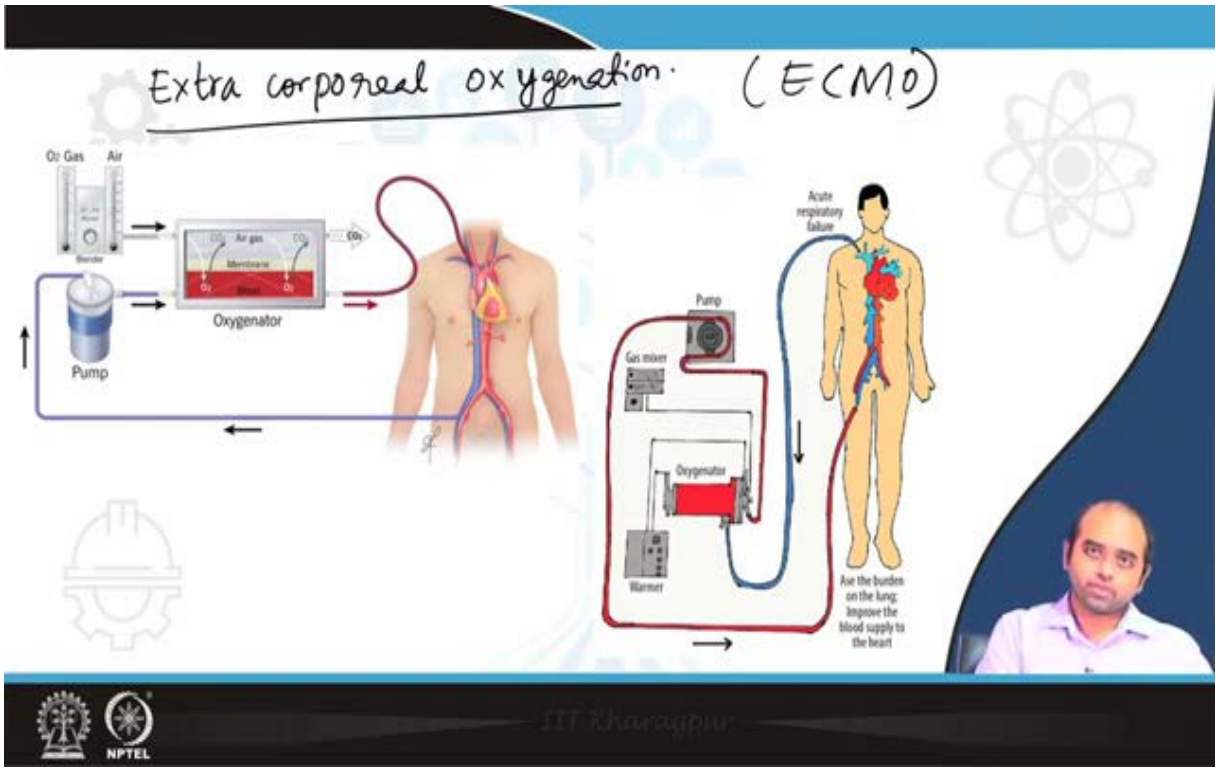

So, let me just give you an idea on the picture of the process. So, this extra corporeal oxygenation is a device which takes blood from the body and then it tries to oxygenate as well as deoxygenate the blood in external unit. Now, of course this functioning of the external oxygenator unit is very important and as you can realize this is a highly sophisticated mass transfer operation where oxygen tries to diffuse through the membrane layer of the oxygenator.

We talk about the details about the oxygenator essentially and in the process the oxygen gets diffused into the blood and the blood oxygenation level is increased. So, apart from the oxygenators this typical device also contains almost 50 to 60 different sensors, heat exchangers, pumps, bubble trap eliminators, a lot of different other things which makes it very complicated operation.

But the heart of this entire extra corporeal oxygenator and also known as ECMO very popularly in the medical world community, this process, I mean heart of this unit is the membrane based oxygenator. So, what happens in the membrane oxygenator is that it contains a series of hollow fiber membranes or you can consider them to be there is oxygen transfer across this membrane barrier.

So, membrane is a porous layer which allows selective diffusion of the oxygen into the bloodstream and of course blood molecules or the platelets, haemoglobin and all those things

does not come out through this membrane. So, the membrane is porous to the air but imporous or impervious to the blood.

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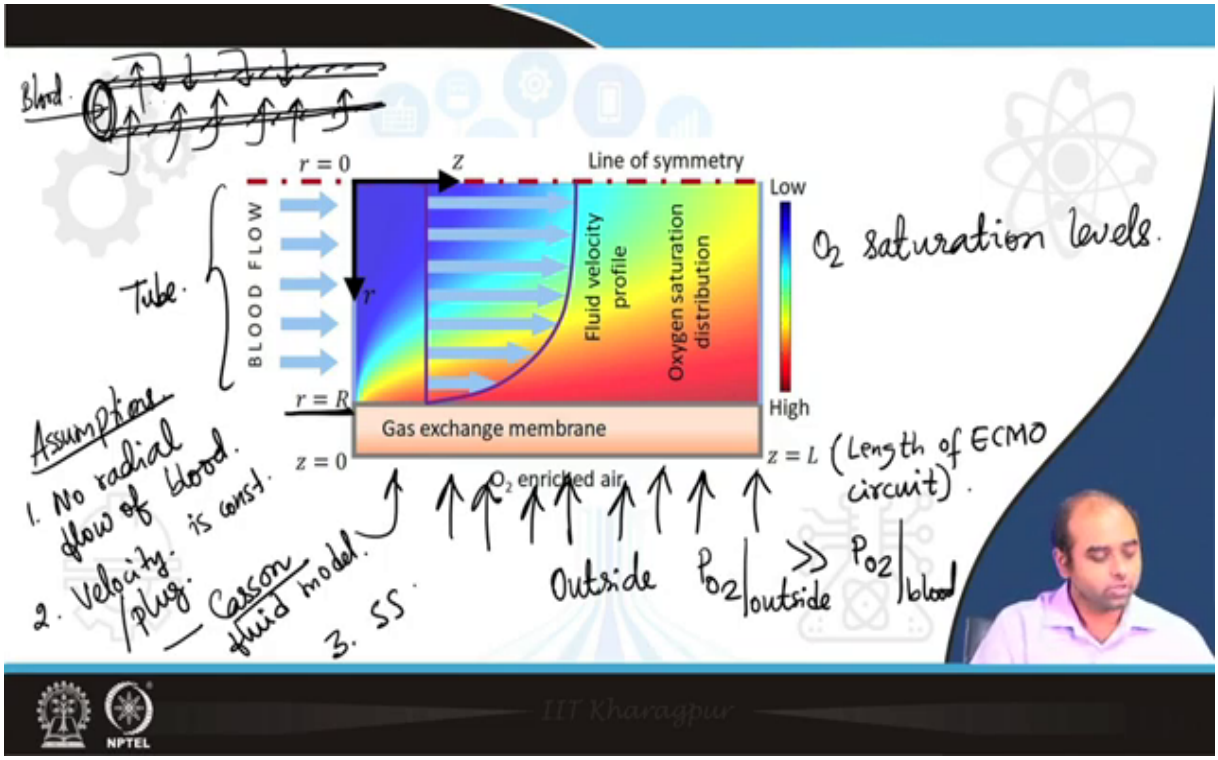

So, let us you can think of this to be a blood so this is like a blood capillary you can think of so these hollow fibers are essentially like fibers where it is hollow and the wall of these fibers is essentially the membrane. And as oxygen, oxygen can flow inside these hollow fibers and the or the blood can also flow inside the fibers.

So, if the oxygen flow inside the fibers there is radial outward diffusion of the oxygen because the oxygen partial pressure in the hollow fibers is higher than in the blood. So, if oxygen is flowing inside the tubes then and blood is outside then it is trying to diffuse outward.

If blood is flowing inside the tube, then oxygen is trying to diffuse from the outside to the inside, both of these are possible configurations and each of them has their own advantage and disadvantages of course, this mode of operation. But you can also have the blood to flow inside of the tubes and oxygen can flow from the outside.

So, you can think of this to be a shell and tube exchanger arrangement where on the tube side you are having the blood flow and on the shell side you are having the oxygen flow. Now, the oxygen partial pressure on the shell side is much higher compared to the oxygen's pressure or

the partial pressure of oxygen in the blood and you can relate them, you can calculate the partial pressure from the Henry's equation of course and you find them to be quite low.

So, there will be a positive diffusion from the shell side to the tube side and in this case the tube walls are porous to the membrane, to the gas. So, this tube or these hollow fibers are essentially a gas exchange membrane. So, let us consider this scenario in this case as you can see let us say this is the part of the tube, the dotted line represents line of the symmetry or the center line, and there is a gas diffusion from the outside of this O2 enriched air we are trying to push in, these are generally not air but high concentration or concentrated, O2 concentrated air in fact.

So, the outside air of course has a partial pressure so P O2 on the outside is much much higher than the partial pressure of O2 in the blood stream, then only this diffusion will happen faster. So, this is consider this to be the tube side, the tube radius is capital R and let us say the this length of the oxygenator or the extra corporeal circuit where the gas diffusion takes place to be of length L, so this is the length of the ECMO circuit where gas diffusion takes place.

And you can clearly understand, so if the gas is diffusing from the outside there will be a high concentration of the gas at the surface of this membrane, so that is what it is marked as red, so red is like more oxygenated blood and blue is like low oxygen levels are very low, so this color codes represent the oxygen O2 saturation levels in the blood.

So, there will be a gradient of the oxygen concentration profile inside the blood. Of course, fluid flow inside the blood also plays a very important role in this case and you can couple of things can be understood very intuitively, one is that if the length of the tube is more then of course the oxygen saturation will be more because of two reasons, one is that the residence time of the blood will be more and second is that the growth of the evolution of the oxygen this saturation will also improve with the axial distance.

But there is one drawback is that if the length of the tube is more, the hold-up volume in the extra corporeal circuit will be more, so there is a limit up to which a certain fraction of the body volume or the blood volume in the body can only be passed on to the external circuit, otherwise there will be heavy haemorrhage to the physiology of the system and can potentially lead to very fatal conditions.

So, there is a limit on how much of the blood can be taken out from a person's body, so the hold-up volume or the residual volume in the oxygenator circuit cannot be too high, so we cannot increase the length as long as we want to improve the oxygen saturation. And the partial pressure of course can be increased but there has to be a limit again otherwise it will have issues on the mechanical strength of these hollow fibers.

The flow rate, we can have a very low flow rate. So, if you reduce the flow rate of course you can realize there will be more time for the oxygenation but again too low of flow rate can lead to coagulation instances so that is something that needs to be taken into account or taken into consideration.

So, there are some medical limitations and based on which the idea of the mass transfer in perfect designing of these systems or operation of these systems becomes very very crucial. Now, if you try to model this mass transport process or the oxygen concentration profile inside the tube we are going to need to write down some mathematical equations and before forming any model writing down the assumptions is very crucial.

So, for this case let us say we make an assumption that the blood flow, so there is no radial flow of blood, so whatever we see is only axial flow of blood. And of course that is true because blood does not, for the blood the membrane acts as a no slip and impervious boundary condition. And let us assume that the velocity is constant or plug type of course the velocity of the blood can be modelled I mean using a non newtonian rheological model known as the Casson fluid, so, and of course the, we will talk about the Casson fluid. And the third boundary condition is steady state, we are considering a steady state phenomena for this problem.

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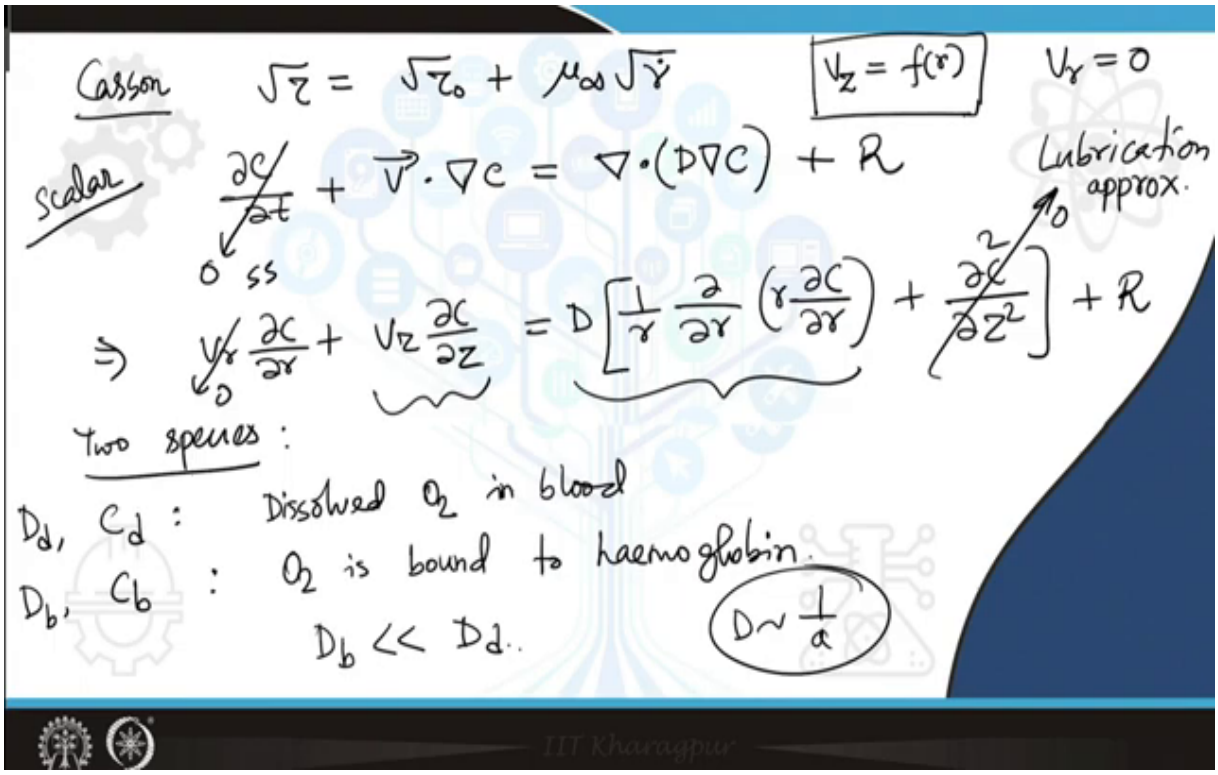

So, what about the Casson fluid model, I mean this is a very popular rheological model generally used for modelling of blood, so tau represents the shear stress and gamma dot represent the shear rate and mu infinity and tau naught are the two constants for this problem. So, let us try to write down the general species balance, so this is the Casson fluid model, for simplicity we can consider that flow rate is constant, of course the flow profile, velocity profile VZ in this case will be a function of r, we can consider it to be fully developed so VZ will not be a function of Z, but it will be a function of r.

And to get an idea and how does it vary with r you need to solve out the Casson fluid model to get an idea about how does this flow, how does u or this velocity in the axial direction plays a role. Vr is of course equal to 0 because there is no radial flow. So, writing down the scalar transport equation the general scalar transport equation is del C del t plus V dot grad C is equal to this the diffusive part or the diffusive flux part. So, this is the general scalar transport model of course if you have any chemical reaction to the problem.

Now, in this case if you expand, of course this will be 0 because it is a steady state problem. So, if you expand you will be having Vr del C del r plus VZ del C del Z Vr is equal to 0 and on the right hand side we consider diffusivity to this oxygen to be constant, it will look something like this, there will be two parts, so this is a cylindrical problem so we write the this cylindrical coordinate system in the r direction and this is the Z direction part.

So, these fibers have generally very small aspect ratio, so based on the lubrication approximation we can easily write this part to be 0. Of course, you can non dimensionalize the entire system based on the lubrication approximation, and then set the aspect ratio to be very small quantity and that part can be ignored out.

So, whatever we get here in this part is primarily of this, if we consider there is no reaction then it is only these two parts, but please remember there is some reaction which takes place in this system which leads to the formation of the oxygen haemoglobin complex. So, this oxygen actually binds to the haemoglobin and forms the oxygen oxyhaemoglobin complex.

So, in general in the case of oxygenation to the blood the oxygen is generally present in two forms. So, of course one of the forms is the dissolved state, so the dissolved oxygen in the blood, so let us call that I mean the concentration of this one let us call the Cd. But there is also oxygen (oxygen) present which is bound to haemoglobin by this hill reaction or a chemical reaction.

So, we write down the concentration of this species that is O2 bound to the haemoglobin as Cb and the dissolved oxygen is Cd. Similarly, diffusivity can also be written down as Dd, so there are two species, these are two distinct species, one is, and both of these cases you have the O2 but one is the free O2 present in the blood in the dissolved state, another is the bound O2 to the haemoglobin which is the oxyhaemoglobin complex.

So, since diffusivity is proportional, diffusivity is proportional to the size of the molecule, the diffusivity of the dissolved or the free O2 in the blood is much higher compared to the diffusivity of this oxyhaemoglobin complex because haemoglobin itself is a big molecule. So, the diffusivity of this oxyhaemoglobin complex is much smaller compared to the diffusivity of the dissolved oxygen. So, you can realize that we will be having two species balance equation, one for the case of the dissolved O2, one for the case of the bound O2.

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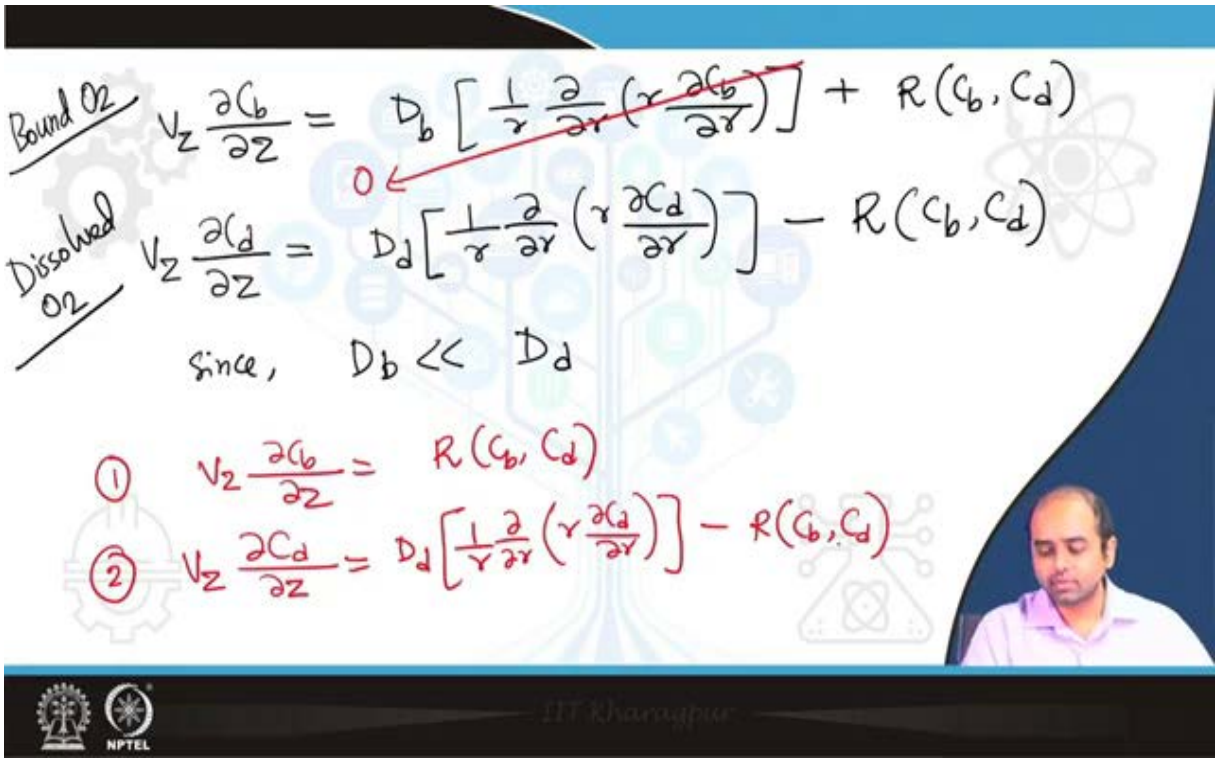

So, this is let us write the bound O2, this is V Z, so this is bound O2 and there is chemical reaction between this bound O2 I mean which depends on the concentration of the bound O2 and the oxyhaemoglobin complex or the dissolved O2, the dissolved oxygen and the bound oxygen. So, this is the part for the bound O2 or forming the oxyhaemoglobin complex.

And similarly, we have the same equation for the dissolved oxygen. So, please note the diffusivities. And in this case, the reaction is minus because as more and more reaction happens from the free oxygen or the dissolved oxygen to the oxyhaemoglobin formation, the free oxygen or this dissolved oxygen decreases.

So, that is the reason why the reaction is written as minus in the second equation and plus in the first equation because as more of this reaction happens the oxygen concentration in the bound state increases or that is leads to the formation or increase in the molar concentration of the oxyhaemoglobin compound.

Now, since as we already said that Db is much much smaller than this dissolved or diffusivity of the dissolved oxygen. So, this component can be ignored easily. So, what do we get? So, first equation is V Z d Cb dZ and you get only capital R Cb Cd. And second equation you have all the terms.

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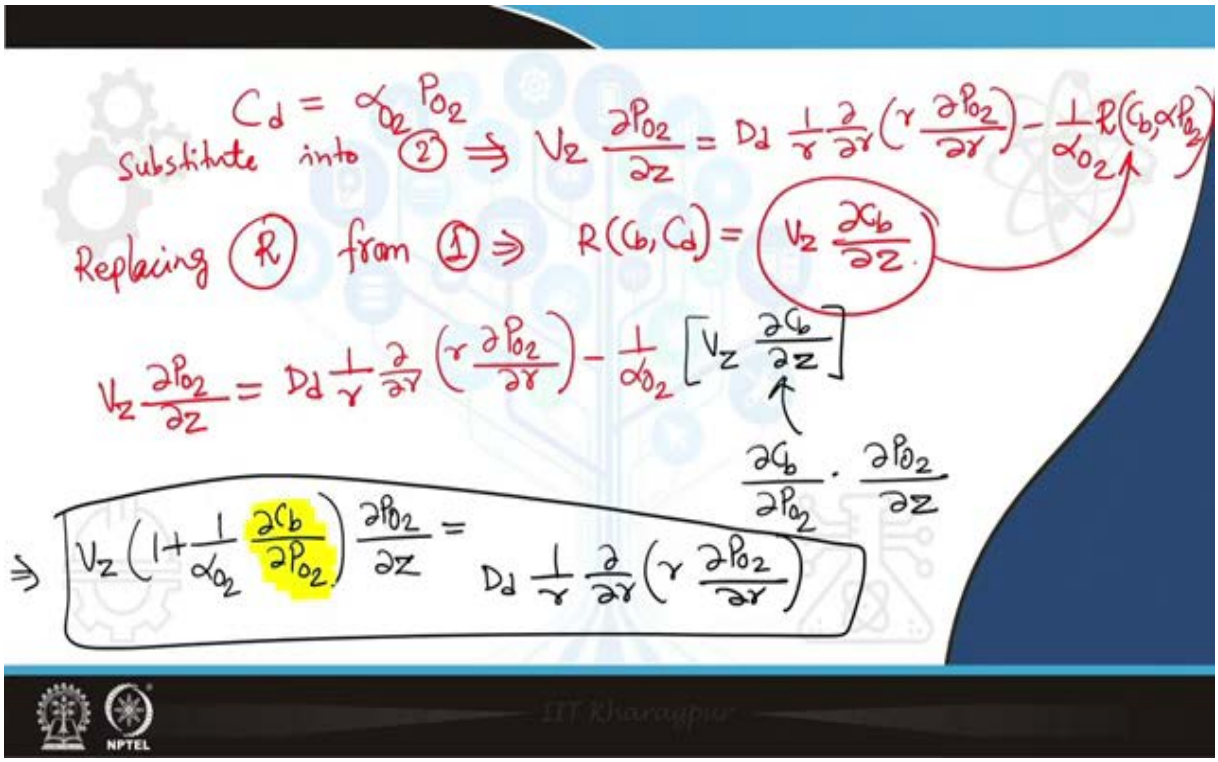

So, now this concentration of the dissolved oxygen can be written down in terms of the partial pressure, alpha O2 you can replace think of this to be some sort of Henry's constant. So, substitute this into equation 2 from the previous slide. Then what do we get? VZ so we convert all the concentration into partial pressure of oxygen, so this is Cb and alpha P O2, so replacing.

So, now what we are trying to do is that replacing the reaction term, this r term, this reaction term from 1, so from reaction, from this 1, we have R Cb Cd is equal to VZ del Cb del Z, so that this is the replacement that I am trying to make into here. So, what do I get? VZ del P O2 del Z Dd t of 1 by r. So, on the last term I write like this, may be using a different color would help in identification. So, this is VZ and then we have d Cb dZ.

Now, please note by chain rule I can write d Cb d P O2 into d P O2 dZ and d P O2 dZ can be, I can bring it in the left hand side, so this becomes slightly modified, I mean slightly organized, this is on the left hand side and on the right hand side I have the this diffusive terms. So, this is the equation that we have. Now, the important part is that how do we calculate out the value of this quantity Cd Cb by dP O2.

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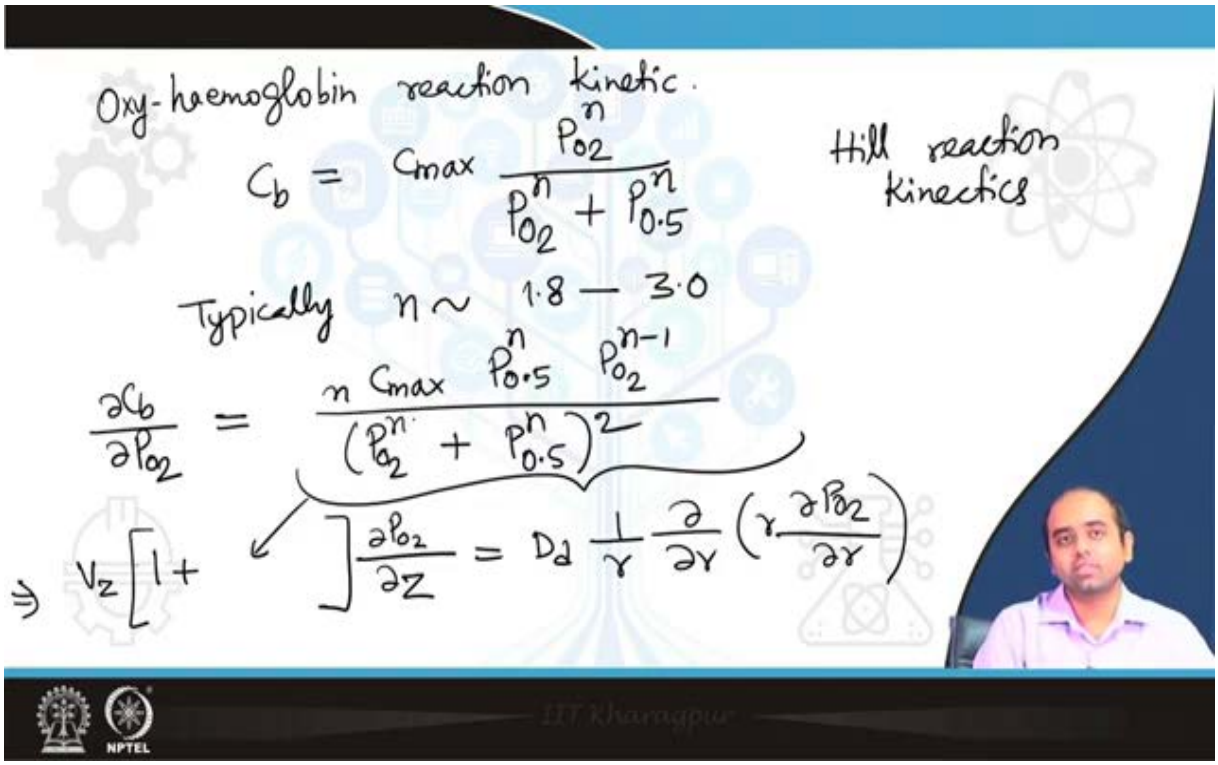

Now this reaction or reaction leading to the formation of this oxyhaemoglobin complex, so this oxyhaemoglobin complex, a reaction kinetic is generally described by the hill reaction. So, what is this hill reaction? That Cb is equal to C max which of course depends on the partial pressure of the oxygen in the free state. So, this is the hill reaction kinetics which tells you that how the concentration of the bound oxygen is related to the partial pressures.

Typically, this n varies from 1.8 to 3. So, from here you can easily work out what is d Cb by dP O2, so d Cb by dP O2 would be equal to n C max P point, so this is P 0.5 so that is the half concentration that is another constant actually n and P 0.5 are two constants. So, from this you can easily write the final equation which looks like 1 plus this entire quantity.

Then you have dP O2 by dZ and on the right hand side you have Dd of 1 by r, so this is the partial differential equation for P O2 and please note that this equation is non-linear because of the presence of higher orders of P O2, since n is not equal to 1, so this has higher powers of P O2, so this is a non-linear equation, so this is a non-linear PDE, so once and of course to solve this profile of P O2 you need the boundary conditions. So, this is first order in Z and second order in r.

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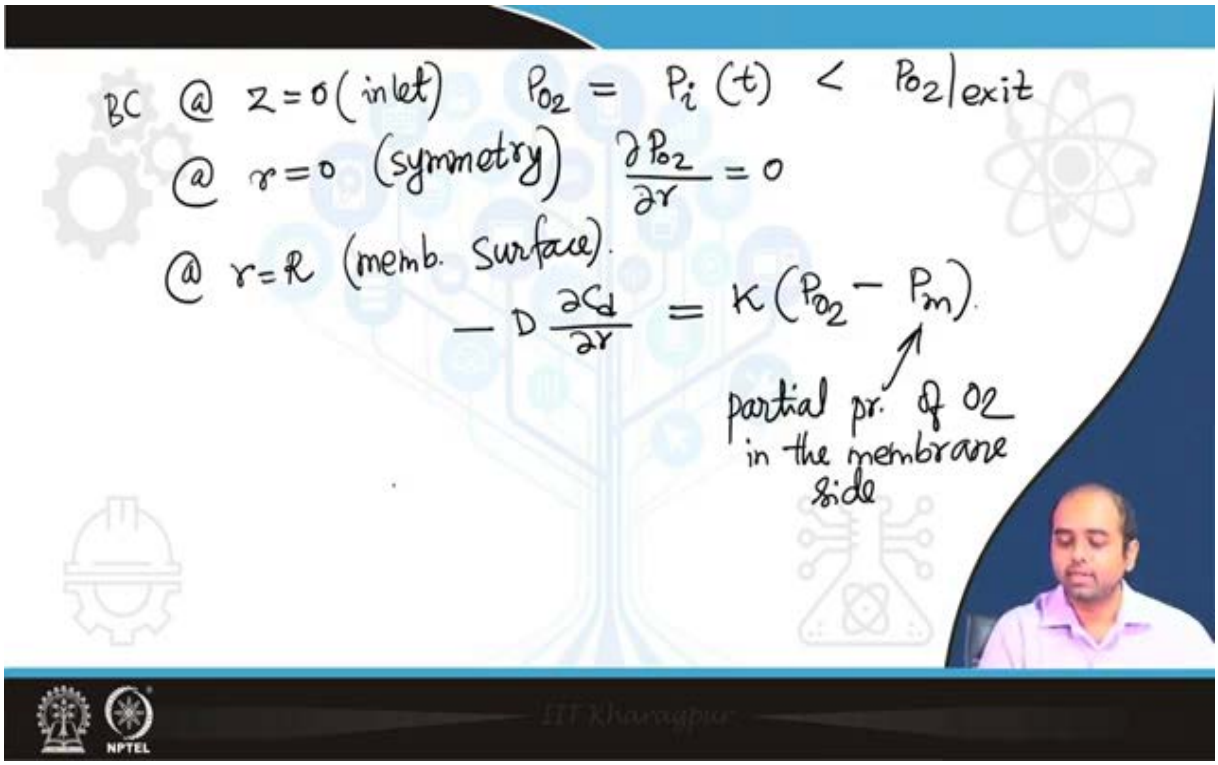

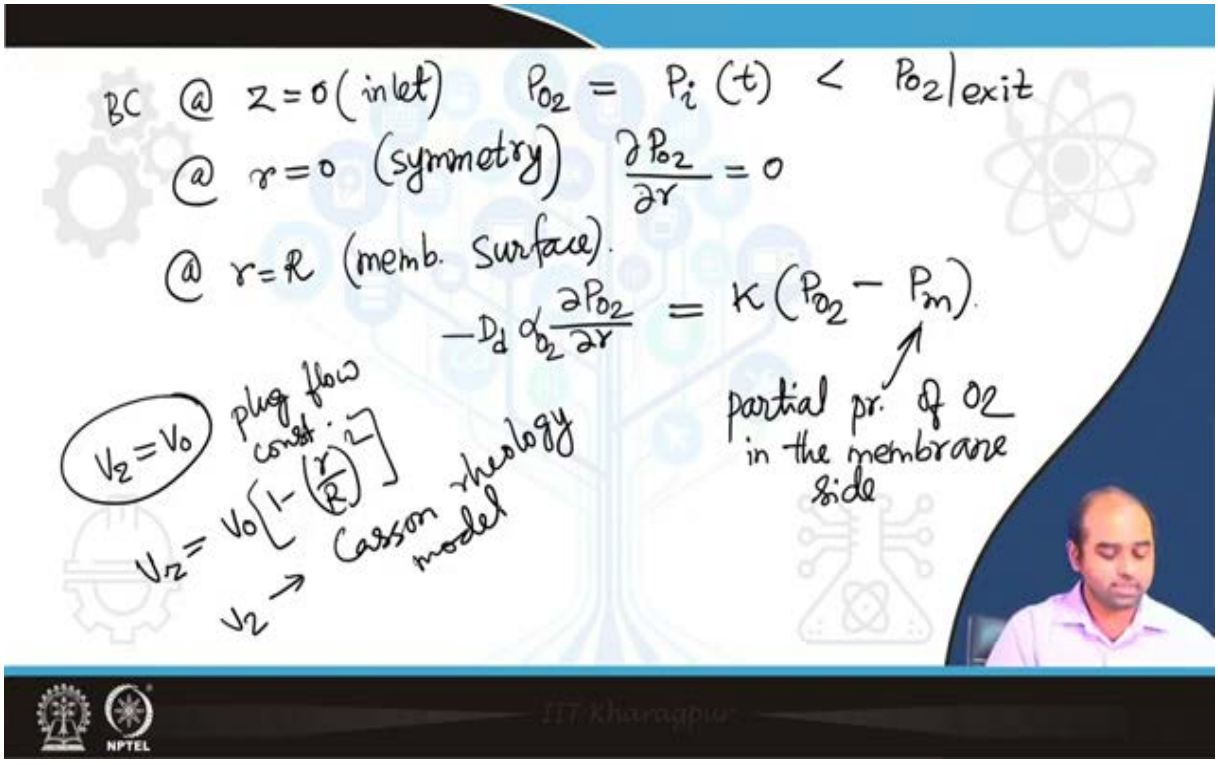

So, we need one boundary condition in Z and two boundary conditions in r. So, at Z is equal to 0 which is the inlet condition this concentration of P O2 is given by like something like P O or P O2, you can say it to be some inlet condition Pi, this could be a function of time

because with time the, so this inlet condition to the oxygenator is nothing but the oxygen level in the body.

So, as more and more blood gets oxygenated the overall oxygen level in the body can increase, so this is quite likely that the inlet blood to the oxygenator will actually change with time but that is very slow change. So, the time scale of the change of the oxygenation level at the entry or in the human body is much slower compared to the this oxygen dynamics present in the oxygenator circuit.

So, you can consider the transient effects in the oxygenator, membrane oxygenator to be in a pseudo steady state but still you can have some temporal effects with respect to the boundary condition changing with time because overall blood oxygenation level increases as time goes on. Of course, this has to be less than P O2 at the, this is always less than at the exit condition. At r is equal to 0 you have the symmetry condition, so which means dP O2 del P O2 del r is equal to 0. At r is equal to capital R which is at the membrane surface, generally the diffusive flux that is d Cd by dr is equal to mass transfer coefficient P O2 minus Pm.

So, Pm is nothing but the partial pressure of O2 in the membrane side. So, this of course depends on the membrane resistance diffusing from the outside through the membrane porous layer. So, all these effects will come into the picture and Cd can already be written down as alpha P O2. So, I can replace this C d as alpha O2, P O2.

So, let me write it that way so this P O2, alpha O2. So, this is the concentration of the dissolved oxygen of course, so that is the reason why I write Dd I mean diffusivity of the dissolved O2. So, this is the boundary condition at the membrane surface which is again mixed type boundary condition.

For the velocity I mean the simplest one is to consider it to be a plug flow or a constant type, plug flow or a constant type, you can also consider VZ to be the parabolic type this could be another reasonable approximation, but the realistic one is that VZ to be obtained from the Casson fluid model rheology, Casson model, Casson rheological model that will give you the exact or the realistic blood flow profile and it depends a lot on the blood flow profile.

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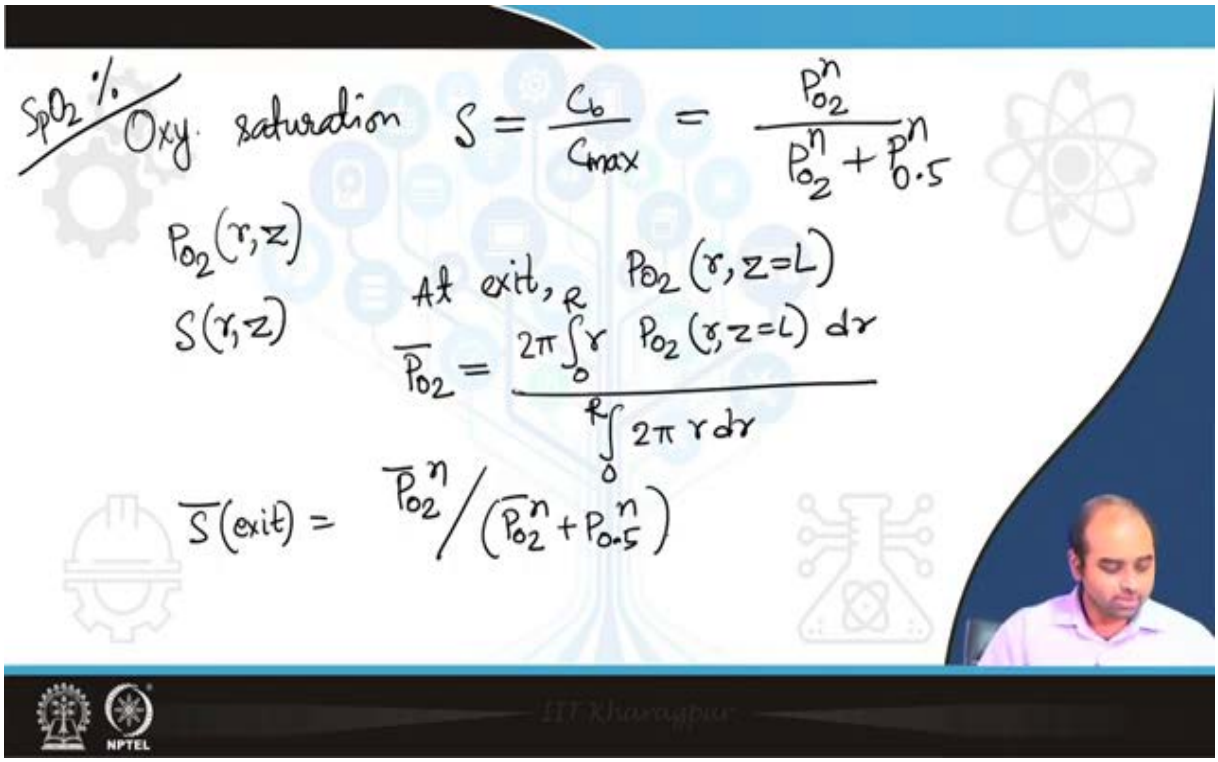

The important characteristic, the important characteristic in this case or how the oxygen saturation is defined. So, oxygen saturation in the blood, the oxygen saturation function S is generally defined by Cb minus C max where from the, it is from the hill reaction essentially, so this can be related to P O2 n by P O2 n plus P 0.5 n. So, once you are able to calculate the this P O2, P O2 as a function of r and z you can calculate out like what is the oxygen saturation at different r and Z. But oxygen saturation at different r levels is not a very realistic quantity.

So, for that what is generally done is that I mean people generally talk about the saturation level when the blood exit the system, that is what it is most important because we do not want to measure saturation inside the oxygenator, whatever the blood that comes out how much is the oxygen saturation level and this saturation is related to the oximeter levels, so that is the S P O2, so this saturation is nothing but the S P O2 percentage that generally you get from the blood oximeters.

So, at the exit, at exit what you can do so that exit concentration is P O2 r, z is equal to L at this condition you calculate the average, the cross sectional average, this partial pressure of the blood. So, how can we do that? So, just do a cross sectional average at the exit condition, so that is at Z is equal to L. So, do not confuse this r with the reaction it is the radius of the capillary tube, that is this hollow fiber.

So, now you consider the this average, cross sectional average, this oxygen saturation at exit as P O2 n by P O2 bar n, so this is something we generally do. So, this is the oxygen saturation when the blood leaves the system. So, I hope all of you get a nice idea on how does this oxygenation profiles inside the membrane oxygenator can be computed, this of course has very interesting implications in the design of this biomedical device as well as performance prediction you can easily have a prediction that with time that how does the for a particular operating condition and then for the particular design specification how does the oxygen concentrator, so not concentrator, oxygen, this membrane oxygenator actually performs.

You can also do the reverse calculation that if the blood oxidation level is very low then how much time it requires before the oxygen saturation actually improves and how we can do that, that is very straightforward.

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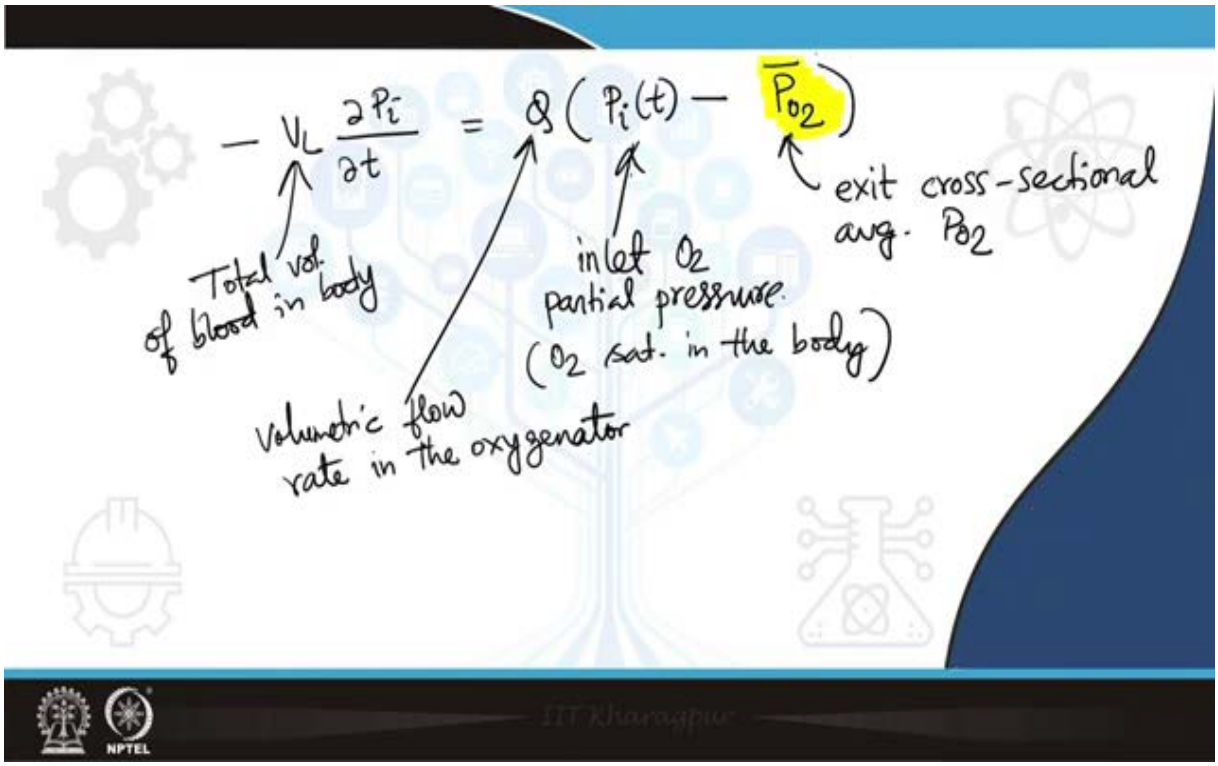

You can simply have, you can simply have this reaction, simply have this equation that can help you in evaluating what is the partial pressures with respect to time. So, let us say this Pi is the entry level concentration and P O2 is the exit concentration, so this is the exit cross sectional average P O2 concentration, I mean the partial pressure, this is the inlet O2 pressure or the O2 partial pressure and which is nothing but the partial pressure which is nothing but

the, this O2 levels. So, this is dependent on the O2 saturation in the body which is what is entering into the system.

And let us say this is the total amount of blood, total volume of the, volume of blood in the body. So, this simple differential equation will tell you that how does the oxygenation, oxygen concentration or the oxygen profile actually improves or increases in the concentrator, in the oxygenator.

So, from the device calculation you will get the idea of this P O2 for a given inlet concentration what is the outlet concentration is something that you will obtain from the calculations that we have just described. And relating this differential equation will help you to understand or correlate that how the actual this oxygen level in the human body will be increasing or will be changing with time.

So, this gives you a very nice idea on the performance prediction of the oxygenator and can help us to take important clinical decisions in respect to monitoring and treatment of respiratory problems in critically ill patients. I hope all of you found this practical problem or a practical application related to mass transport very interesting. And we hope that in the next class we will be looking towards another very interesting mass transport problem. Thank you, I hope all of you like this lecture.