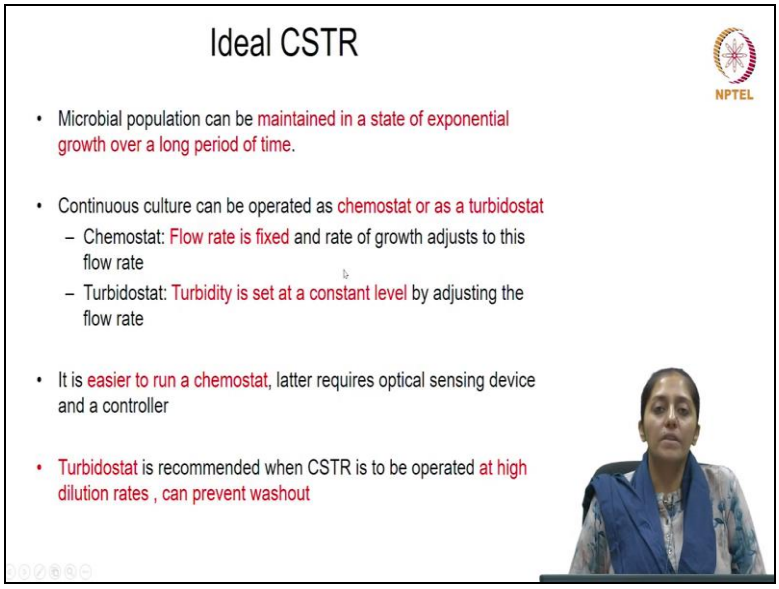
Bioreactor Design and Analysis
Dr. Smita Srivastava
Department of Biotechnology
Indian Institute of Science – Madras

Lecture 13
Design of Continuous Bioreactors - Part 1

Welcome back students. So today we are going to talk about continuous bioreactors and their designing. So we have been able to now discuss about what a bioreactors? Then we also then discussed the design of batch bioreactors. Then further discuss the design of fed batch bioreactors and the application of fed batch cultivations in fermentation industry. And now today we are going to discuss about continuous fermentation their applications and then design of a Continuous Bioreactor.

(Refer Slide Time: 00:58)



So what is an ideal CSTR? Sorry, you must have heard the term a lot of time CSTR. So the CSTR stands for continuous stirred tank reactor. Now in ideal CSTR, we say ideal because it is a perfectly mixed stirred tank bioreactor. Now ideal CSTR we can assume that the microbial population is being maintained in a state of exponential growth over a very long period of time. Now continuous culture they can be operated either as chemostat or as a turbidostat.

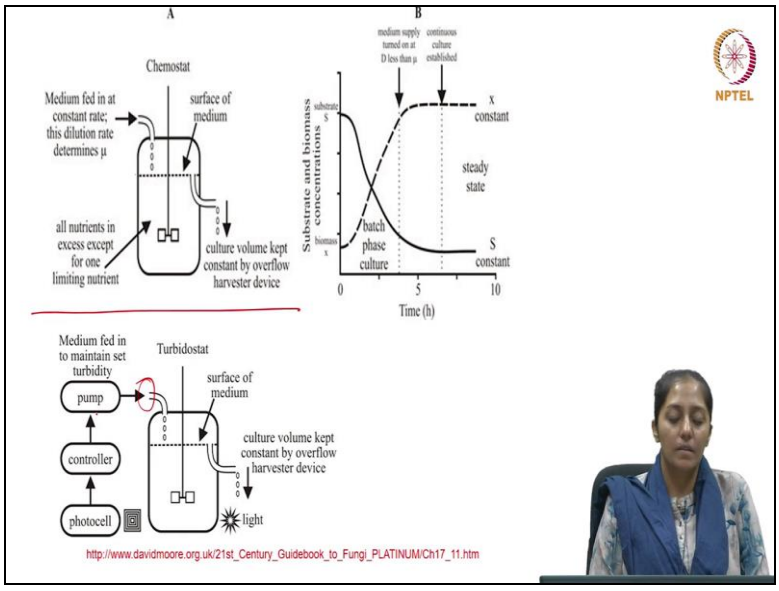
What does chemostat mean? The flow rate is fixed on the rate of growth of the culture is being adjusted to the flow rate. So this gives us an opportunity to manipulate the growth rate of the culture as the modulation is in the flow rates. Turbidostat, now in a turbidostat the

turbidity inside the medium is set at a constant value. How? This is done by adjusting the flow rate. So the flow rate is no more constant.

We have to keep changing and adjusting the flow rate. So as to keep the turbidity at the constant level inside the reactor, so this more difficult to operate than a chemostat because when you need an inline device which can continuously monitor the turbidity and we also need to ensure that the pumps are calibrated properly. And they are functioning all through the fermentation process, properly.

Because the flow rates will have to be manipulated in order to keep the turbidity constant. So it is much easier to run a chemostat because turbidostat would require and optical sensing device and a controller to control the flow rates. Turbidostat is however recommended when CSTR is to be operated at high dilution rates and therefore can prevent washouts. We will see, what is a washout phenomenon? And then we can come back to this point that how turbidostat can be more useful when the reactor is to be run at very high dilution rates where the risk of washout is very high. Washout means the cells getting washed away from the reactor in the outlet stream.

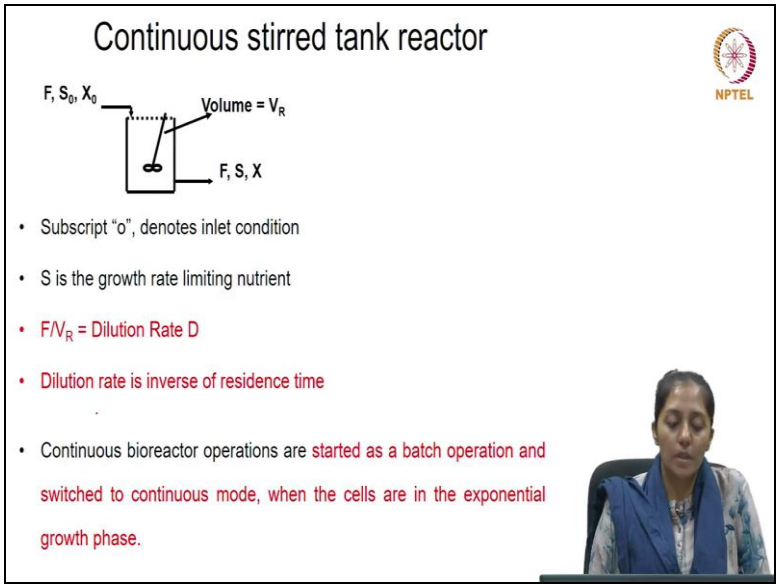
(Refer Slide Time: 04:03)



So, this is a simple schematic of a chemostat and turbidostat. So as I said earlier if you see the chemostat given on the top here the volume will remain constant shown by the dotted line. It is not changing and here in a turbidostat there is a controller which controls the flow rate of the pump and the calibration of the pump. And there is an optical sensing device which will continuously monitor inside the reactor or the broth.

So the culture volume can be kept constant by an overharvesting device. So there we need to ensure but that the turbidity inside the reactor which is related to the cell density is constant by maintaining the; or by adjusting the flow rate inside the system.

(Refer Slide Time: 05:08)

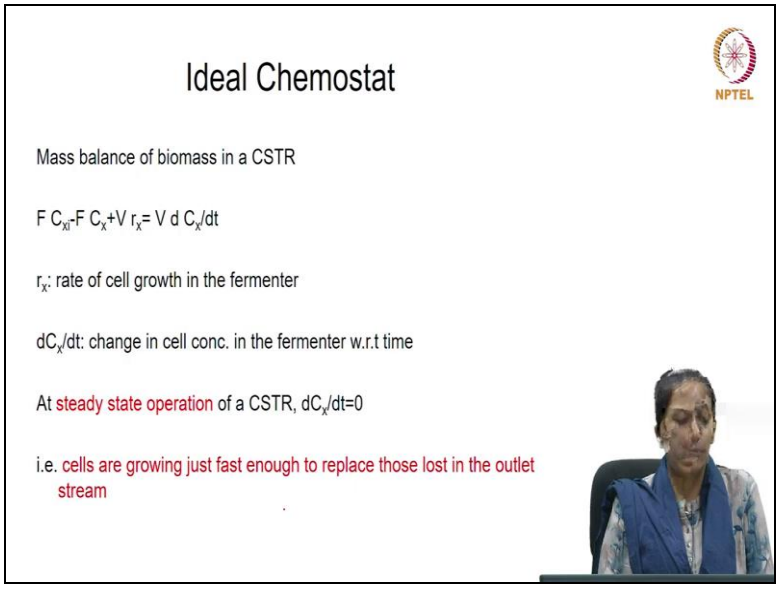


So let us note down some of the notations which will be used when will be designing continuous stirred tank reactor. If you can see the schematic on the screen that is an inlet stream showing F are the volumetric flow rate of the field. S 0 as the field substrate concentration and X 0 as the Biomass concentration present in the feed coming inside the reactor. The volume of the reactor is V R.

And outlet stream has the flow rate F substrate concentration S and X. Now, it is an ideal CSTR and running as a chemostat. So which means that what is coming out what we are measuring in the outlet streams, the variables their values will be the same inside the reactor. So, O stands denote the inlet conditions of the subscript. S is the growth limiting substrate. So we know now the dilution rate is F by V.

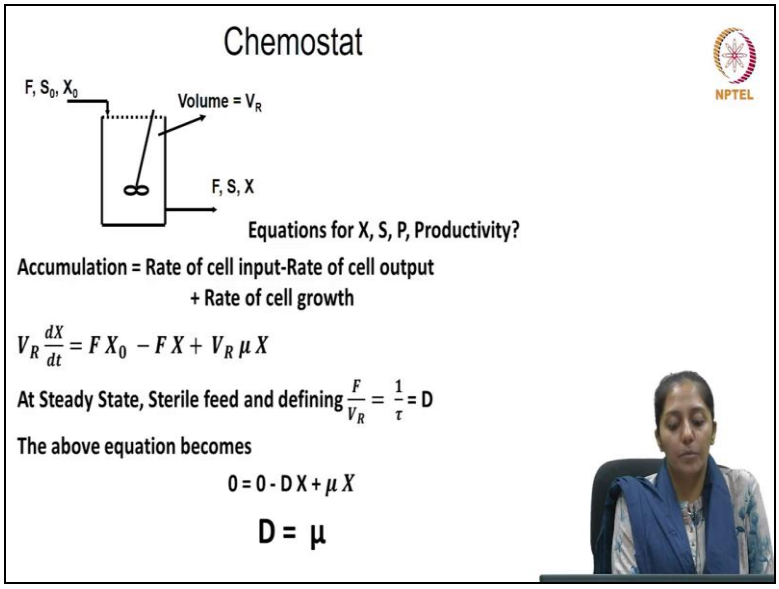
So here because the volume is V R, so the dilution rate can be given as F by V R which is the inverse of the residence time of the reactor. Now continuous reactor operations they are generally like in case of fed batch. They are started as batch and its purpose is to continue the growth phase continue the culture to remain in the exponential phase to avoid nutrient limitation, then it is switch to continuous mode when the cells reach the exponential phase.

(Refer Slide Time: 07:04)



Now ideal chemostat as I was mentioning.

(Refer Slide Time: 07:14)



If you do a mass balance across this ideal chemostat for the biomass and reply, so if you do a mass balance, which means if we apply the content equation the rate of accumulation of the Biomass will be equal to the rate at which the cell is coming inside the reactor minus the rate at which the cell mass is going outside the reactor plus the rate of cell growth. Obviously we are assuming an obviously there is no under all practical conditions. There is no consumption of biomass taking place.

So if we expand now accumulation rate is being represented. So now again in a chemostat the volume of the reactor is fixed because the inlet and outlet flow rates are constant at F. So your excess Biomass concentration so it is a mass balance but now the volume being fixed

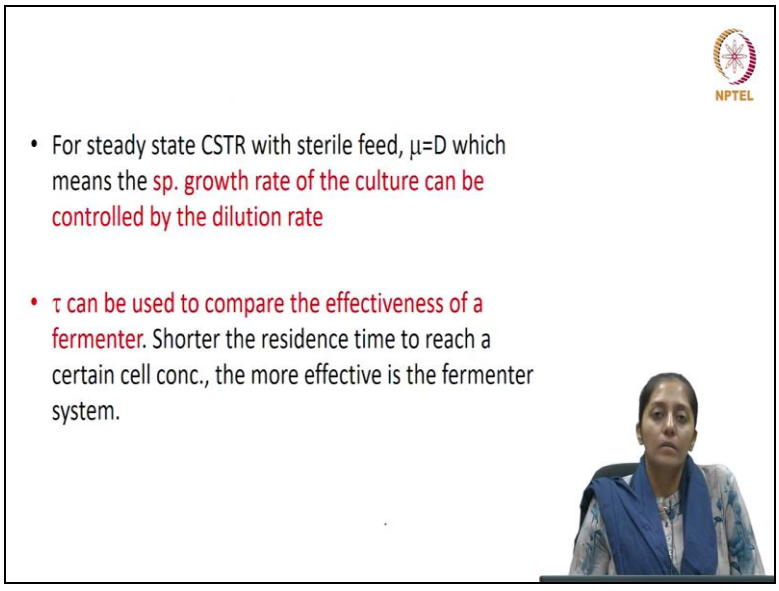
and it has been taken out. So we can be represented as V R times dx by dt this is the rate at which the Biomass is coming inside the reactor.

This is the rate at which the Biomass is leaving the reactor. And this is the rate at which the Biomass is right growing specific growth rate growing inside the reactor or increasing inside the reactor the growth happening. Now assuming that it is a sterile field, so, there is no Biomass in the inlet stream so this term goes to 0. And assuming it is a chemostat which means these containers bioreactor is running at steady state.

So there is no net accumulation of biomass, which means there is no change in the Biomass concentration. It is time in the reactor. So if you do the rearrangement again X and X gets cancelled and you will see that as in case of quasi steady state of fed batch reactors. In continuous bioreactors running a chemostat at steady state specific growth rate becomes equal to the dilution rate now.

I hope you can understand the advantage of running a continuous reactor, which I just mentioned few slides back that there is an opportunity to control the growth rate of the culture by manipulating flow rate because D is the function of flow rate. The above equation therefore we are able to prove that a steady state the specific growth rate of the culture becomes equal to the dilution rate.

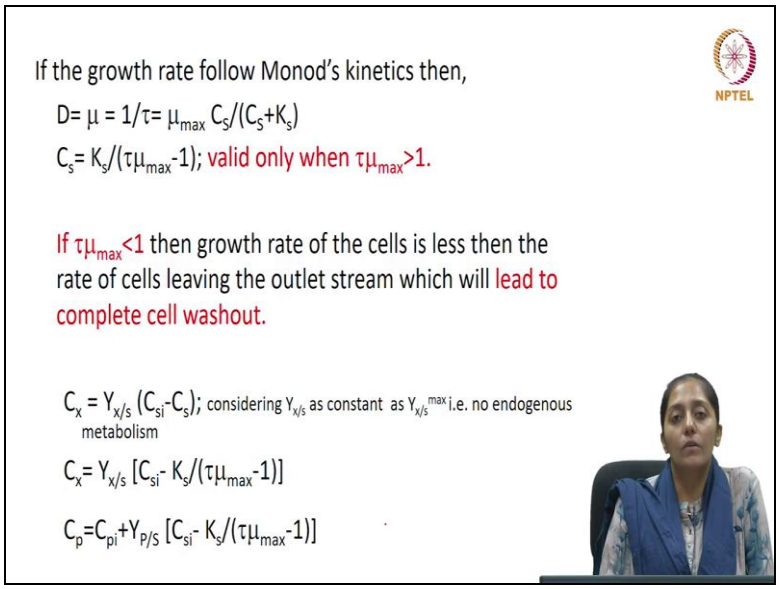
(Refer Slide Time: 10:13)



So because now the specific growth rate of the culture can be controlled by manipulating the dilution rates the residence times can be used or the dilution rates can be used to compare the

effectiveness of the fomenters. Which means what? For maximum productivity which is shorter the residence, time to reach the desired cell mass concentration. Though more effective will be the fomenter.

(Refer Slide Time: 10:48)



Let us see how to calculate the study state substrate concentrations. Now we have understood how the growth rate will be related with the dilution rate. Now let us see how can, we find out the substrate concentrations study state substrate concentration of the product concentration and corresponding productivity of biomass and product. Now we know and steady state D is equals to mu. If the sculpture is following Monod's model again substituting Monod's model.

And rearranging and D is the inverse of the residence time. So if you now use these equations do the rearrangement to find how C S is related to the residence time you will find that it becomes equal to K S divided by residence time multiplied by Mu Max which is mu M -1. Now this demonstrates what? This is valid only when the denominator which is tau Mu max -1 is greater than 0, less than 0 becomes negative.

So it has no physical significance, meaning so this in turn means that Tau mu max has to be greater than 1. So again bring tau as an inverse of dilution rate. So Mu Max has to be greater than the dilution rate for substrate concentration to have any valid numeral value. If suppose this becomes less than zero then what happens? Less than 1 so let us see if your dilution rate becomes greater than Mu max what will happen?

If your dilution rate greater than Mu max which means your tau mu max is less than 1 is not it tau tau times mu max is less than 1. This effectively means start the growth rate of the cells is now less than the rate at which the cells are living the outlet stream is not it this would mean effectively that it will lead to the complete wash out of the cells from the reactor. This is what is washout phenomenon.

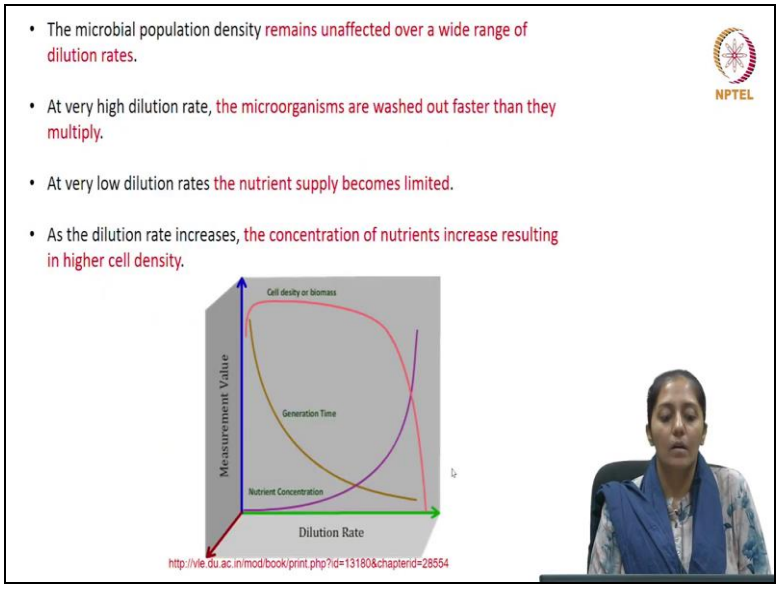
When the dilution rate becomes greater than the maximum specific growth rate of the culture beyond which the culture cannot grow. Then the rate at which the cells are living the reactor becomes more than the rate at which the cells are growing inside the reactor or getting accumulated inside the reactor. So this can lead to the complete washout of the cell. So there will be no cells remaining inside the reactor.

Hence this will lead to complete washout and this is called as washout phenomenon. So this is the condition which has to be followed to prevent washout. So tau Mu max should be greater than 1. Now for continuous reactors sterile steam your Biomass can be a function of Y X by S this is the field concentration and this is a concentration in the outlet stream. Now as you mean that Y X by S is constant which is it is; theoretical value with no endogenous metabolism.

Which means so then you are Biomass concentration at steady state in the outlet stream can be calculated in terms of the steady state substrate concentration in the outlet stream which we just found above in equation 2. So if you substitute C S from here in this as given here then you will end up here. So this is how your study state Biomass concentration can be obtained if you know the dilution rate at which the continuous reactor is running and knowing the inlet feed stream and the culture of kinetic constants.

Now how to determine the steady state product concentration? Again we will make use of the yield coefficient by P by S is nothing but C Si – C S which is equals to C P minus C Pi, C Pi is the initial product concentration initial in the sense in the inlet stream. Now inlet stream again, there is no product. So your product concentration can be written as. So your study state substrate concentration has been substitute like above. Then you can calculate the value of product concentration.

(Refer Slide Time: 17:51)



So microbial population density it remains unaffected over a wide range of dilution rates. So if you see the plot given here X axis shows the dilution rate, your orange plot is the cell mass density. So if you see as the dilution rate is changing that is a very little change in the cell mass density where with increasing dilution rates the cell mass density reaches to a point where after beyond a certain point of the dilution rate suddenly starts decreasing.

So which shows at very high dilution rates the washout has started happening because of which the cell mass starts decreasing inside the reactor. Similarly at very low dilution rates here again the nutrient supply becomes limited and therefore the Biomass concentration is less. As the dilution rate increases the concentration of the nutrients increases resulting in higher cell density. And then over a wide range that is not much significant change before the washout happens.