Bioreactor Design and Analysis
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Lecture 15
Design of Continuous Bioreactors - Part 3

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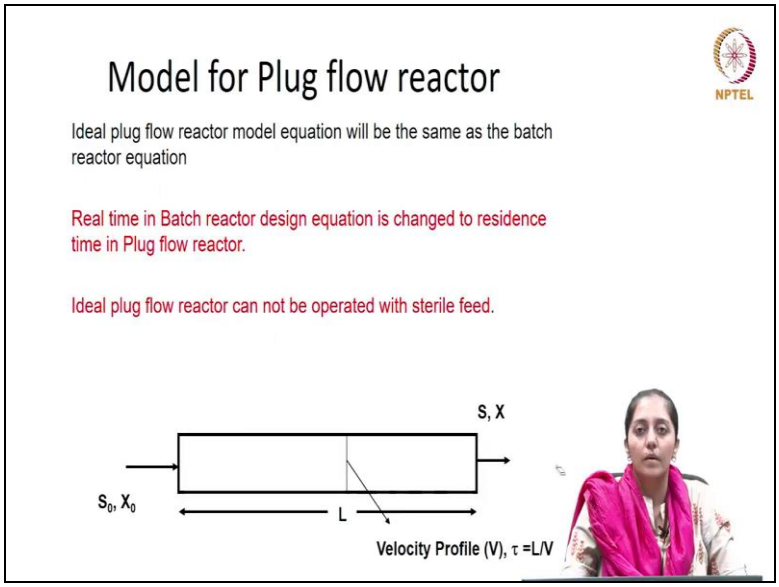

Welcome back students, so in the last class we were discussing design of continuous bioreactors. So we will continue the same topic let us begin with the model for plug flow reactor which is the kinetics is like a batch reactor but the flow is continuous which means that the substrate is continuously being fed in and as it moves through the tubular reactor the substrate gets converted to product.

So the ideal plug flow reactor model equation is the same as that of the batch reactor equation. Real time in batch reactor design equation is changed to the residence time in the block flow reactor. Ideal plug flow reactor cannot be operated with sterile feed. So if you see the slide the picture on the slide the length of the tubular reactor is L the inlet substrate which is being fed in inside the tubular reactor is S 0.

And because it is not sterile the biomass concentration is X 0 and as it comes out from the other end the substrate gets converted and the residual substrate concentration therefore changes. So the outgoing substrate concentration has been represented as S and the biomass due to growth due to substrate consumption has changed to X from X 0. So it is an ideal plug

flow reactor if L is the length of the tubular reactor and V is the linear velocity that the resonance time be calculated as L by V of this plug flow reactor.

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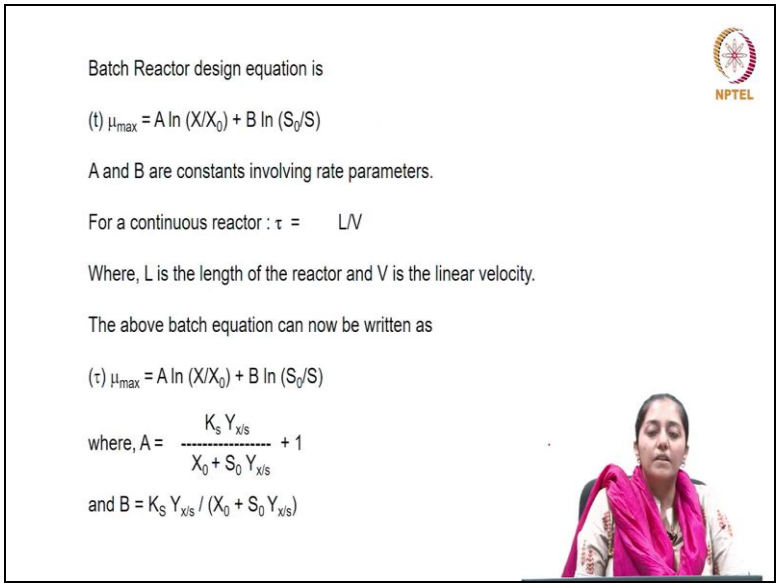

The batch reactor design we have already established the design equation as shown on the slide given as equation 1 where A and B were constants which involved rate parameters for a continuous reactor. We know now the residence time of this plug flow reactor can be given as L by V where L is the length of the reactor and V is the linear velocity. Now this batch equation can now be written as so we can substitute this t in the form of tau which is the residence time given as L by V and A and B were the constants based on kinetic parameters and your inlet biomass and substrate concentration.

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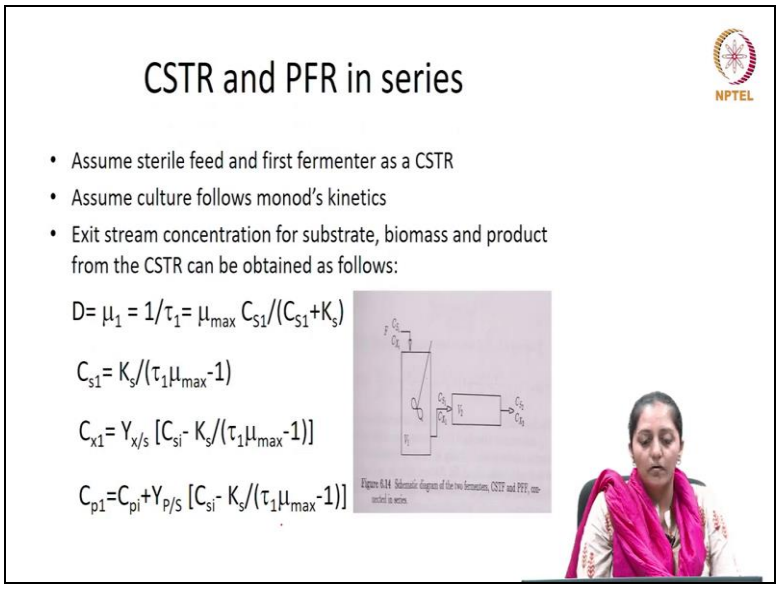

So let us see how and in what situations we need to use the plug flow reactor model. Now let us assume that it is a sterile feed in a combination of 2 reactors the first one is the continuous reactor ideal CSTR followed by a plug flow reactor an ideal plug flow reactor. So I said the incoming stream we are assuming it is a sterile feed and the inlet substrate concentration for the first reactor will be represented by the subscript one.

And for the second reactor the variables have been represented by subscript 2. So being sterile feed C x1 is zero but there is C s1 as the incoming substrate feed inside the continuous reactor with the volume V 1. So because it is an ideal CSTR running at steady state we have already now reduced that dilution rate becomes equal to the specific growth rate of the culture in a steady state CSTR.

So if we again use a subscript one for the first reactor then the dilution rate in the first reactor will become equal to mu 1 where mu 1 is the specific growth rate of the culture in the first reactor. Now if the culture is following Monod's kinetics or Monod's model we can further expand mu 1 in the form of Monod's model which is a function of substrate concentration. So now the substrate concentration inside the reactor is C s1.

Now because it is an ideal steady state CSTR whatever is the concentration inside the reactor will be the same concentration which is coming outside the reactor which we are giving a notation 1. The inlet substrate feed has been given the notation C si and C si because it is a sterile field is zero. So if you see this equation one it is in terms of the dilution rate the specific growth rate of the first of the culture in the first reactor which is again an inverse of the residence time of the first reactor which has been represented as tower one.

And it has been further expanded the mu has been expanded as a function of substrate concentration inside the reactor at steady state as C s1 because it is following Monod's kinetics. Then C s1 therefore after rearrangement of this equation one can be represented under steady state as a function of residence time and culture kinetic constants. So now if C s1 is known and the yield coefficient is known for the culture we can find out the outlet biomass concentration from this first CSTR.

So as a function of the inlet substrate concentration and the outlet substrate concentration and YX by S we have determined C S1 because c si here goes to 0. So this is how we can

determine now C s1. And similarly if we know the yield coefficient by P by S this we already know. Assuming the initial sum product is already there which has been represented as C pi which can you also assume as zero.

Then your outgoing product concentration or in the or the product concentration in the outlet stream can again in a similar manner can be represent represented as shown in equation 3 as a function of again the inlet substrate concentration. And the outlet substrate concentration and yield coefficient of product with respect to substrate consumed.

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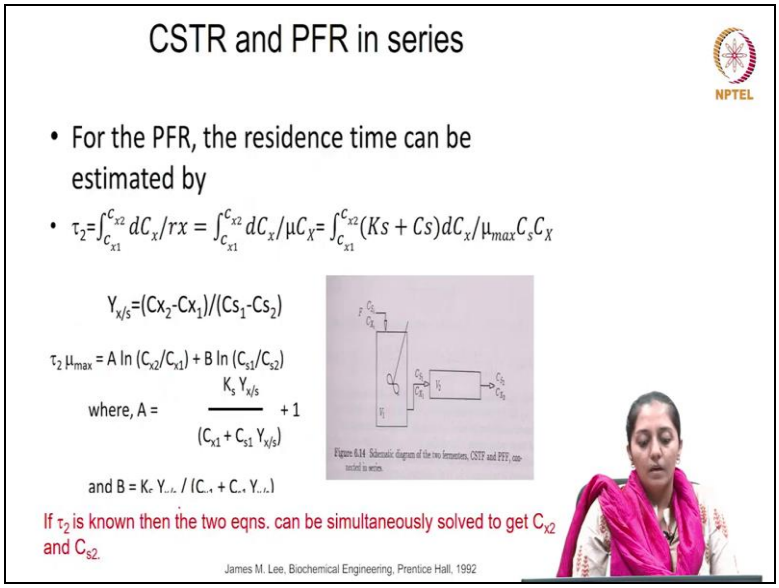

Now we have already come to know what is the substrate concentration product concentration and biomass concentration coming outside reactor 1 which is now an inlet to the reactor 2 which is a plug flow reactor. The volume has been represented as V 2 of this plus plug flow reactor the outlet substrate and the biomass concentrations in this ideal plug flow reactor have been represented as C s2 and C x2 and the inlet we know now are the outlet from the first reactors for this reactor which is C x1 and C s1.

Now residence time for the second reactor because it is follows batch kinetics can be estimated as shown here. So your residence time can be calculated by using the limits of the initial biomass concentration which is the inlet biomass concentration which is C x1 and the final biomass concentration from this reactor which comes out of this reactor which has been represented as C x2. So the limits are for the C x have been given as C x1 and C x2 of the integral and r x is your rate of reaction.

So the biomass formation rate, so now if you substitute this biomass formation rate is nothing but mu times C x it has been substituted here in place of r x and then integration has been done after substituting mu in terms of C s. So now this has 2 variables C s and C x. Now in order to integrate this we first need to remove one of the variables or substitute one variable in terms of the other.

So for that we again have another equation of yield coefficient Y X by S which shows C x2 - C x1 by C s1 - C s2. So the numerator is the amount of biomass produced in this batch reactor and the denominator is the amount of substrate consumed in this batch reactor. So, using equation 1 and 2 so 2 has been used to substitute C s in terms of C x and then the equation 1 can be integrated and solved which will lead to again batch design equation which will take this form as given in equation 3.

And A and B we have already seen in batch reactor design will be constants which are a function of the inlet substrate and biomass concentration and yield coefficients with Monod's model parameters. Now tower 2 here was the residence time of the plug flow reactor. So now once we have these 2 equations which can be used for the plug flow reactor and for the CSTR. If suppose tau 2 is known which means the resonance time of the second reactor is known then the 2 equations can be simultaneously solved to get C x2 the 2 equations equation 2 and equation 3.

Now equation three has been obtained from equation one it is the same as the batch design equation. So now there are 2 variables C x2, C x1, C s1, C s2 are the substrate variables. Now C s1 and C x1 are known there are 2 variables which are unknown C s2 and C x2 which we will use equation 2. So substitute one in place of the other and then solve the 2 equations equation 2 and 3 simultaneously.

Now the second reactor is the plug flow reactor for this plug flow reactor the residence time can be obtained can be given as we know that r x is dC x by dt for a batch reactor and r x is the growth rate which is mu C x dC x by dt which is the rate of accumulation of the biomass. Now here residence time once we integrate let us assume tau 2 is the residence time and here we have dC x by mu C x.

The integral limits it is C x1 and C x2. C x1 is the inlet biomass concentration and C x2 is the outlet biomass concentration in this plug flow reactor. Now further because mu is following Monod's can be represented by the Monod's model as a function of the substrate concentration. If we substitute here so as shown here we can write it like this and once we now solve it tau 2 is the residence time this is nothing but your batch design equation which we have already done earlier.

And if you put your limits then it becomes a function of C x2 C x1 C s1 and C s2. Now in terms of yield coefficient so yield coefficient of the culture was Y X by S which is biomass produced per unit substrate consumed in this reactor. So now we have 2 equations with 2 variables unknown variables which are C x2 and C s2. C s1 and C x1 are already now known from the first reactor.

So now we substitute one variable as a function of other variable in any one of the equations. So using equation one we will do the substitution in equation 2 and then if tau 2 is known then we can simultaneously solve these.

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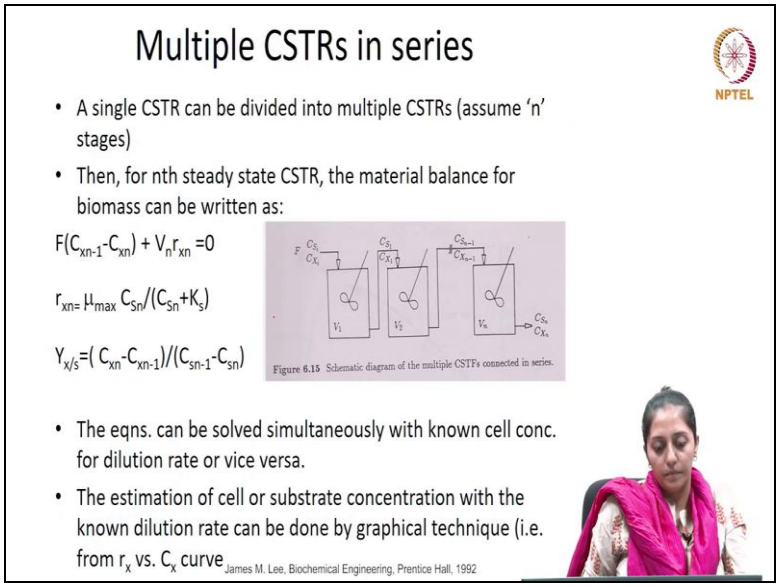

Now let us see a case where multiple CSTR's are connected in series. A single CSTR can be divided into multiple CSTR's assuming there are n such CSTRs linked together in series. Then for the nth steady state CSTR the material balance for the biomass can be given as shown here. If F is the volumetric flow rate and C xn - 1 is the inlet biomass to the nth reactor and r xn is the reaction rate of the biomass formation rate in the nth reactor.

V n is the volume of the nth reactor then at steady state the material balance of the biomass can be represented by equation one because there is no net accumulation rate happening. So now r xn can be expanded in the form of Monod's model another relationship between the X and the S can be obtained using the yield coefficient. So for the nth stage reactor we can have 2 equations one is the mass balance for the biomass across this reactor and the second is the in terms of the yield coefficient.

The amount of biomass produced is in the numerator per unit substrate consumed in the is equal to Y X by S. The equations can be solved. So, now again similarly as we did earlier the equation can be simultaneously solved with known cell concentrations and the dilution rates. The estimation of cell or substrate concentration with the known dilution rate can be done also by a graphical technique in this case.

So if you can see the subscripts used for the nth reactor have been shown here C x i and C si are the inlet to the first reactor and C sn and C xn will be the outlet from the nth reactor here.

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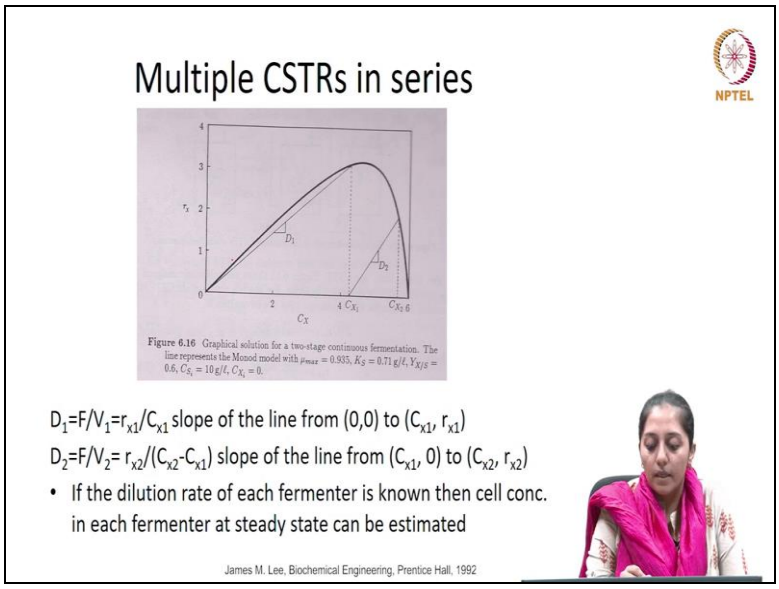

Now for one CSTR they have shown with this dark line the plot if you see how the biomass formation rate will change. So it will keep on increasing it reaches its maximum and then comes down because of the substrate depletion. So because this is a single CSTR as the dilution rate increases the biomass formation rate also increases and then it reaches its maximum and very sharply goes to 0 at washout shown as this point.

Now if this one CSTR can be divided into series of CSTR's multiple CSTRs then for the first reactor if the dilution rate d1 is known which is; nothing but the slope of this line. So if the slope is known wherever this line will cut this curve we can determine the biomass. The exit biomass concentration from that particular reactor again if the dilution rate of the second reactor is known then from this point another line can be drawn with that slope and wherever it cuts the curve again its corresponding X value will give us the exit cell mass concentration from that second reactor.

So if the dilution rate of each fermenter is known then the cell concentration in each fermenter at steady state can be estimated by this graphical technique.

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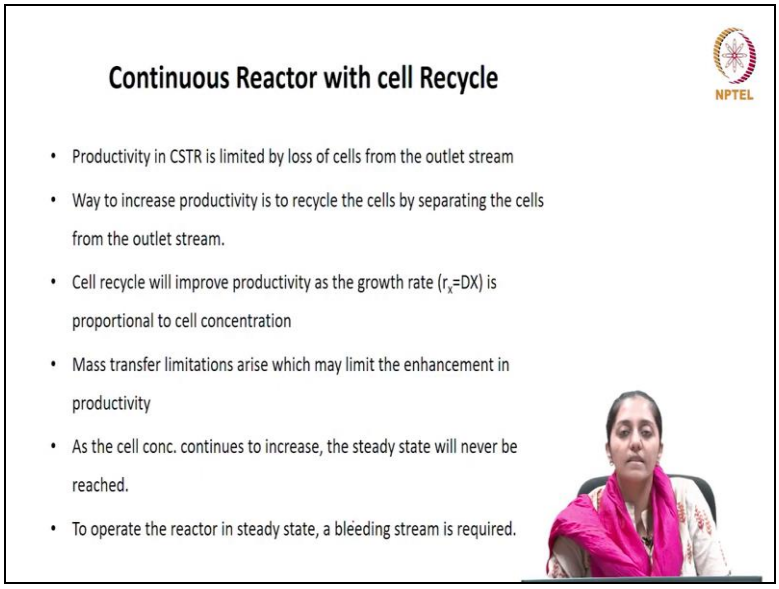

Now let us see if we are running a continuous reactor with cell recycle then how do we design such systems. So the productivity in a CSTR is limited by the loss of cells from the outlet stream is not it because we cannot run a CSTR at dilution rates greater than mu max. So the productivity is limited by the loss of cells which is happening in the outlet streams. Way therefore to increase the productivity can be to recycle the cells by separating the cells from the outlet stream.

So cell recycle therefore can improve productivity as the growth rate is a function of the dilution rate and the biomass so which is productivity. So productivity is nothing but dx so if X can be continuously increased then your productivity will increase and it is proportional to the; because it is proportional to the cell concentration. So cell recycle will improve

productivity why as the growth rate is proportional to the cell concentration r x is equals to D times X in a steady state CSTR.

Now mass transfer limitations can arise which may eventually limit the enhancement in productivity as the cell concentration continues to increase the steady state will never be able to reach. So now we know that we can increase the cell concentration and therefore the productivity. But if you keep on continuously increase the cell concentration the productivity after a while is compromised why because as the cell concentration will increase mass transfer limitations will start appearing.

And the mass transfer limitations can eventually then cause reduction in the growth rate of the cells and can limit therefore the productivity enhancement. Now as the cell concentration is continuously increasing in such systems the steady state is not able to reach. So to operate such reactors in steady state what we need is called a bleeding stream.

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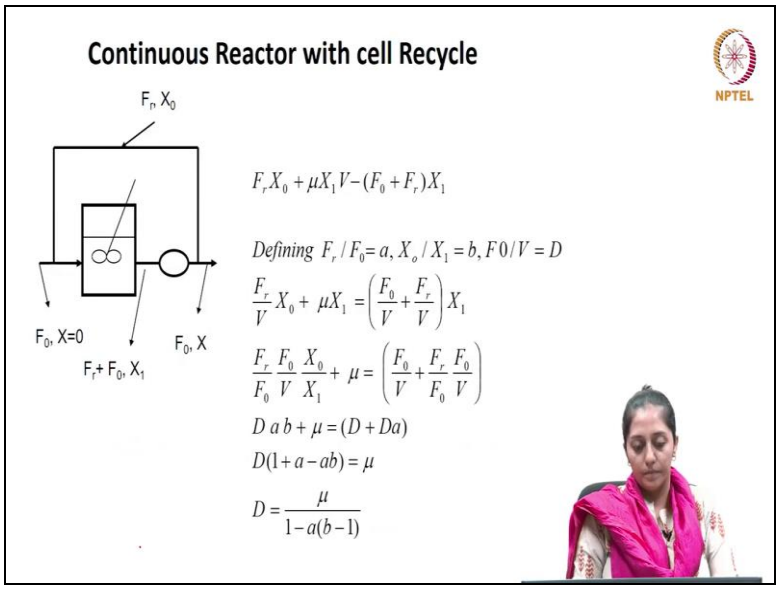

So let us design a continuous reactor with cell recycle. So please note the schematic shown on the slide the notations have been given as F naught for the inlet stream to the reactor and F r is the fraction of the stream which has been sent back as a recycle. And the cell separating device is at the outlet of the reactor as shown here as a small circle, oval shaped circle and this is the stream which is going back as the recycle.

So please note the notations for the biomass the volumetric flow rates of each of the streams and x1 is the biomass concentration inside the reactor which is running at steady state

therefore the outlet is also x1 from this steady state continuous reactor. So if you do a mass balance across the reactor then you will end up in equation 1 let us understand this. So the first term is the rate at which the biomass is coming inside the reactor the second one now because it is a steady state CSTR and a chemostat the flow rates have to be the same.

So here let us assume inside is F r + F naught so your inlet stream here is being given as F naught and it is a sterile stream so that has been not considered then here the recycle stream has a volumetric flow rate of F r with a biomass concentration of X 0. So the first term represents the rate at which the biomass is coming inside the reactor. So they have not shown the term F naught into X which is 0 because it is a sterile feed stream.

Then mu X1 times V so V is the volume of the reactor X1 is the steady state biomass concentration inside the reactor and mu is the specific growth rate of the culture. So the second term represents the rate of increase of the biomass due to growth minus F naught X1 so X1 comes out of the reactor. So it is the outlet, so F naught + F r should be the flow rate outside the reactor if the volume is constant of this CSTR.

So this was F naught and this is F r it combines so the stream flow rate is F naught + F r. So F naught + F r times x1 is your rate at which the biomass is going outside this reactor loss output and it is a steady state no accumulation so this is zero. So input - output plus growth in this is equal to 0 for this reactor mass balance for biomass. Now again F r by F naught has been represented as fraction a X 0 by X 1 again this fraction has been represented as b and F naught by V has been represented as the D which is dilution rate.

So the F naught which was the inlet stream here divided by the volume of this reactor has been represented as D. So now if we divide this equation by the volume there is F r by V term into X 0 mu X 1 V gets cancelled and again this has been divided by V so this is times X 1. So now all these have been brought in the form of F naught by V. So F naught has been multiplied and divided in the first term, so this has been then replaced as D F r by F naught given here has been replaced as a and X 0 by X 1 given here.

So the entire equation has also been further divided by X 1 and V. So x1 has been divided so this fraction is then represented as b and x1 gets cancelled. So this only mu remains in the second term and on the RHS F naught by V has been given as D and again in the second term

F r by V F naught has been multiplied and divided and again F r by F naught has been so F naught by V has been represented as D and F r by F naught has been represented as a.

So now again D has been taken common inside we will have 1 + a - ab as the fractions and on the one side only specific growth rate terms remains. So now if you see for a continuous reactor with cell recycle at steady state it is no more D is equals to mu but it is a function of mu and the recycle stream flow rates and the inlet flow rate fraction F r by F naught where F r was the volumetric flow rate of the recycle stream.

And also a function of b which is a fraction X 0 by X 1 where X 0 was your biomass concentration in the recycle stream and X 1 is your biomass concentration coming outside the reactor. So biomass separator this device is a biomass separator. So some biomass in the recycle stream of fraction X 0 so of concentration X 0 has been sent back and the outlet is X.