Biochemical Engineering

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Module No. # 01

Lecture No. # 24

Effect of Mass Transfer on Microbial and Fungal Growth

In the last lecture, we started off with microbial growth models and we will continue from where we left; a little bit may be, earlier. So, we talked about the process of growth and what are the nutrients that are necessary, what are the chemical reactions that happened during growth.

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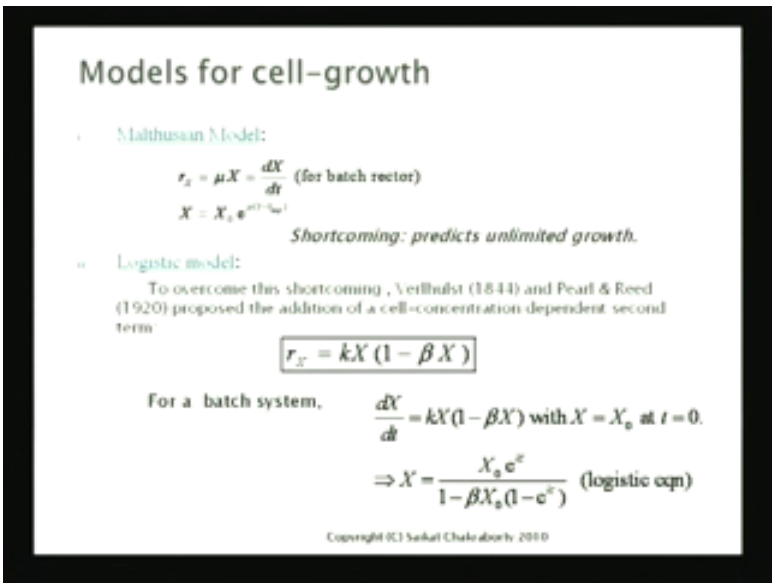

And then, we started to look at the different kinds of growth models that is there. So, if you look at that screen here, so, we started off with the Malthusian model, which simply said that, the r x is d x d t. And then, we went on to look at the Logistics model, which tried to propose the dependent, second order dependence of, of of, on the reaction rate of the substrate and, and then, we got d x d t is k x times 1 minus beta x.

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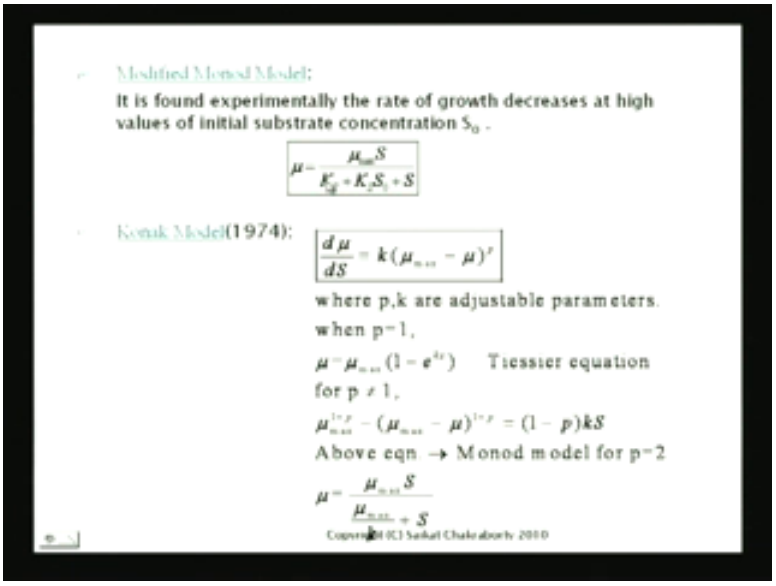

And then, the next model was the most important model we looked at, which was the Monod growth model. Just check; so, I think something skipped here. So, we, we had the Monod model to start with, which was mu times S over k S plus S. And then, we modified it using the Monod growth model, which we called the modified Monod model; we added the K S plus S 0 term in the denominator. And then, we had the Konak model. As you can see over here, what happens in the Konak model is, that Konak model is for the limit of p going to 2, for the case of p going to 2, goes to the Monod model, right. So, this is where we stopped, if I remember.

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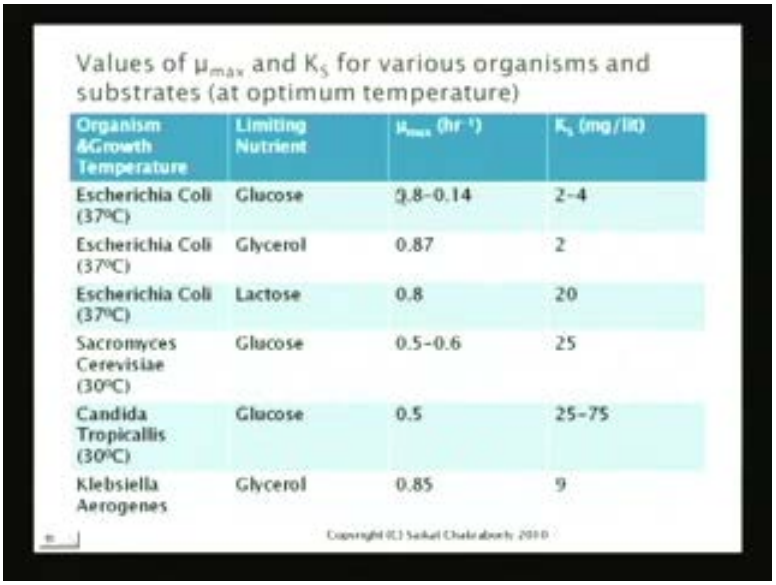

Now, where we will start today is the value. So, if you are doing a Monod model for example, you have these K S, the rate constant and the mu max, maximum rate. And so, we, what we going to start with today, are the values of mu max and K S, for various organisms and substrates, fine. So, the first one, we look at is the Escherichia coli, e coli that is, and these are growth temperatures that you see over here, or the optimum temperature; that, as I told you before, that there is a range within which, which these microorganisms can grow; but then, within that range also, there is a temperature that is an ideal, or optimum temperature. As, as we discussed before, what happens here is that, for an ideal, or optimum temperature, and I talked about this point, you know, tropical or subtropical countries, you have the growth of these bacteria are a lot more than colder countries; the reason being that, the optimal temperature, as we can see over here, is ideally suited for a tropical or subtropical climate. So, excuse me. So, e coli, for example, it can grow under different kinds of nutrients. So, depending on the nutrients that it is growing in, the mu max, and the K S are obviously going to be different, obviously; very straightforward; because, you know, if you change the substrate, the growth rate is going to change.

So, if you look here for glucose, for example, the, if the limiting reactant nutrient is glucose for example, if you are using the glucose to grow the bacteria, to grow the microorganism, then, mu max is 0.8 to 0.14 and the K S in between 2 to 4. If you are using glycerol to grow e coli, then, the mu max is 0.87; K S is 2. If you are using lactose, then, it is 0.8 and 20. So, K S is much high, larger over here. And, sacromyces cerevisiae which is yeast, you know, if you are growing, if you are using glucose to grow that and the mu max is 0.5 to 0.6 and K S is 25; and, this Candida tropicalis and this, this if you are growing with glucose, the mu max is 0.5 and K S varies between 25 and 75. And, Klebsiella aerogenes, if you are using the glycerol, then, mu max is 0.85 and K S is 9. So, what you find is that, the mu max, more or less, you know, is independent, irrespective of whatever bacteria you are growing, or microorganism you are growing, and what is the substrate you are using, more or less remains around the same number, whereas, K S kind of changes; but again, the range of K S for many of these is around 20, and some of these in the 10; but again, you know the order of, what I am trying to say here is, the order of magnitude remains more or less the same. So, the order of magnitude does not change too much; it still is in the range of 1 to 100, that order.

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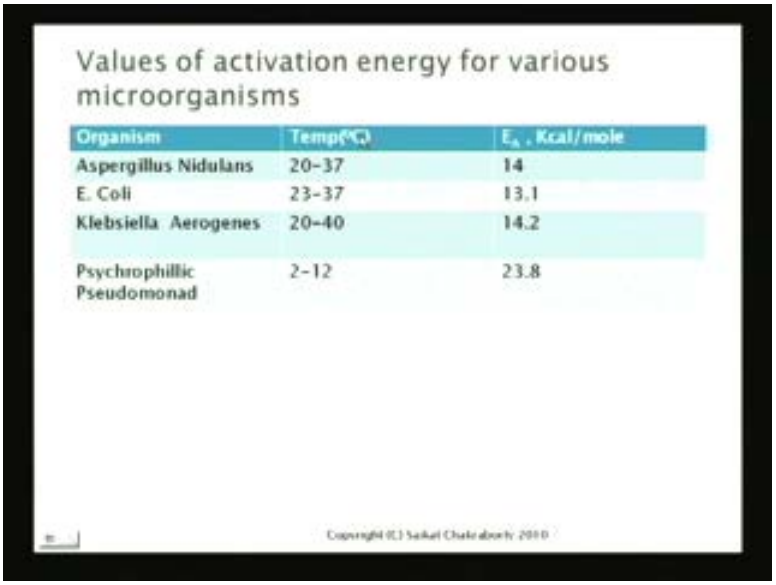

And then, the values of activation energy and we had discussed, if you remember, we had discussed this in the, when we were doing enzymes, the dependence of temperature. So, whenever there is a dependence on temperature, there is a effect of activation energy and that is also related to the question that, why a certain temperature is optimal, or good to grow certain microorganism and why other temperatures are not good, right. And then, you know, the question of tropical and subtropical climates and other things arrived; because, if it is, for example, if the, these are the temperature ranges and if the temperatures are too low, then, this is an activation energy. Now, the, the activation energy is required, but the total amount of heat that is generated, or required, is dependent on temperature. So, if the temperature is very low, for example, that amount of heat would not be generated, or, or required to do that. So, that is why, this gives you the range for the e S for the different bacteria. So, most of them as you see, are growing between 20 to 37; this is 20 to 40; but essentially, that is the growth range. Then, that as I said, again, is a very ideal climate, you know, the subtropical climate and these numbers are around 13 and 14. This psychrophilic pseudomonad, the temperature range is lower here and the, it grows in colder, you know, cold temperature and the e a for that is, obviously, larger, right; because, its temperature, activation temperature is low, lower, then, e a has to be larger.

And, you know, certain, there are certain bacteria, or virus, for example, these, the bacteria that we are used to, at some point of time, including this time, that is, the

common cold virus. So, it is a, it is, you know, so, for example, it show your mom will say that you caught a cold. What do you mean by you caught a cold? You did not catch a cold; cold is not a thing that you can catch; it is the virus that you catch. So, the reason people say this so easily that you caught a cold, then, it, it is kind of, becomes a part of our everyday linguistics; but essentially, we are talking about viruses. When people say that you caught a cold, what they mean is, you caught the common cold virus. So, you know, if you expand the statement that, that is what it means, you caught the common cold virus. So, it is one of the rare viruses which actually can exist in a cold, colder climate; in a, lot more than the summer climates. So, you would not have the common cold virus even in summer or high temperature season, whereas you would have this especially during the cold temperature. So, this is one of those, so, just, you know, the, so, which grows in 2 to 12, then, common cold virus actually grows in temperature this and much lower than this.

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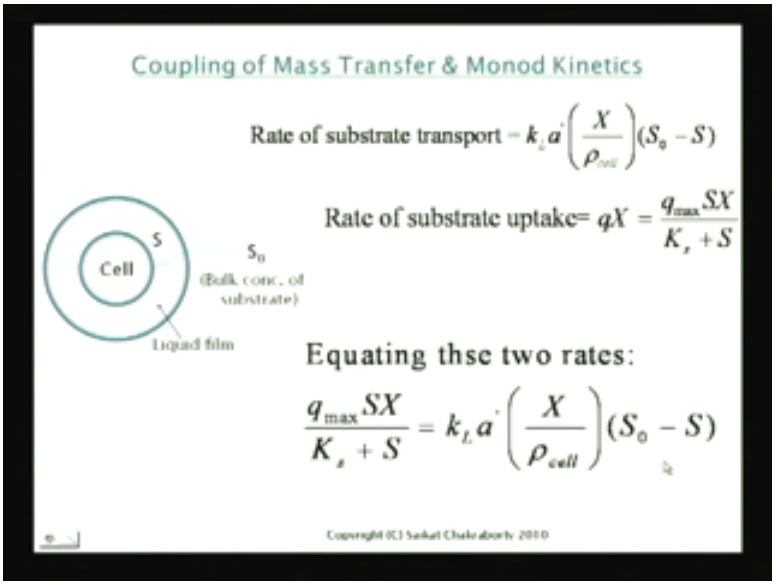

Now, what we are going look at is essentially, the major topic of today, is the effect of mass transfer and growth. Now, if you remember, this is exactly how we did the enzyme. So, we look, looked at kinetics of the problem. So, we looked at the effect, the reaction aspect of it and then, we looked in immobilized enzyme, enzyme we looked at the transport aspect, it was the mass transfer aspect. And then, what you did, much of the first half of the semester was, the combined effect of mass transfer and reaction, which was, I think, sort of something new, you know; I am not sure, exactly what you did in the

last, previous courses, but, sort of something new, as compared to what you might have done in previous courses. You would have done, I mean, there are courses where would have done mass transfer, or transport and then, there are courses where you have done reaction, but what, but, in real life, what happens is, these two things, kind of compete with each other. So, reactions and mass transfer, either occur in series, or occur parallelly, or simultaneously.

So, then, we, if you remember, what we did in the last part of the semester was, we looked at these several, if, cases, where reaction follows mass transfer and there are cases, where reaction occur simultaneously with mass transfer. And, the same thing is actually applicable to growth model, the reason being that, growth is essentially a reactive process. It is a reactive uptake process. And, if you remember, you know, just because, in a few days, where I can go back and show you the reactions over here. Some reason, I think, something happened. Anyway, so, so the, if you remember, I do not have the reactions with me right now, but, if you remember, the reaction that we wrote was, the reaction of glucose, or some kind of carbohydrate and nitrogen with the cell, which resulted in an uptake of carbon, hydrogen, oxygen and nitrogen to the cell, right. And, one of the confusion that you might have, see for example, what we are doing in the model are, we are using 2 symbols, x and S. So, what does the x stands for? x stands for the cell and S stands for the substrate. So, please make a note of that, you know; do not, do not forget this. So, S stands for the substrate.

So, S is the substrate as a whole; so, it could be the nitrogen; it could be the oxygen; it could be the carbon, or the hydrogen; but, substrate as a whole, in general and x stands for the, stands for the cell. So, essentially, there is an reactive uptake of these substrates by the cell and the cell grows as a result of, result of it. So, there is a reaction aspect of it, but, there is a mass transfer aspect of it to, mass transfer aspect to that as well. And, why is that because, the substrate essentially has to overcome some mass transfer limitations, or transport limitations, to go to the point, where the cell can actually uptake it through a reactive process, exactly like the enzyme thing, that immobilized enzyme thing that we did, and we will do some, few cases today, or may be tomorrow as well.

So, this is an example that we are looking at here. This is the cell; this inner, inner circle that you see over here is the cell and the outer circle that you see over here is the liquid film, or the boundary layer. So, so, what happens essentially that, you, this is, this is cell

and it is the cell is growing in a medium, right. I discussed this in the last lecture, all of it. The cell is growing in the medium and you might have (( )) in the medium, may not have (( )) in the medium; you might have (( )), you can use a plate inside the incubator to kind of, shake it. So, whether you have (( )) in the medium or not, there is always going to be a liquid layer, you know, a stagnant layer; it is not really a boundary layer, but, it is a stagnant layer, which is similar to a boundary layer; boundary layer is for a moving system, but, you know, even if you have (( )) or not ((stirring)); so, what happens, because the cell is solid, there is always going to be a stagnant layer of liquid around the cell, right; is it clear to everybody, or is that something that you are agree with? So, then, this layer, liquid layer, say, has a thickness of d, or something, whatever (( )), I might say.

Now, what happens as a result of the presence of this liquid layer is that, the substrate has a concentration S 0 outside and the concentration at the interface of the liquid layer and the cell is obviously, going to be lower than the concentration outside, which means that there is a concentration gradient in between the bulk and this one. Now, unlike in the case of the enzyme, we may not actually want to go and solve for the concentration profile of, in the, in this liquid layer, stagnant cell; the reason being, the stagnant cells are typically very thin, and it is probably of not much practical use, to actually go and solve for the concentration profile in this.

So, what we do, we simply use the concept of the mass transport coefficient. So, what you see over on, here on the screen, k L times a prime x over rho cell times S 0 minus S. Let us, let me explain each little thing. So, k l times a, a prime is, the k l is probably the mass transfer, mass transfer coefficient you (( )) times this area and then, x over rho cell is the volumetric increase of the, you know, increase of the cell volume, volumetric increase. So, we divide it, say x s by weight and you divide it by the density. So, you get the volume of the cell. So, this is, sorry, this is, k l times a prime would then be for unit volume. The unit of this would be for unit volume. So, this would be volume. So, k l times a prime times x, x over rho cell would be the, for, for a particular given volume, so, this would be the mass transfer coefficient times, the difference, of course, S 0 minus S. So, this is the amount of substrate transport. Why is it proportional to x? Why is that proportional to x, because, the more is the, more is the volume of the cell, more is a total transport going to be, right; and, the volume of the cell is proportional to its weight; is it

clear? The more is the volume of the cell, the more is the total transport going to be. Is it something you agree with?

So, next is the...So, this is the rate of substrate transport and then, what would be, what, what is that we, we are going to balance it with what is going to happen. So, at the interface, for example, (( )) the rate of substrate transport at the interface. So, at the interface, for example, if there are no internal mass transfer gradient inside the cell, it is very likely that, there are internal mass transfer gradient inside the cell, and you know, we did this in another course, at some point of time; some of you did that course, ignore that; what happens, we solve for the concentration profile within the cytoplasm; you can, you can even solve for concentration profiles of certain materials of substrate within the cytoplasm, if possible. But here, we assume the cell to be very small and we assume that, the reaction within the cell is more or less uniform; we do not assume a mass transfer gradient within the cell, which is not an unreasonable assumption, let me tell you. It is possible to go, see, you decide what is the level of details you want to go into. So, you can look at, for example, if you want to, this model that we are solving, if you want to solve a really detailed (( )) model, what would you do? You would take the liquid film and then, solve for the profile within the liquid film; solve for the profile within the cell, and then balance all of that. What we are doing instead is that, we not solving for any of the profile even within the cell, or the profile within the liquid film; we are simply saying, the rate of substrate transport is mass transfer coefficient times volume of the cell times S 0 minus S; and, for the cell, what is now, what is the uptake. So, the uptake is due to the reaction in the cell, right.

So, what would the uptake be? We already did that, you know, the growth. What is a uptake? We did the growth model. So, if you are using a Monod model, for example here, what would be the uptake? The uptake is, you know, what I gave here. So, which is S times x divided by K S times K S plus S times q max. So, q times x is exactly the Monod growth model, if you remember. So, I used mu; instead of mu I use q, over here, and I will come to the reason of it,in a moment; you will see why I used that. But, the same thing exactly, so, q times x. So, q is the growth rate per unit weight of the cell, fine. Growth rate for unit cell times number of cell again, because more is the amount of cell, you know, more is a growth; is it clear? Linearly dependent on growth, cell. So, q. So, q is given as q max S over K S plus S, Monod growth model times x. So, what happens is

that, at steady state, these two should balance each other. So, these are, this is my basic equation that you have, q max S X divided by K S plus S equals k L a prime X over rho cell times S minus S 0.

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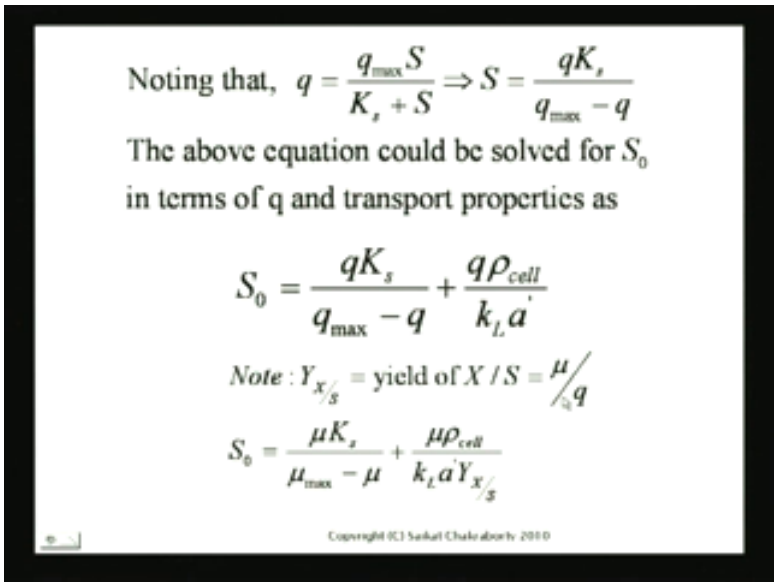

Then, so, this is a basic equation. What it entails is that, the rate of substrate transport at steady state equals the rate of reactive uptake by the cell. Now, so, here, q is just as which mentioned here; q is q max S over K S plus S. So, what we do here is that, we expressed S as a function of q. So, we expressed S as a function of q. Why do we do that? I will come to that; it is written here. So, once you do that, we express S; so, S becomes q times K S over q max minus q. Once you do that, what you can do is, look at this equation; you can go and put back your S here in terms of all of the variables; then, this becomes in equation in S 0 and you can solve for S 0 straightaway. And, this becomes a linear equation in S 0. You can solve for S 0 straightaway, and this is what you get for S 0. So, S 0 is now expressed in terms of different transport properties and q. So, q is a variable remember, but everything else, is a constant out here. We will see in a minute, why I am trying to do that, you know.

Now, what I do is, now, this new thing comes in over here, is that, I defined the yield of x per unit S. See, here, when you were writing a balance, let us see, when you are writing a balance, your are writing a balance for the substrate; remember, you are not writing a balance for the cell; you are writing a balance for the substrate; that is why, I used q over

here. Now, if I am doing it, if I am want to convert it into the cell, the yield of cell, so, when you did the, that is a only little bit different between what we did to the Monod growth model and here. Monod growth model was quantifying the amount of cell growth. Therefore, it was given as mu times S, mu times x; whereas, this one quantifies the amount of substrate uptake and Y is the one that gives the yield of x per unit S. What does it mean that, see, there, it is not necessary that, there has to be a one is to one relationship between the uptake of the substrate and the production of the cell. It is not necessary that, one mole of the substrate should produce one mole of, of the cell.

So, mu is that ratio; it could be that, 2 moles of the substrate produce one moles of, of cell. So, mu, sorry, Y is the ratio that would give that. So, mu over q. So, Y could be half; Y could be 0.3, 0.4; Y could be 2, or 3 even, unlikely; but, you know, it could be 2, or 3, but, you understand the concept very, very clearly; should I explain one more time? So, what happens is that, when I wrote this equation, I used q, because q (( )) for the substrate, whereas, when you use these notations, you have to remember. So, for the, when you use it for the cell, it is mu, and when you use it for the substrate, it is q; and, q over, mu over q is the amount of cell produced, amount of x produced per unit amount of S, that comes in; is that clear? So, now, I can write the same equation in terms of mu. How do I do that? See, for example, so, q is mu over Y, right, from this equation, here, look. So, Y is mu over q; therefore, mu, q itself is mu over Y right. So, you substitute that. So, then, let me use the pen here.

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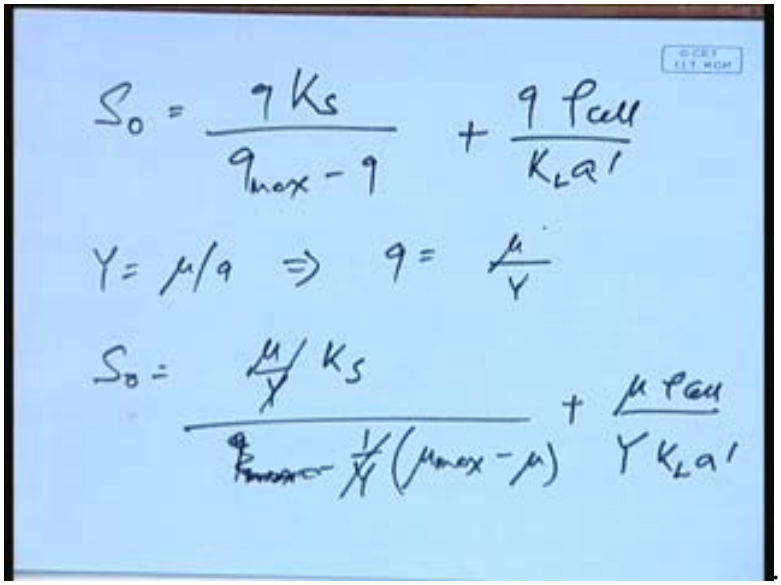

So, S 0 here q K S, q max minus q plus. So, Y being mu over q, which means that, q itself is mu over Y. So, S 0 then becomes, mu over Y times K S, Y is the number, remember; it is not a variable, just a number; 1 over Y mu max. So, 1 over Y, 1 over Y cancels out here. So, you have mu K S divided by mu max minus mu plus mu rho cell by K L prime. So, if I go back to the screen now, so, the last thing you see is exactly what I did just now. So, mu K S over mu max minus mu plus mu rho cell over K L a prime Y, fine.

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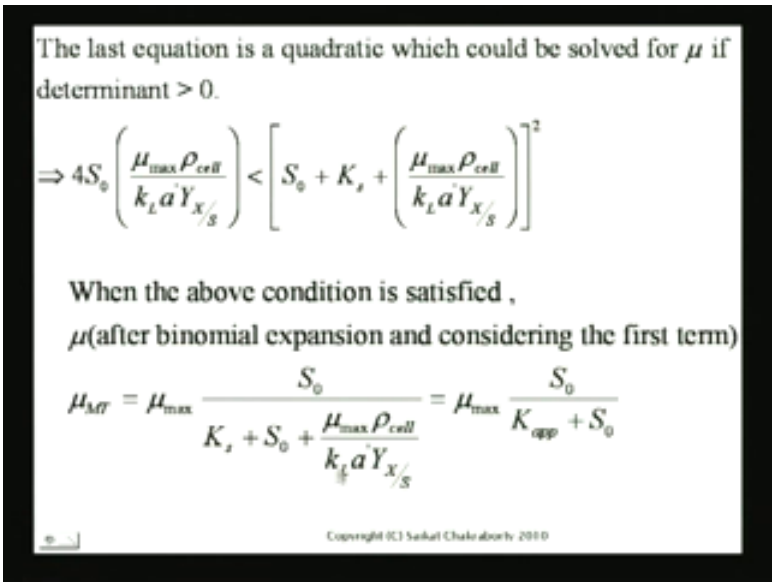

So, if you look at this equation that you get over here, you can solve for mu in this equation. You can solve for, yes, mu in this equation provided, because mu is a variable; now, q earlier. So, what we did was, you, what, what did we do essentially, it was a variable; if you put your S over there, then, it was variable in S; but, we did not want to put my, our S in that. So, we put in terms of q. Then, we converted q to mu and then, you can solve for mu, because mu is a variable, which is unknown over here and that could be solved for, if the determinant is greater than the 0. So, you may want to take a minute and look at this and you, if you want, I can show you this. Maybe, that is what I will do. So, here.

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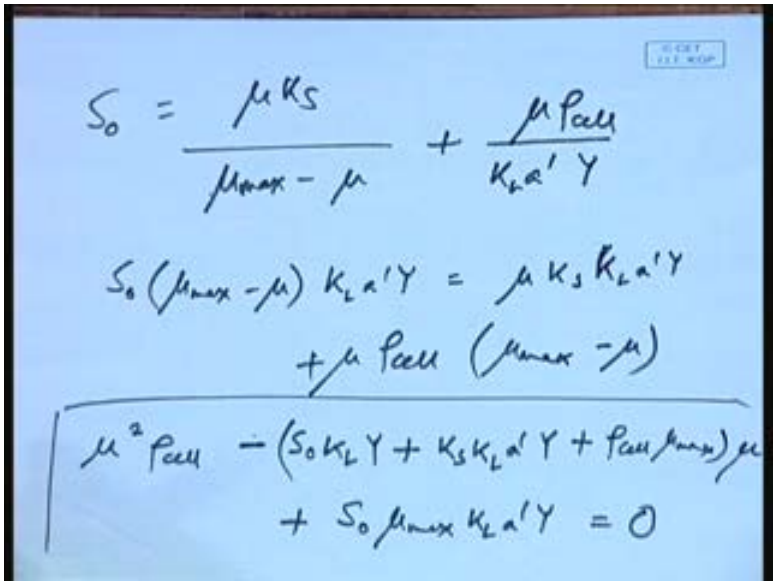

So, your equation is mu K S mu max minus mu plus mu rho cell K L a prime Y. Then, you, you know, multiply the whole thing by mu max minus mu and so on. So, you get mu max minus mu times K L a prime Y equals mu K S K L a prime Y plus mu rho cell mu max minus mu, right. So, this becomes a quadratic in mu. So, this, if you take it, so, you get mu square times rho cell, plus, let us see, minus, sorry. So, minus S 0 K L Y plus K S K L a prime Y, plus rho cell mu max times mu, plus S 0 mu max K L a prime Y equals 0. So, this is your quadratic, and, so, all you need to do is, look at the determinant of this. So, this is what I do over here; and, for this to have a solution, for the equation that I just wrote, the quadratic equation, for that to have a solution, the determinant has to be greater than 0, which is what we use. What are, why are we trying to do this? See, what we are trying? Can you have, do you have a sense, why we are trying to do this? You know, this looks too complicated mathematically, but physically, what we are trying to aim at? What we are trying to find over here?

(( ))

Yes, minimum concentration of what?

Substrate (( ))...

Yes. So, initial, S 0 is initial amount of substrate that is, that is there, and what is my initial amount of substrate that I require for the cell to grow; because, that is very

important. We need to figure out. See, if you, if you undernourished the cells, they are never going to grow. So, what we are going to find out is that, what is minimum amount of substrate that is required for the cells to grow. See, we had the equations at the, at long back, you know; if you look at what is here on the screen, see, we have the equation right here, and what we could have done is, straightforward, gone and solved, gone and solved for S, right. This is a quadratic equation in S. We have it and you can go where, go and straightforward get it, solve it and get a solution; but, we did not go that way. We went another route and the reason was, it is more important to actually find out that, what is the minimum amount of initial substrate that you need to nourish the cells experimentally; for experimental growth, rather than to actually solve for what your substrate amount is. So, that is exactly what we are trying to do. We can always solve that; that is not a big deal to solve that quadratic equation; but, what we are trying to find out is, what is my minimum amount of substrate and how do you get that. You get that straight from the equation, fine; because everything else is, you see over here, mu max, rho cell, K L, Y and K S, these are all constants.

So, the only unknown over here, or thing, that you want to control, rather; so, these are the things that you cannot control; mu max is the property of the cell; you cannot control; rho cell is the property of the cell; you cannot control; K L again, is the property of the cell and the substrate and substrate liquid, and the cell, you cannot control. Y is the property of the cell and the substrate, you cannot control. So, these are the things you cannot control; the only thing, controlling parameter that you have here, is S 0. So, what you want do from here is that, equate this, you know; so, you put for S 0, this equal 0 and solve for S 0, to get, what that would give you the minimum amount of substrate that is required for the growth and nourishment, and therefore, the growth of the cell; is it clear to all of you?

So, then, once you do that, you know, so, you can, once this condition is satisfied, then, mu, that you had over there in the equation itself, could be written in this form. What, what I am trying to do over here is that, what I am trying to do, do you have a sense? So, this part, is that clear? So, this, this is separate from what I have below, below; do not worry about this; is that, upto that, is that clear to everybody? The S 0 thing, that what we do is, figured out, what is the minimum amount of substrate that is necessary. Now, this is something different, I am trying to do here. What I am trying to do here is, see, my

model that I have over here, this one, is a model for the Monod growth; but, the actual growth that is taking place, is not the Monod growth. Why because, it is limited by mass transfer; because, it is limited by, by transport; and therefore, the actual growth is not the same as the Monod growth. So, what I am trying to do is, trying to find out that, what is my actual growth; and, that, with a little bit of algebra that is here and you can have a look at that, when you go back home is that, you convert this. So, S, you can, how, what you do is that, what is a difference. So, if my, if I have Monod growth for example, let us see.

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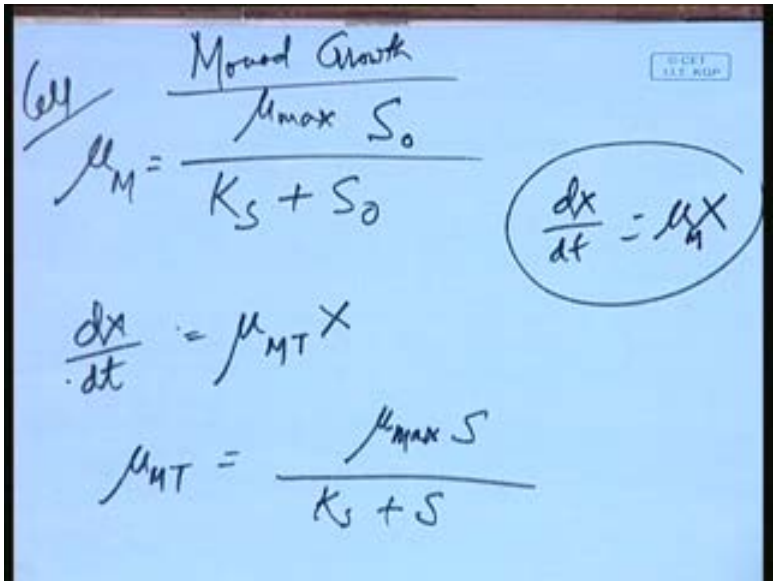

What would be my growth, if I had Monod growth for the cell? This is for the cell. Monod growth. You simply have mu max S times S 0 times K S plus S 0, right. And, of course, multiplied by x, that is always there. But, so, your mu Monod, let us call this mu Monod is this, and your growth rate is d x d t would be mu times x, fine. Now, in the presence of mass transfer, how is this going to alter? What is the growth rate going to be, in terms of presence of mass transfer? This is going to be mu; let us call this mu Monod. So, mu m times x. So, this is going to be mu something else; let us call this mu m t times x. How it is going to be different, mu m t, equals, use what; it still follows the same thing, you know. What is the mu m t? times S plus K S plus S. We did that before, here; then look. So, this is the one. So, what is the difference? The difference is, for pure Monod growth is, there is no mass transfer with S 0; but, in the presence of mass transfer, you have S. And, what you need to do is, we simply need to substitute for S.

How would you substitute? If you, let us look at the screen here. So, this is here, my equation. Now, that I have figured out, what my (( )), so, my major first motivation was to figure out what is the amount of, minimum amount of nutrient that I required. Once I have figured that out, I go ahead and simply solve for the S, which is the quadratic equation. Now, I will have two solution; one would be unfeasible solution; one would be a feasible solution. Take that solution, and then, I can put it back into, look, look here. So, I put it back. So, I get the solution of a, put it back over here. So, you know. So, my, my S, that is the solution S that I get is, S 0 plus, I am sorry; S 0 thing, that you get, yes, I think, what will happen is, it is little bit of algebra out there.

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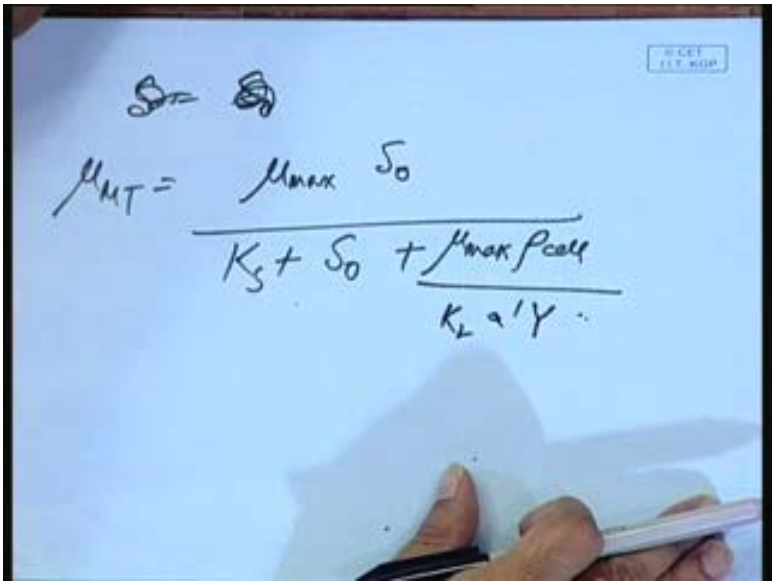

So, I am skipping the step; you can just go and check, you will get mu max S 0, K S plus S 0 plus mu max, rho cell plus K L, a prime into Y. So, this is what you get and so, this is what you get. So, the algebra out here is that, you will have a denominator, you know, it will get cancelled; little bit of algebra is out there, once you solve for the S 0. So, what you need to do is, go back, solve for S. So, take the quadratic equation, solve for S in terms of S 0. If I need to explain, I will do it. I think, I have it here, yes. So, this was, no, sorry, this is not that (( )) equation. Let me write down, you know, (( )), I do not want confusion in this.

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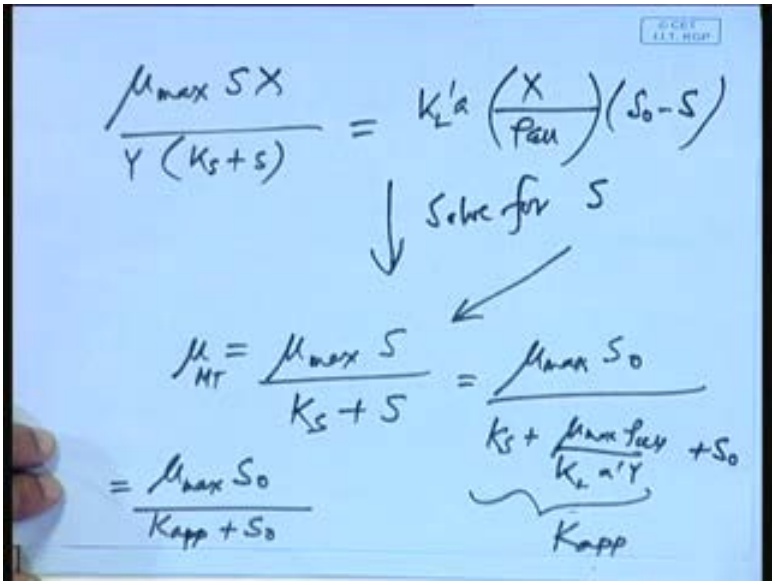

So, mu max S, mu max times S times x over Y K S plus S equals K L prime a x over rho cell S 0 minus S. So, this is your quadratic equation that you now need to solve for S. Is it clear? Solve for S using this quadratic equation and the solution that you get, put it in mu. So, mu equals, or mu m t let us say, equals mu max S over K S plus S; put that, put that solution that you get, into this; what you will get is mu max S 0 K S plus mu max rho cell K L a prime Y plus S 0. This is what you will get. So, solve for S, put this into this and after a little bit of algebra, (( )) denominator which will get cancelled and some things will happen and this is what you get. Now, what we are going to do is, how does this look? This looks similar to the Monod model, if you look at it, except that, if you call this K apparent. So, if you call this K apparent, then, this simply becomes mu max S 0 K apparent plus S 0, right. So, then again, it looks like the Monod growth model, but with a difference.

Now, let us go to the screen. So, this is my K apparent. So, if you want to write, write the, if you did not write what I wrote, this is what it is. So, mu m t is mu max S 0 over K S plus S 0 plus this term, which could be written in the Monod form, mu max S 0 over K apparent plus S 0, where K apparent is K S plus S.

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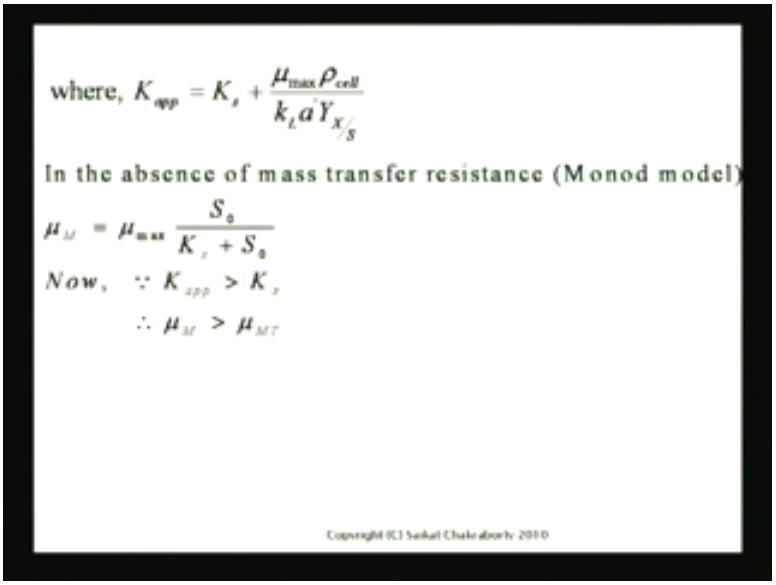

So, what it means is that, K S, because this term, you know, mu max rho cell over K L Y, which is larger than 0, of course, greater than 0, which means that, K apparent is larger than K S; which means that, the overall growth process is slowed down; which is obvious, if you have mass transfer resistance, overall growth processes is obviously, going to be slowed down; excuse me. So, in the absence of mass transfer, my mu max, mu m was mu max times S 0 over K S plus S, and in the presence of growth transfer, my mu m is going to be small, mu, mu m t is going to be smaller than mu m; or, in other words, mu, mu, growth rate, or the specific growth rate, mu is called the specific growth rate, the new specific growth rate is going to be smaller than the old specific growth rate, right. Is there any question on this, anybody? So, so just, you know, is it fine with everybody?

So, let us move on to the next part, that we will do today is, the growth of fungi; slightly different from the growth of the cell. The reason is, the growth of fungi is different from the growth of cell, then, you probably know this, is that, you have seen, you know, fungi growing in, in trees, right; you have seen how fungi grow, in trees and you know, this mushroom like structure, they sometimes form. So, what is the major difference, that in the way the cell grows, from that a fungi will grow. The major difference is that, the cell they grow, along each other and with each other, but, they are separated from each other within the, in the, in the cell growth chamber. So, if I am to draw the process, yes, so,

take something like this, and then, the cell, one cell will grow...Let us start with one cell, for example.

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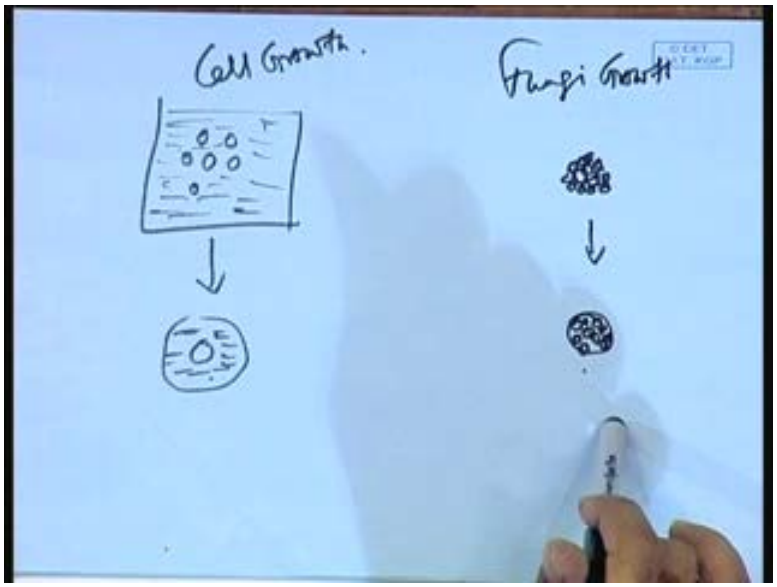

And then, we have, 2 cell, 4, you know, 4 cell and so on. So, this, this is going to continue, let us say; but, it grows like this. So, you have the medium out here. So, the medium is out here, all of them; that is why, we could do a model like this, where we took the cell and we took the medium around it. This is the cell growth, general cell, normal microbial cell growth. And, and, fungi growth is different in the sense that, again, if you, you can start with one cell, but, they grow in colonies; there is no medium out around; the only medium you have, is outside the colonies, you know. So, they, they grow like this. Now, can you, this is, this is the interesting question I want to ask you that, can you, can you tell me from, in the evolutionary prospective that, which one is better? Which kind of growth is better? So, you have this growth, as you know, so, there is no way, you can take this. So, if you have to take this, you have to take the whole thing together, as a colony. So, you know, whereas, you can isolate a single cell over here; but you cannot a isolate single cell over here; you have to it growth like a colony. So, tumours also grow like that, in colony. So, from a evolutionary prospective, can you tell me that, which one makes more sense? Which one is better from an evolutionary prospective? I will give you the answer, in a way almost, that...

(( )) mass transfer rate will be there (( ))

Yes. So, what is my, what is the answer to my question? Which is better, from an evolutionary prospective? Which kind of growth?

(( ))

Better, right; that is correct. So, the single cell growth is better from an evolutionary prospective than the fungal growth. The reason, and, and you know the answer is there almost that, that you know, the cell growth includes all kinds of cell growth, including human cell growth. So, this cell growth that we are talking of, are of course, more evolved species. So, all kinds of cells, whereas, fungal, fungus is a lot more primitive species and you know, much of earlier cell growth, actually started like fungal growth. Fungal, fungus is a lot more primitive species than, than cell, normal cell, and normal cells are the more evolved species, and, and the whole of evolution, more or less is even put towards, getting towards the more intelligent, creating more intelligent cells and, and species. So, that is why, human beings thinks that, they are the most evolved because, they were the last formed, you know, the last species formed. So, if there is another species formed after human being, they will be more evolved because, evolution always, you know, works along the path of intelligence. So, whatever is the more intelligent, self sustaining process, they will work towards that. So, what is the major difference between this, this cell growth that you see over here, and the fungal growth is, what he just, you know, ((Kaushik)) just mentioned is, this mass transfer resistance is lot lesser here, as compared to here, because, you have fluid around it.

So, which means that, nutrients can enter each and every cell, each and every cell; for each and every cell nutrient is made available; whereas, what happens is that, there is a hierarchy almost here that, in a, in a fungal growth, first the outside cell, the outline cells near the border, should have nutrients and they should grow; only after they have eaten, they will pass on what is left, to the one that is inside. So, both mass transfer resistance are both here and there; it is a lot more over here actually, and so, from sustainability point of view, nutrient sustainability point of view, what happens is that, the accessibility of nutrient to the species inside, to the cells inside, is lot less than the accessibility of nutrient to, in, in the species outside, right. So, that is the evolutionary perspective; from a simple, chemical engineering point of view, you, you can kind of try, sort of trivialize it almost, and say that, the surface area for the mass transfer that is available, is more when a single cell is there, as compared to the surface area of mass transfer, when the

colony of cell; but, I would not go to that level, because as I said, that will be almost trivializing a process, that is as complicated as, grand and as revolutionary as this one.

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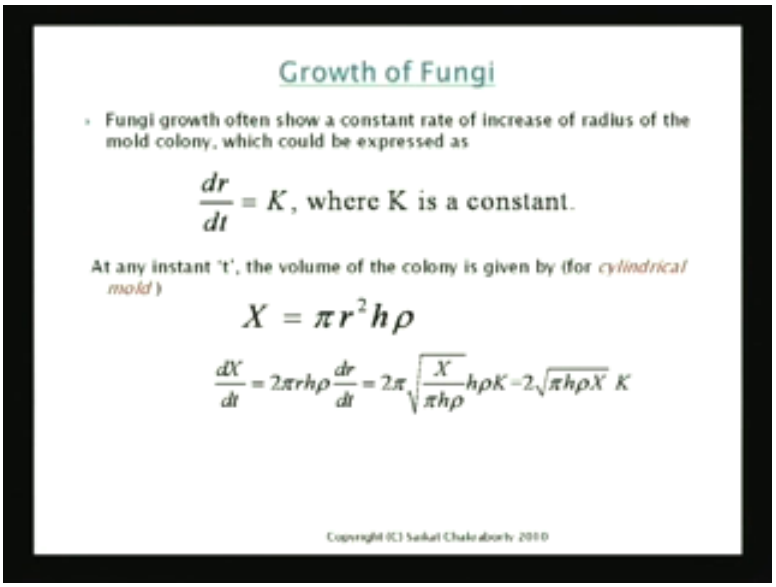

So, the basic thing about fungal growth, something that I just discussed is that, it grows as a colony, as a mold colony. ((So, this will be here was I write)). So, it grows as the mold colony, and it shows a constant rate of increase of radius, and, and you know, this is happens, whenever some species, anything, grows as a colony; for example, the question I gave you in the test was about this growth of tumour, and tumour also grows as a mold, like a mold. So, it grows together as a colony, and therefore, this shows a constant rate of increase of the radius. So, anything that grows as a, as a mold, mold colony, shows a constant growth of, rate of growth of the radius; constant rate of increase of radius. The reason being that, you know, why, because, see the, it is that, total amount of nutrient that is, that is entering the system is a constant. So, it is not a single cell; it is, I mean, sorry, it is...So, all the cells together, are acting like a single cell over here, right. So, that is the major difference. So, whatever nutrient is available, is available to the whole colony of cells. And then, there is a gradient within it, and we will study, look at the gradient, how, what happens and so on.

So, so, if you have d r d t, which is a rate of increase of the radius with time, that equals K constant and at any instant t...

K is a constant

K is a constant, yes, because that is what happens in the fungal growth; the radial...

Fungi (( ))

(( ))

No, we are talking about single mold over here; it is not the, a mold that is not breaking; a single colony of cells, that is growing. See, there is a process which can break only after it has reached the threshold; it is not that, every fungus will, will lead to another fungus, to fungus; it will reach the...What happens is, a mold will reach a certain threshold of radius, beyond which, it cannot take itself and then, it will break; and, I will also come to what is that threshold; I will, I will, I will show you that. So, this is the process, where the, the fungus itself is growing as a mold; the single fungus is growing as a mold and the rate of increase of radius is the constant over here and the...So, we considered here, the, in this problem that we do today, we considered a cylindrical mold. So, if you have cylindrical mold, then, the x is pi r square over h times rho.

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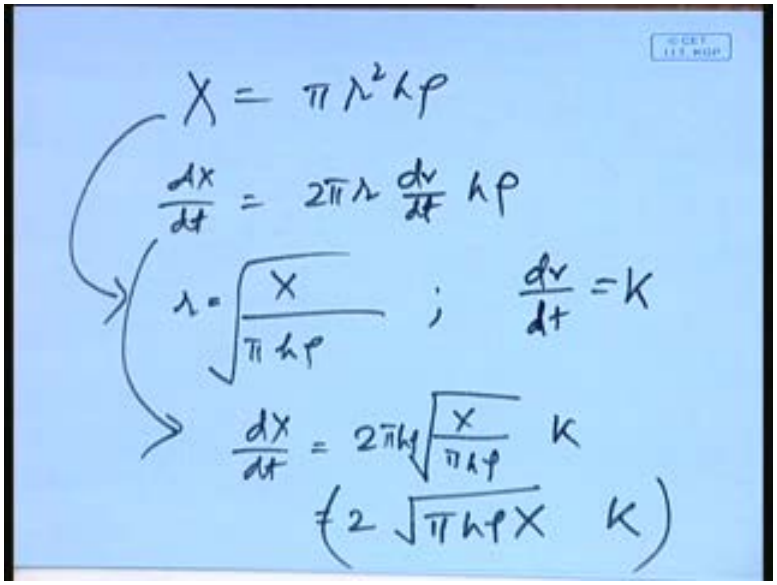

So, this is the radius at each point of time, which is increasing; this is the height of the mold and rho equals the density, fine. So, this is what you have. Now, d x d t would there, therefore be, since the height is not increasing, d x d t, it simply depends on the increase of the radius of the mold, fine. So, this is what we do; we differentiate both sides of the problem. So, you get, you get 2 2 pi r h rho times d r d t, fine.

So, what we are trying to do over here, next, what we are trying to do is, simply express everything, in terms of x. See, when we did the last model, we had everything in terms x. So, we want the growth rate, not in terms of the radius, but in terms of the cell itself. So, d x d t. Then, what we do is, simply replace your r over here, by square root of x, that you get here, from this equation, right. So, and then, you get this; let me show it here, without any confusion. So, x is equals pi r square h. So, d x d t is 2 pi r d r d t times h row. Now, from here, what I get is that, r equals x over pi h rho square root of that, and I know that, d r d t equals K. So, I put that over here. Again, d x d t equals 2 pi square root of x over pi h rho, h rho and K, which is 2 and K, right. So, then, you can simply go ahead and integrate this and find out, how the mold changes with time. So, You assume that, at the start, the mold had a total weight of x 0 or something, and then, you can just quickly go and integrate it, and then, you get x as a function of time and x 0; straightforward integration. Fine, clear?

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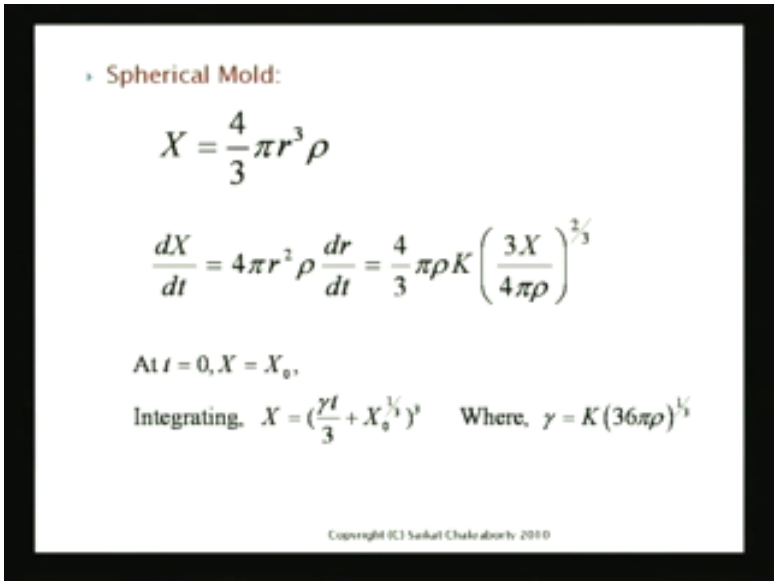

Now, what we look at, is a same problem, but, we are now looking at spherical mold and you know, some fungi will grow cylindrical, some are spherical. So, again, you can repeat the same steps. So, x equals 4 third pi r cubed rho. So, d x d t would be 4 pi r square d r d t rho and then, you can replace again, r from that, and then, you instead of half, you will get a 2 third over here, which you can again integrate ((no audio 45:58 to 46:34)).

So, integrate, this is what you get, x equals, some gamma t times over 3 plus x 0 to the one third whole, whole cubed. So, what was your expression for the spherical mold? It was some lambda t times something square and this one, you get gamma t times cubed. So, which means that, the spherical mold will grow much faster than a cylindrical mold, right; because, this is cube of time and that has a square of time.

(( ))

K, got K d r d t as constant, right, to start with; that was the assumption. It is not a strictly valid assumption, but, sort of, reasonably valid assumption. Once you are done, just let me know. Finished?

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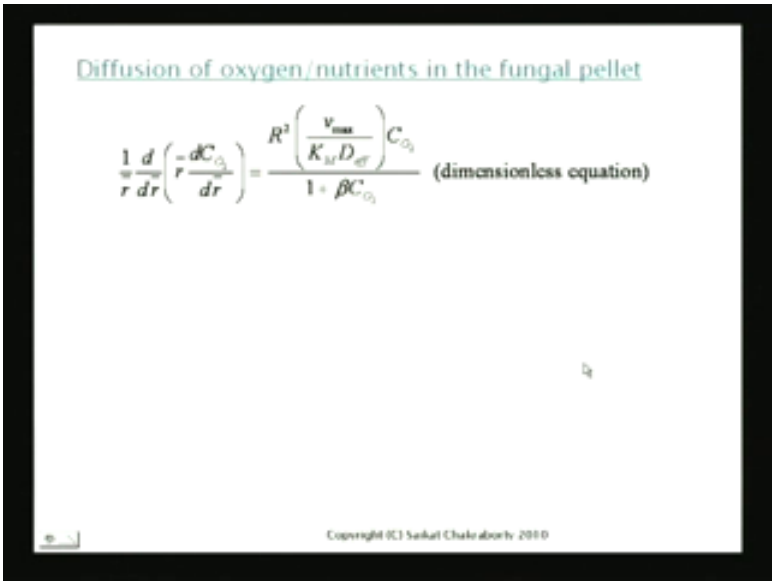

Now, comes the question that, if just like, like we did for the, in, for the growth of the, for enzymatic reaction, then, we did the same thing for normal cell, cellular growth; first, we looked at the, looked at the aspect of growth, that reactive aspect, and then, we looked at a mass transfer aspect. So, same thing, we are going to look at exactly, now, that is, look at the set of mass transfer, that will partly answer your question about the threshold, and which is the point that, it can keep growing. So, when it cannot keep growing any further, it will break into 2, to reduce. So, that is again evolutionary thing, to reduce the mass, amount of mass transfer resistance, that is offered to it. So, the, that, that is about we are going to look at now. So, excuse me. So, this is a cylindrical, cylindrical model that we are taking; cell cylindrical fungal palette; let me just go back.

So, this is what we did for the growth process, but, this growth process that we are talking of, is not, not a complete growth process, the reason being that, there is mass transfer resistance, that is offered to the substrate; so, because, the substrate can only reach the outside. So, that is the major difference from here, as I explained, to with, major difference between this and the single cell model. So, this is the substrate; I had referred to that as an, at oxygen, but, it does not have to be oxygen; you know, it should be everything else, oxygen, carbon dioxide, carbon, hydrogen, everything put together, let us say; but, let us assume it to be oxygen.

So, this is the equation in dimensionless form and the reason I wrote it this way is that, you know, we can go back and we did already, we did this already for the enzymes and you can go back and look at the dimensionless form, for the immobilized enzyme; if you remember, just before the exams, (( )). We showed how to make a dimensionless for the immobilized enzyme and exactly the same thing and so, beta you know. So, these are all these, same, same coefficient that we had before, and this has to do with, yes, this has to do with the Michaelis-Menten kinetics over there. So, this is dimensionless form, but, if you do not trust this form completely, then, we can go and derive it from what you had, but the reason I am not repeating is because, we had already done this in the immobilized enzyme part.

So, so, 1 over r. So, r bar, this is r bar, is the dimensionless form of r. And, how do you make it dimensionless? Just make it dimensionless with some initial radius, because the radius is growing. So, just make it dimensionless with an initial radius. So, d r r r bar times d d c d r times, this is the reaction. So, what is happening is that, this is the diffusion that is occurring of the substrate, inside the, inside the mold, and there is reaction that is occurring. Couple of things that we need to understand this, you know, before we go further with this; one is that, as in the cell, you know, while in the cell, we neglected the gradient, mass transfer gradient of the substrate within the cell, if you remember, but, we cannot do it here; why is that, because, the cell is much smaller entity.

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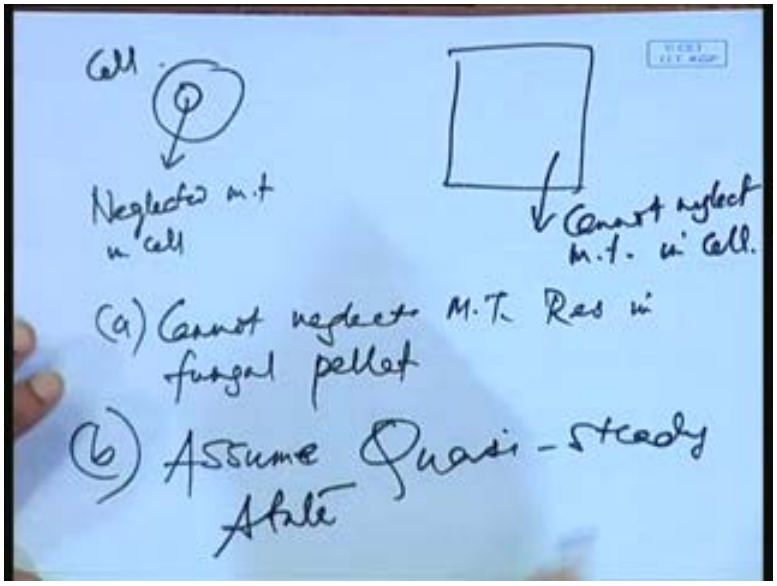

So, what we did here, when we did the cell example was, and this is the fungal model. So, we neglected the mass transfer gradient, neglected m t in cell; we cannot neglect m t in cell, because, the length scales are much larger here. So, the diffusional gradients are going to be much larger over here. Second is that, this is it, cannot neglect mass transfer resistance in fungal pellet and b, let us go back to the screen over here, what you see is a steady state; this is the question I have for you; what you see is the steady state equation; but, the fungal pellet is growing. So, where is (( ))? Why is (( ))? There should be, right; fungal pellet is growing. So, if you have an, the whole process is steady. So, what is happening here? ((no audio 52:33 to 53:03)) Why do we assume steady state? We are running out of time today, but, I will just explain quickly, why. What we do is, let us, let me write it here. Assume, this is a very important thing, and as we will start tomorrow, next class with this quasi-steady state. Again, this may be a new concept that we are, you are dealing with today.

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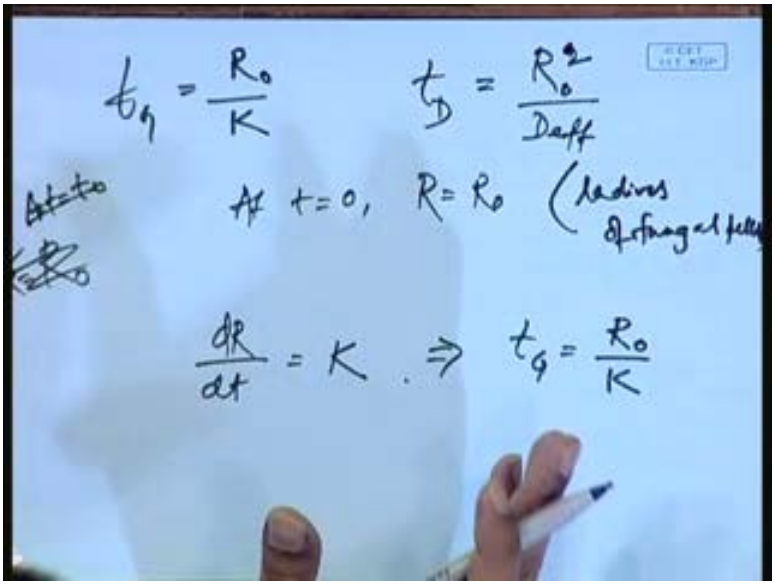

So, this is a, this is different from the assumption of quasi-steady state in the enzymatic case; please understand. What is happening is that, there is an unsteady process that is happening, that is the growth of the fungus; and, there is another, probably another unsteady process, which is the diffusion of oxygen into the cell. Now, whenever there are a couple of processes, two or three processes, and we want to make some assumption about one of these processes, what we do; we compared the time scales of these processes, fine. So, what are the time scales over here? How do we compare the time scales? One is the time scale of growth, fungal growth; t g, let us call it; the other is a time scale of diffusion of the oxygen. So, what is the time scale for diffusion? Let us assume that, at any point of time, at a certain point of time, at t equals t 0, R equals R 0; that is, the, at t equals t 0, R equals R 0; that is, the radius of the fungal pellet; is some value, we need to assume some value; otherwise, we cannot do radius of fungal pellet. So, what would be my diffusion time scale?

(( ))

R 0 square by d effective, fine. What would be my growth time scale? What would be my growth? So, if the fungus is, if the fungus is growing, in general, right, the radius of the fungus is increasing. So, what would be my growth time scale? We had it in the last example we did; just have to use that; what is d r d t? K. So, what would be my growth time scale?

(( ))

T g would be, not into, r 0 over K; r 0 over K, fine. So, if you have to assume quasi-steady state, what is, what quasi-steady state of what? (( )). What does the quasi-steady state mean? Quasi-steady state, that you have assumed, if I go, let me go back to the screen here, what it means is that, quasi-steady state means is that, I wrote a steady state equation for the diffusion of oxygen; but, I am writing a steady state equation for the growth of the pellet; for the growth of radius of pellet, which means that, the diffusion of oxygen is much, much faster, than the growth of the, the radius movement of the radius of the pellet, the radius of the pellet, the fungus radius, and this is not true; you know, in real life, the fungus radius, it does not change every second; it changes over a period of days; whereas, oxygen diffusion is taking place over, over the, over time scales of minutes; is that clear to all of you?

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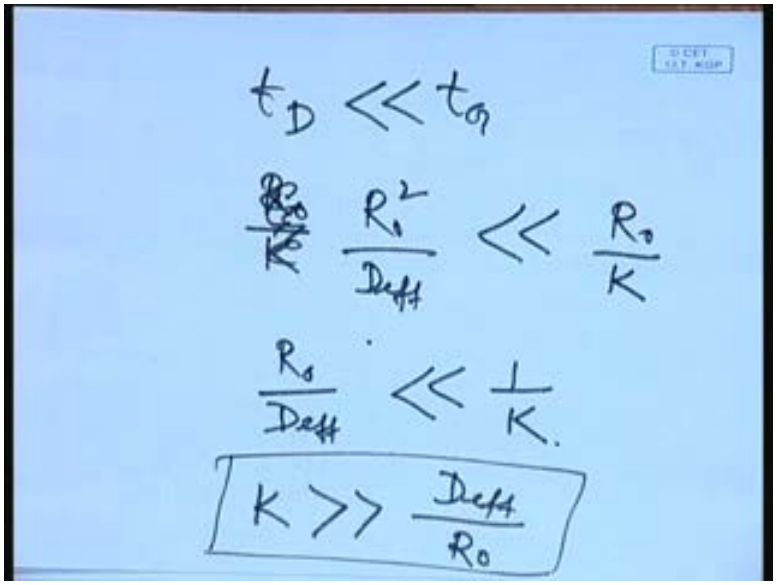

So, what I need is that, the diffusion time scale t D, what is the relation between the diffusion time scale and the growth time scale, and t G over here; what would be the relation? t D should be...

(( ))

Much much greater.

(( ))

Time scale, should be much, much smaller than t G. So, t D should be much, much smaller than t g; that is my requirement; which means that, if I put t g, t d should be much, much smaller than t g; which means, R 0 over K should be, sorry; not R 0 over K, R 0 over D effect, R 0 square over D effective should be much, much smaller than R 0 over K; which means that, R 0 should be, R 0 over D effective should be much, much smaller than 1 over K; or K should be much, much greater than D effective over R 0, fine. So, this is the criteria that we need, for quasi-steady state to be valid. If quasi-steady state is to be valid, then, we can go ahead and write this; if quasi-steady state is not valid, then, what you would do?

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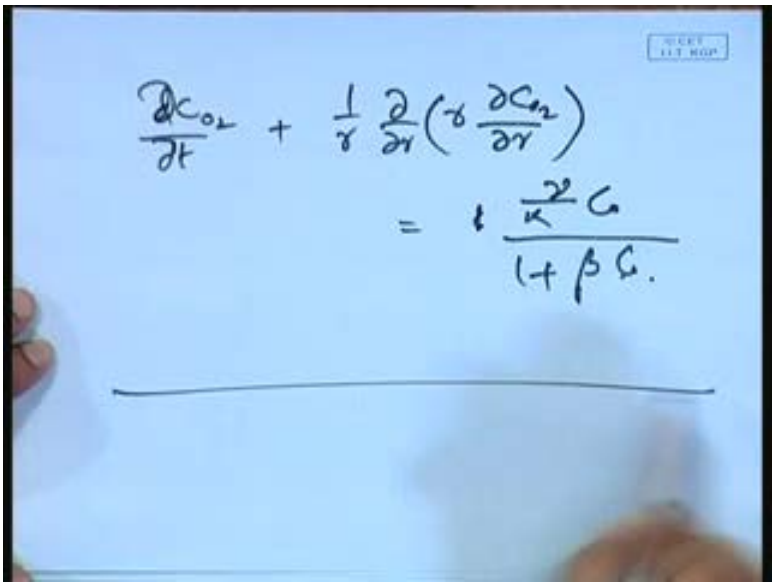

Then, you have to write, d d c over d t, del c over del t, sorry, plus 1 over r del del r of r del c o 2 del r, equals some c o 2, c o times mu over K 1 plus beta c o. So, we will stop here today. We have run out of time and we will continue from here in the next class.