Bioreactor Design and Analysis
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Lecture 05
Design of Batch Bioreactors - Part 3

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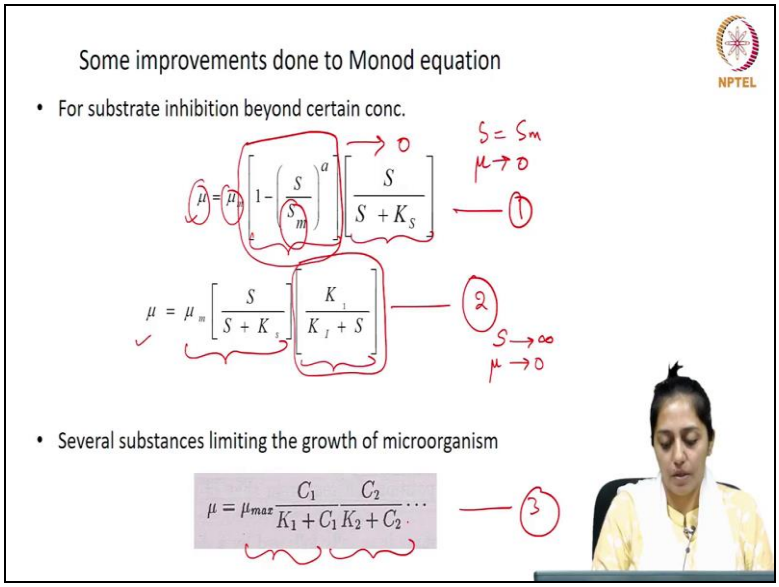

Welcome back so uh yesterday we were talking about some of the modifications which have been made in Monod's growth model to depict growth rate of the cultures in fermentations. So let us see some of these modifications for substrate inhibition beyond certain concentration the equation number one. Where the first term of the equation is what which is demonstrating the inhibition effect of the inhibitory substrate on the specific growth rate.

If you see the second equation the first sorry the second term in the second equation is what is depicting the substrate inhibition effect on the specific growth rate of the culture. So if you remember Monod's model the first term multiplied by the maximum specific growth rate in equation 2 is nothing but our Monod's model and the second term is what has been incorporated in it to account for the substrate inhibition during growth.

In the equation one similarly the second term is what is the limiting term of the Monod's model and the first term here is the term which will take into account the substrate inhibition effect on the specific growth rate of the culture. Now the difference between equation 1 and equation 2 is the fact that the equation 1 demonstrates a phenomena where there is a defined

substrate concentration called as S m at which the specific growth rate will become nearly equal to zero.

So to understand this you can do a substitution of S in the equation as equal to S m and you will be able to find that mu then becomes equal to 0 while in the equation 2 if S tends to infinity your mu then only tends to zero which means that if you make a plot of specific growth rate versus substrate concentration.

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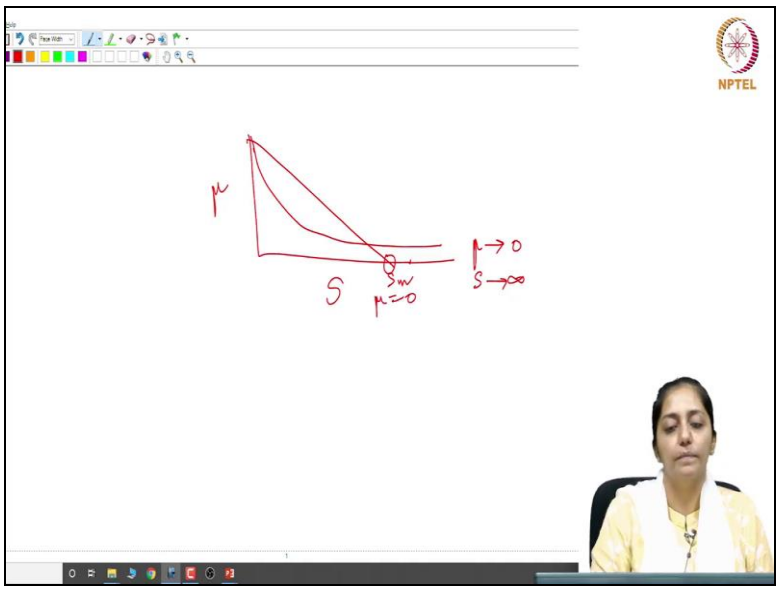

Then you will observed an asymptotic behaviour which states that mu is tending to 0 as S tends to infinity. While in the other case at S some defined concentration S m mu will become equal to zero. Then you can see at the bottom of the slide equation number three it is demonstrating the limiting effect of more than once critical substrates present in the medium. So Monod's model assumes that there is only one critical substrate present in the medium limiting substrate.

But if suppose you are finding there are more than one limiting substrates which are present in the medium then the limiting terms with respect to those substrates can be incorporated in the Monod's model equation.

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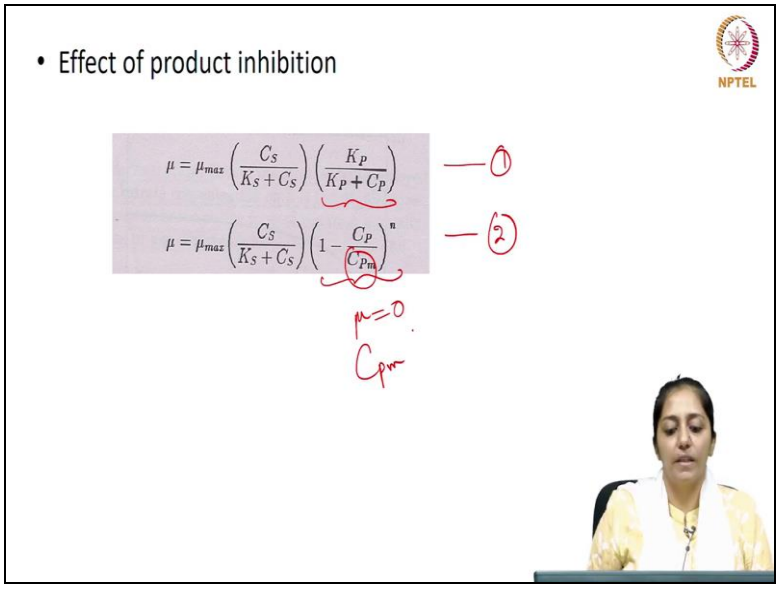

Similarly there are models which can take into account the effect of product inhibition. So if you see here the two equations they are showing a similar behaviour as the substrate inhibition where the equation one shows an asymptotic behaviour in which the specific growth rate of the culture will be reducing to 0 or nearly 0 at infinite concentrations of the product. While in the second equation at a defined concentration given as C Pm the specific growth rate of the culture will become equal to 0 which means complete inhibition can be observed complete growth inhibition can be observed at a defined concentration of the product.

So as you see in your branch kinetics the behaviour of the culture in the presence of a substrate or a product accordingly you should adapt a mathematical equation to demonstrate its effect on specific growth rate.

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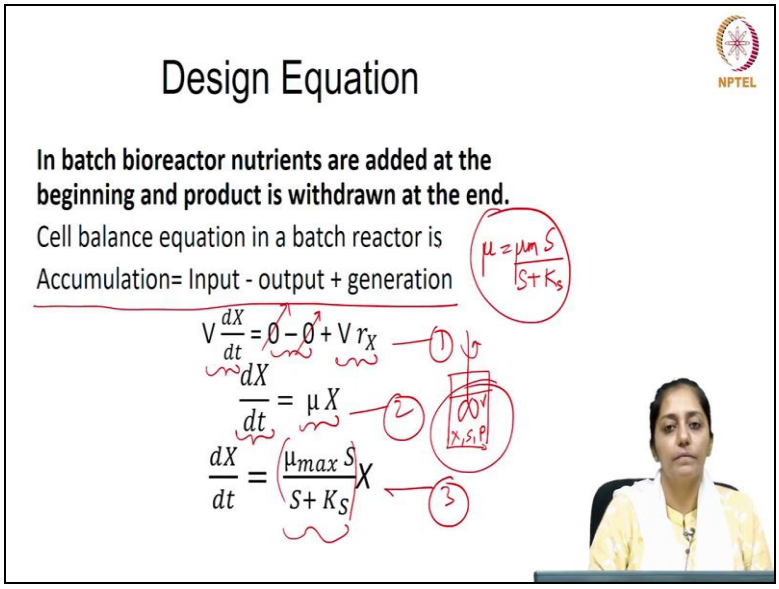

Let us move on to the design equation for a batch reactor. So in a batch bioreactor nutrients are added at the beginning and the products are withdrawn at the end. So there is no intervention during the cultivation period and hence it is called a closed system. So, if you do a cell mass balance for a batch reactor and apply law of conservation. So if we do a mass balance for the reactor then the rate of accumulation of biomass which is on the RHS becomes equal to the rate of growth of the biomass which is shown on the LHS in a reactor especially in a batch reactor.

And the terms which have been brought to zero one is the input term and the other is the output term in the continuity equation. So if you can see the continuity equation which states here the rate of accumulation of biomass is equal to the rate at which the biomass is coming in minus the rate at which the biomass is moving out plus the rate at which the biomass is getting generated inside the space or the reactor here and minus if the biomass is getting consumed.

So we know that the biomass is not getting consumed during the batch cultivation it is only getting generated the consumption term is not shown here. So for a batch bioreactor the rate of accumulation of biomass or the rate at which the biomass concentration is changing with time becomes equal to the growth rate of the culture inside the reactor. Now if the specific growth rate of the culture can be defined by Monads model as shown in equation three then you can further expand equation 2 as equation 3.

So this term is what we know as Monod's model which talks about how specific growth rate is related to the limiting substrate concentration.

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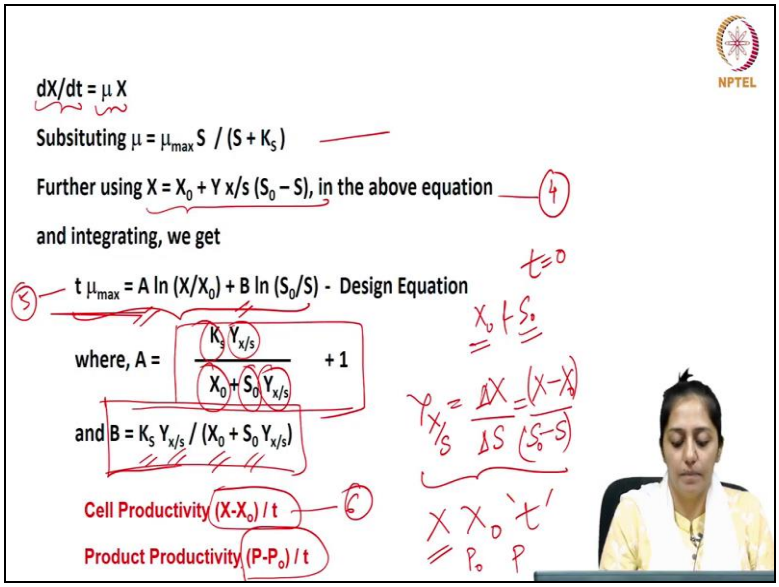

So we know dx by dt was the rate at which the growth is happening which is nothing but specific growth rate multiplied by the cell mass concentration. Now if we further substitute this equation let us call it as equation 4 we know the yield coefficient as I said in the last class is can be written as delta X by delta S so this is yield of biomass with respect to substrate. So in case let us assume that X 0 and S 0 are the initial biomass concentration.

And S 0 is the initial substrate concentration inside the reactor initial means at t time equals to 0. So Y by X can be therefore written as if X is the final concentration then Y by X is given as for a batch as a fraction of X - X 0 by S 0 - S which is the amount of biomass produced in the batch fermentation per unit the substrate consumed. Now if now in the equation 3 if you see equation 3 there are two variables X and S.

Now in order to have one variable X or S so that you can integrate the equation you need to have another equation which can relate X and S. So this equation 4 can be used as the second equation to solve or predict X or S versus t when we do the substitution and we integrate the equation 3 we end up in a design equation which is given as equation 5. And A and B in this equation are constants given below.

In terms of the initial biomass concentration the initial substrate concentration the yield coefficient and the Monod saturation constant. So this entire entity is therefore a constant.

Similarly B is a club of the constants K S by X by S X 0 and S 0. Now for a batch fermentation the cell productivity or cell volumetric productivity where X is the biomass concentration X 0 was the initial biomass concentration.

So volumetric productivity is defined as the amount of biomass produced per unit time we know this much amount of biomass which is X is getting produced in time t which is batch time so then the volumetric productivity is given as X - X 0 by t as shown in this equation. If you see product productivity again if P 0 was the initial product concentration at time t is equals to 0 and P is the final product concentration after batch time t then the product productivity can be given as the amount of product produced during the batch per unit time as shown in equation 7.

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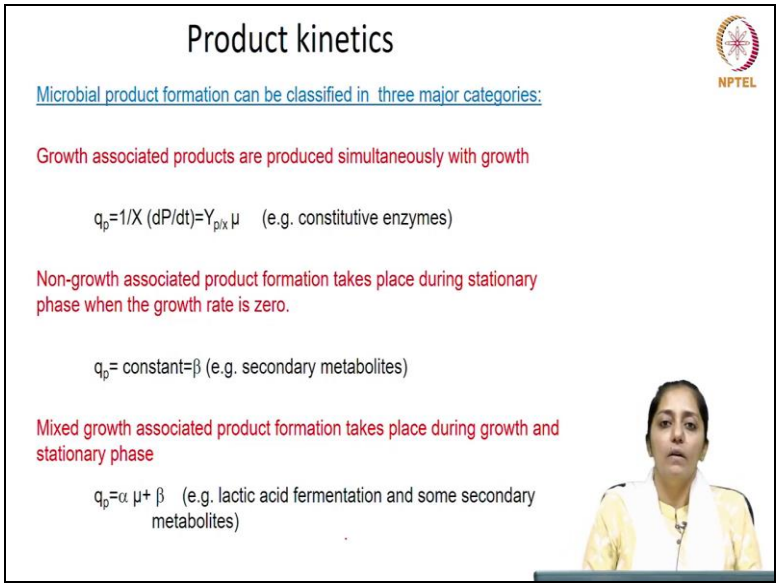

So now let us talk about the product kinetics. Product kinetics would mean the rate at which the product is getting formed or how the product concentration in a batch is changing with time. Like growth models there are various models which can demonstrate product formation kinetics in batch fermentations. One of the well-known model equations is called ludicking pirate equation which can very well demonstrate growth associated and non-growth associated product formation rates.

So product kinetics in microbial fermentations can be classified into three major categories the growth associated products which are produced simultaneously with growth like for example constitutive enzymes. So if you see the first equation on the slide where q p stands for specific product formation rate.

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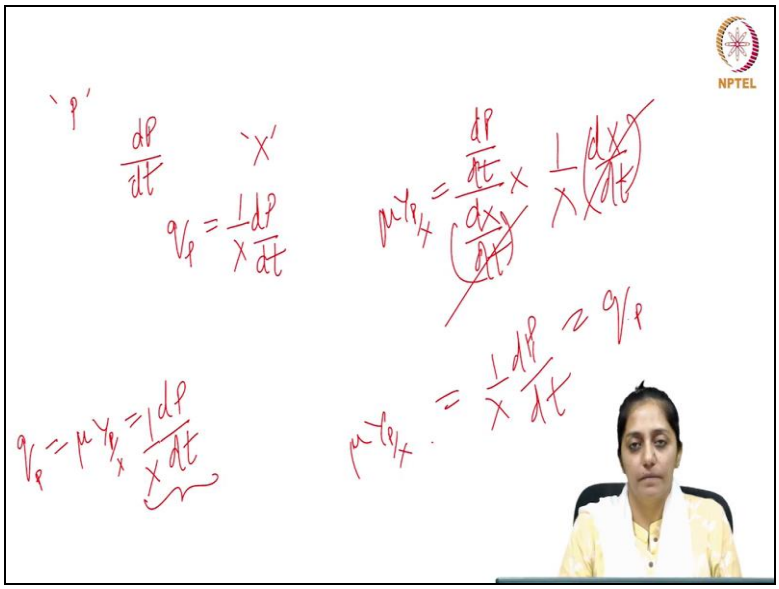

So as I said earlier so if p is your product concentration then the rate of product formation is your dp by dt q p is your specific product formation rate which means it is 1 by x dp by dt where x is your biomass concentration. So qp is what is written as 1 by x dp by dt now which in other terms can be written as the yield coefficient multiplied by the specific growth rate. Now Y p by x is the amount of product formed per unit biomass produced.

And mu is specific growth rate can be written as 1 by x dp by dt this is equation 1 this is equation 2. So if we want to relate q p in terms of Y p by x and mu if we multiply mu by Y p by x you will see you end up in dp by dt multiplied by 1 by x substituting equation 1 and equation 2. So your equation 1 is Y p by x dp by dt by dx by dt and equation 2 is specific growth rate which is 1 by x dx by dt the typo has been corrected down.

So now I hope you can understand when you multiply equation 1 and equation 2 the RHS you will end up in so your mu times Y p by x becomes 1 by X dp by dt which is equal to q p which is specific product formation rate. So this is what is equation 1. So this is used to demonstrate growth associated product formation which means that the product formation is a function of the growth rate.

Now let us talk about another type of product formation which is non-growth associated product formation in which the product formation takes place during the stationary phase when the growth is not happening or the growth is zero. So then your specific product

formation rate is said to be constant it is no more a function of growth rate. This behaviour is generally observed in secondary metabolite formations during fermentations.

When it is a mixed growth associated product formation then your q p is not only a function of the growth associated part but it is also a function of non-growth associated phase. So then you combine both the growth associated and non-growth associated terms and you demonstrate the specific product formation rate as a club of both the functions. So Y p by x has been replaced as a constant alpha and your beta is it is the same.

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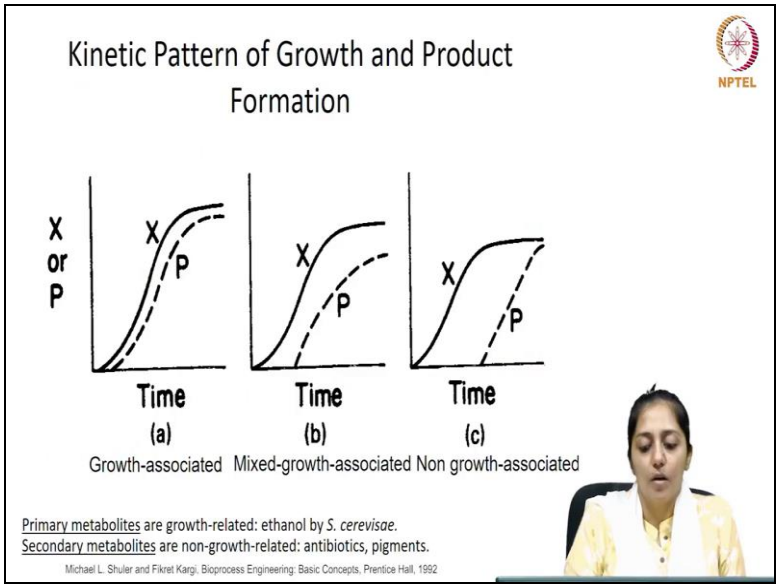

So this is how if you make a plot of the biomass or the product with respect to time in a batch culture you may observe these different kinds of profiles. If you see profile a the product concentration is changing having the same trend as the biomass formation. This depicts growth associated product formation if you see curve b the product starts getting formed during the growth phase of the culture and is continuing in the stationary phase as well.

So this is a big growth associated product formation. Whereas in the plot 3 you will observe that the growth has stopped at a point where the product formation has begin which means that it is a non-growth associated product formation and that too the rate of product formation is constant. So an example for growth associated product formation is primary metabolites formation and non-growth associated kinetics behaviour will be observed for secondary metabolites.

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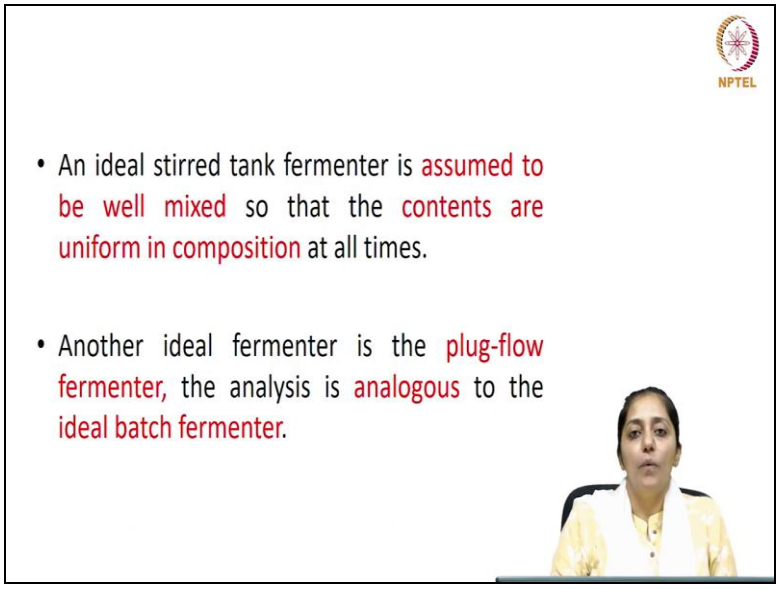

Now apart from well mixed stir tank reactor configuration which is assumed to be ideal when it is well mixed so that the contents are uniform in suspension all the time. Another ideal fermenter is the pluck flow fermenter and the kinetics is analogous to the ideal batch mixed flow fermenter.

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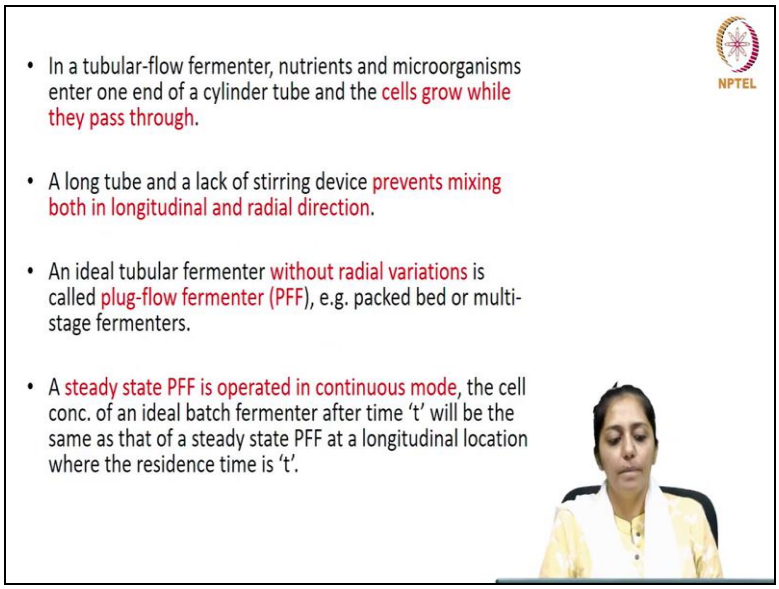

So what is a plug flow fermenter? It is a tubular flow fermenter in which the nutrients and micro organisms enter one end of the cylindrical tube and the cells grow while they pass through that tube. So it is a long tube and there is a lack of steering device which prevents mixing both in the longitudinal as well as in the radial direction of the tube. Now an ideal tubular fermenter which we call as pluck flow fermenter we assume is without radial variations which means that there is no variations across the radii.

Examples of plaque flow fermenter are packed beds or multiple stage fermenter when there are continuous reactors combined then also the kinetics can be equated to a plug flow fermenter type. A steady state plug flow fermenter is operated in continuous mode which means that continuously the broth is coming inside with the starter culture and there is a broth leaving the other end with the grown culture.

A steady state plug flow fermenter the cell concentration of an ideal batch fermenter after time t will be the same as that of the steady state plug flow fermenter at a longitudinal location where the residence time is t.

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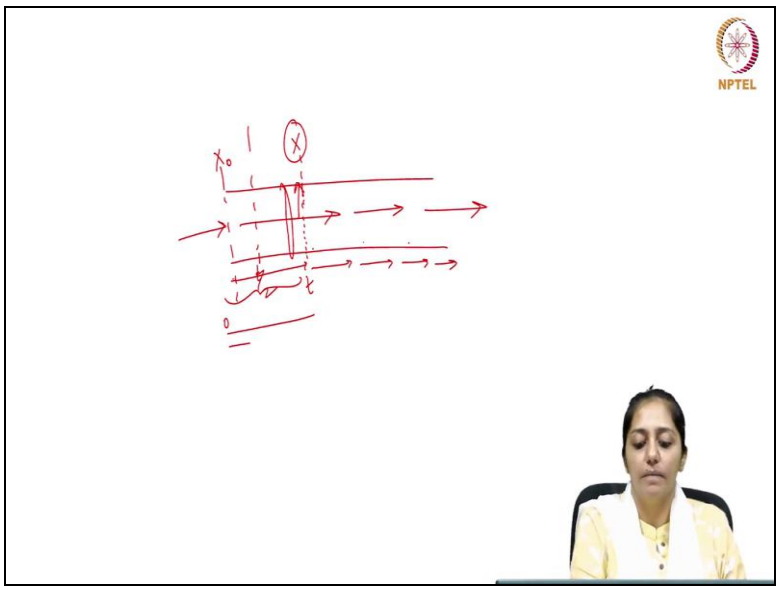

Let us see, so a tubular fermenter is a longitudinal tube and in there is an inlet an outlet a containers flow. There are no variations radially the concentration is only changing longitudinally. And the kinetics of a plug flow fermenter running at steady state is same as that of a ideal batch reactor. It means that suppose at time t the biomass is X so it means that it can be equated to a batch reactor which has run for a batch time of t starting from X 0.

And the harvest time which is the batch time t the final biomass is X. So the distance corresponds to the time spent by the culture in the fermentation or the cultivation time. So at time t half there is some biomass and this is how it keeps changing longitudinally. So just for clarity I will repeat. A steady state plug flow fermenter is operated in a continuous mode where the cell concentration of an ideal batch fermenter which we have just studied after time t will be the same as that of a steady state pluck flow fermenter at a longitudinal location where the residence time is t.