Optimization in Chemical Engineering
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Lecture – 55
Applications of Optimization (Contd.)

Welcome to lecture 55, this is the last lecture of week 11. In this week we have talked about various Applications of Optimizations and you have taken examples from Chemical Engineering as of now. In today's lecture we will take an example from biochemical engineering; specifically, we will talk about optimization of a continuous bioreactor. So, Optimization of a Continuous Bioreactor as specifically we will discuss Microbial Growth in a Chemostat.

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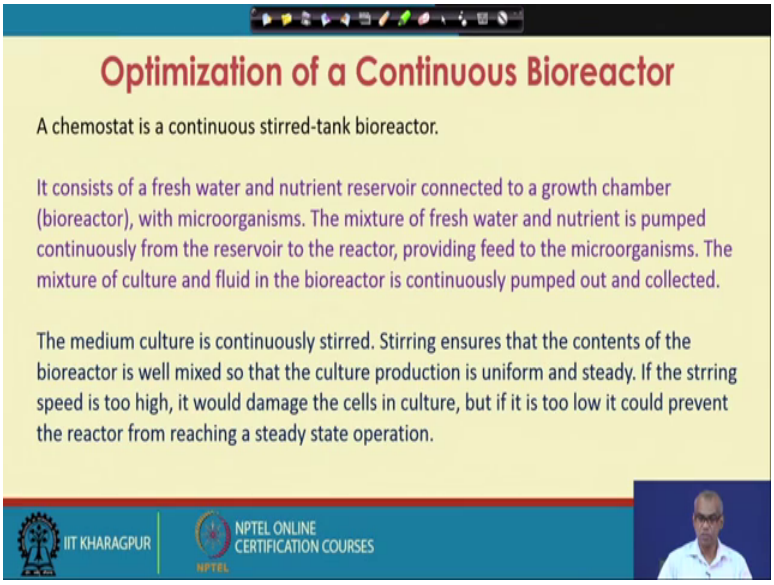

A chemostat is a continuous stirred tank bioreactor. It consists of a freshwater and nutrient reservoir connected to a growth chamber which is called bioreactor with microorganisms. The mixture of freshwater and nutrient is pumped continuously from the reservoir to the reactor providing feed to the microorganisms. The mixture of culture and fluid in the bioreactor is continuously pumped out and collected. The medium culture is continuously stirred, stirring ensures that the contents of the bioreactor is well mixed.

So, that the culture production is uniform and steady. If the stirring speed is too high it would damage the cells in culture, but if it is too low it could prevent the reactor from reaching a steady state operation.

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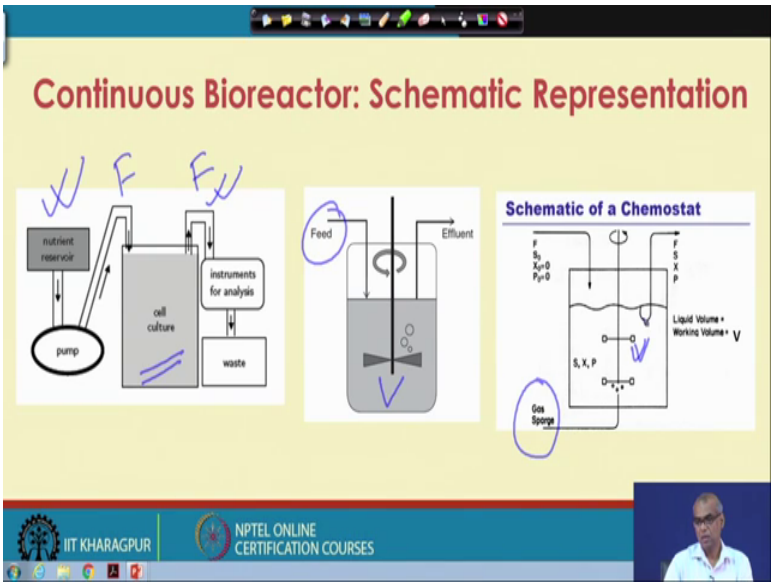

This is some schematic representation of the chemostat or continuous bioreactor. As we discussed, we have a neutron reservoir from which the nutrient is continuously pumped to this bioreactor. Also the flow rate of that exist stream is same as the flow rate of this inlet stream.

So, the volume of this bioreactor remains constant. You also spurge gas to the bioreactor, you can spurge air so that the level of oxygen in the bioreactor is maintained at some optimal value. Note that in the bioreactor the feed steam contains the nutrients which the microorganisms present in the reactor eats and grows. So, they will multiply grow in number. So, there will be production of more amount of biomass. They can also produce some product and the with the exit stream you will have the substrate the cell mass or the biomass as well as the products.

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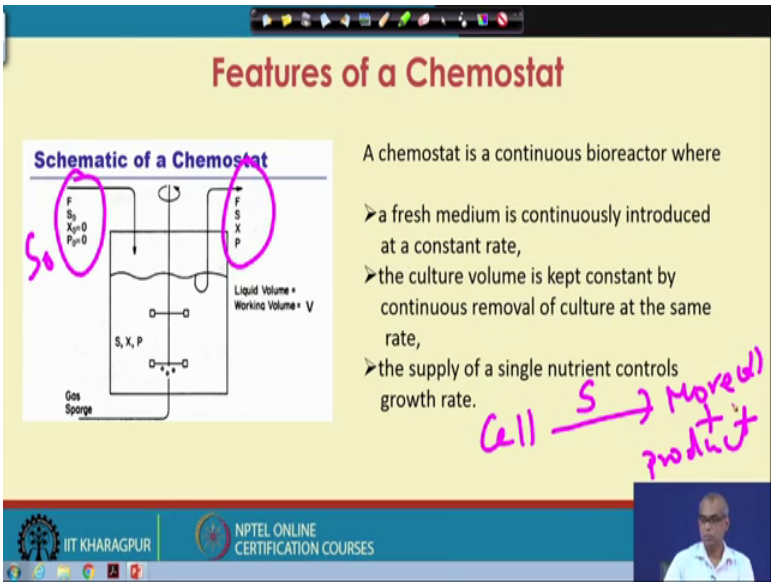

The stirred tank bioreactor is one of the most commonly used types for large scale production in the industrial applications such as food pharmaceuticals various commodity and specialty chemicals. The chemo state is a widely used apparatus for the study of microbial physiology. The features of a chemostate are as follows.

A chemo stat is a continuous bioreactor where a fresh medium is continuously introduced at a constant rate. The culture volume is kept constant by continuous removal of culture at the same rate. The supply of a single nutrient controls the growth rate. So, the supply of a single nutrient which we call the limiting nutrient controls the growth rate.

So, when you write down the equations that describe the growth of microorganisms in the bioreactor. We consider, the balance on the consumption of the substrate and that substrate is the limiting substrate. So, in a bioreactor you have microorganisms let us call them cell. So, from cell it is substrate and then it produces more cell, it can also produce product. For example, you may be interested in growing yeast in a chemostat in a bioreactor.

So, you can supply glucose the yeast will eat glucose consume glucose and grow. We can also produce ethanol from the fermentation.

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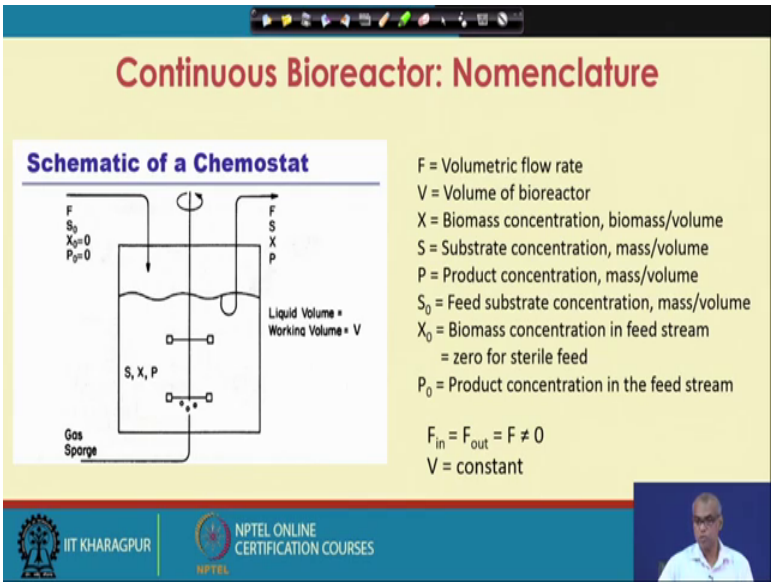

So, let us look at the notations in the schematic of the chemostat shown F is the volumetric flow rate, V is the volume of bioreactor. So, the volumetric flow rate maybe say liter per hour, meter cube per hour, volume of the bioreactor may be liter or meter cube etcetera, X is biomass concentration.

So, this is gram by mass bio mass per unit volume. S is sub state concentration again mass per volume, so maybe gram per liter. P is product concentration, again mass per volume maybe gram per liter. S 0 equal to feed sub state concentration. So, this is the limiting substrate concentration. Again unit is mass per volume of meaning gram per liter. X 0 equal to bio mass concentration with the feed stream. X 0 is the biomass concentration in the feed stream. So, if the feed stain is sterile as often is the case X 0 is 0, because then there will not be any biomass in the feed stream.

You can have initially biomass within the bioreactor. And you can enter or feed as a sterile stream and it will have no biomass in it. So, X 0 will be equal to 0. P 0 is the product concentration in the feed stream again normally that will be 0. So, the input flow rate and the output flow rate are same. So, V e volume equal to constant. So, these are the notations we will use while writing down the model equations.

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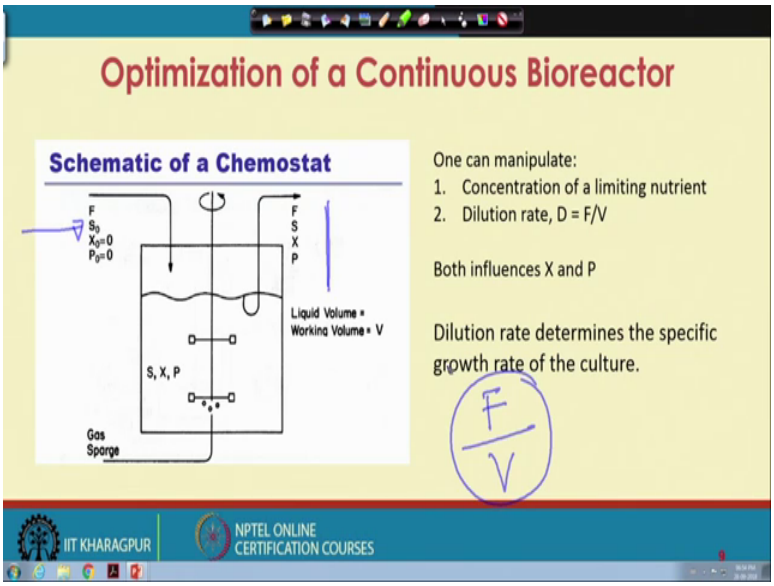

So, one can manipulate the concentration of the limiting nutrient in the feed stream. So, S 0 one can manipulate to influence the outcome of this bioreactor. One can also manipulate the flow rate or more specifically a quantity called dilution rate which is the flow rate divided by the volume of the reactor. So, in a chemostat by changing the substrate concentration in the feed and or by changing the dilution rate, we can influence both the cell mass or the biomass as well as product concentration. Dilution that determines the specific growth rate of the culture.

So, the production rate of the biomass is dependent on the dilution rate. In that case the substrate consumption will also change upon change in the dilution rate. So, dilution rate is a good handle to influence the outcome of the continuous bioreactor chemo stat. So, in this lecture we will see how to determine the optimal bioreactor, sorry the optimal dilution rate for a continuous bioreactor.

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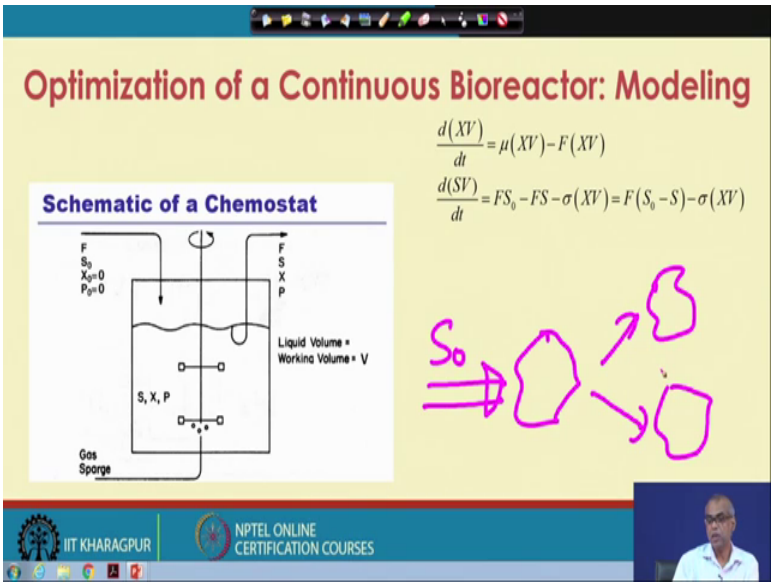

So, first let us write down the modeling equations that will describe the working of chemo stat.

For simplicity let us consider only the growth of the microorganisms, in other words we have the microorganisms in the bioreactor, and then I have a feed stream which contains the limiting nutrient. We are not considering any product formation. So, we have to write down thus 2 mass balance equation. One is for growth of the microorganisms, another is for the consumption of the substrate. So, the physical phenomenon that is taking place is, you have the microorganisms, and you are supplying the substrate, so then it grows in numbers.

So, let us define the amount of biomass and the amount of substrate in the reactor as state variables. So, how or what will be the change or rate of change of the biomass in the reactor, what will be the rate of change of the biomass in the reactor?

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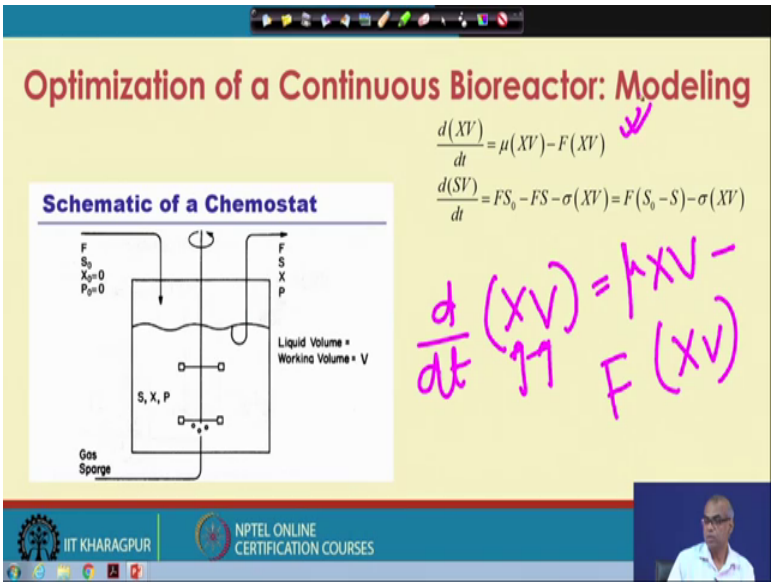

That will be given as d dt of amount of biomass which is concentration of biomass multiplied by volume. So, this is concentration and this is volume, so this gives me the amount of biomass. So, rate of change of biomass will be equal to input minus output we are considering sterile feed.

So, there is no input of biomass with the feed stream, but the biomass grows. So, we get more biomass when there is some biomass already present in the bioreactor. So, you have to define a term known as specific growth rate. So, if I multiply the amount of biomass by the specific growth rate, this will give me the how much biomass grows in the bioreactor. So, this nu into xv is the quantity corresponding to the growth of the biomass. And then the biomass leaves with the exit stream so that will be flow rate in to xp.

So, this is how I get the first equation; which is the mass balance equation on the biomass. Next how do I account for the rate of change of substrate in the reactor? Again we write the mass balance equation.

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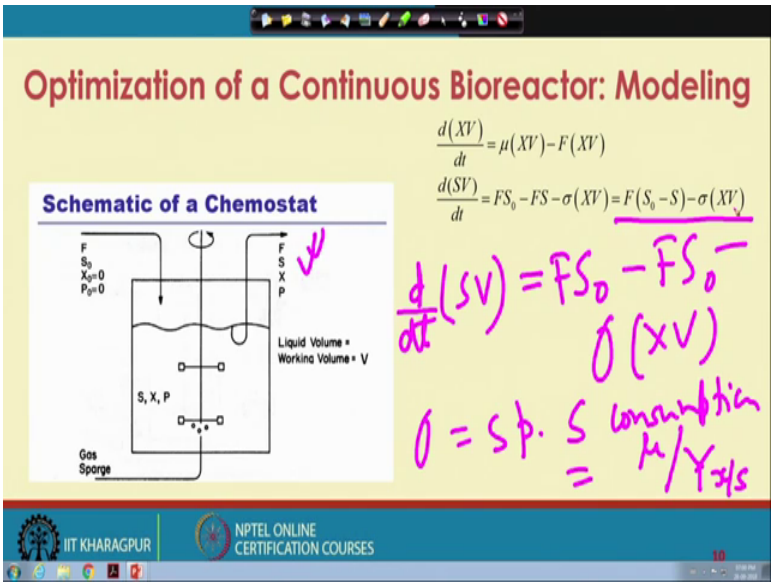

So, d dt of SV S is the substrate concentration times volume. So, the amount of substrate is, the amount of substrate that is coming in with the feed, so that is F into S 0. The amount of substrate that goes out with the exit stream; that is minus F into S 0, and then the microorganisms consumes S. So, microorganisms consume substrate.

So, as we multiplied the specific growth rate with the amount of biomass to get the biomass grown, if I define the term called specific consumption rate and multiply the specific consumption rate with the amount of biomass I will get the amount of substrate consumed by the biomass. So, that is will be sigma into XV, where sigma is the specific substrate consumption rate. And this is equal to the specific growth rate divided by yield. Yield of cell mass for substrate. So, this is how you get the second equation; which can be rearranged and you get this.

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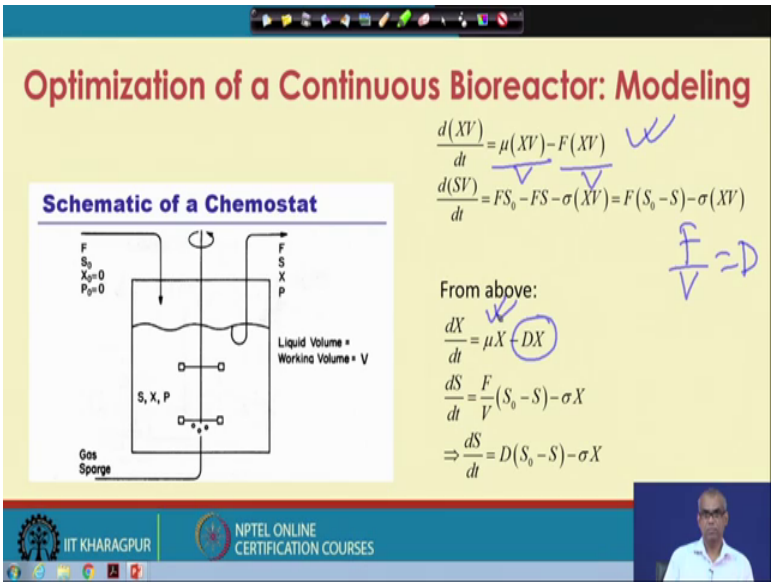

So, I now have the 2 mass balance equations. Note that V remains constant. So, you can take out V from this equation and then if you take out V in this part will be divided by V this part will be divided by V. So, you will get mu X here and you will get F by V here which is D. So, that is why you get D X here.

So, this is how you get the D X D t equation. Similarly, take out V because it is constant and then you get dS dt equal to F by D into S 0 minus S minus sigma S. Note that if you take out V this will be multi divided by V this will also be divided by V.

So, we will get this part and this part. F by V is defined as dilution rate D. So, dS dt can be written finally, as dS dt equal to D into S 0 minus S minus sigma S; where S 0 is a substrate concentration in the feed stream. And S is the substrate concentration in the reactor; which is same as substrate concentration in the exit stream.

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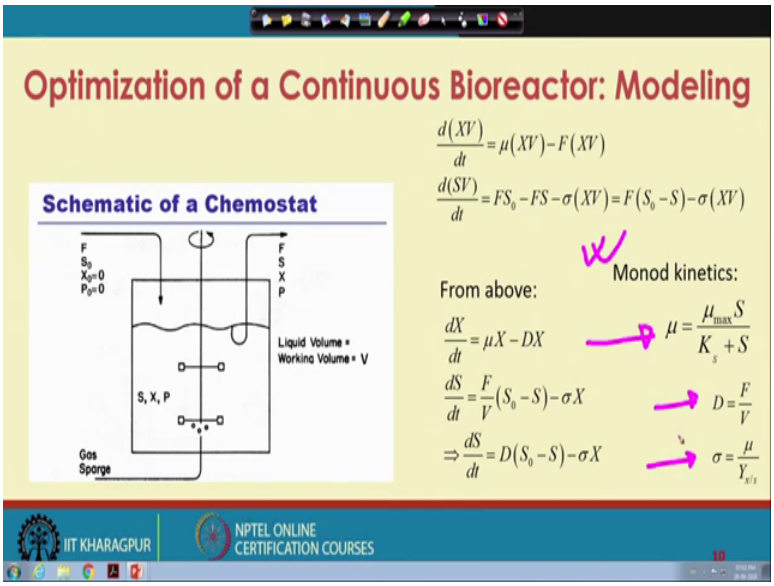

The growth rate follows different kinetics one of the simplest kinetics is the Monod kinetic, which is written as the growth rate mu equal to mu max into S divided by K S plus S. This is how you find the dilution rate, and this is the substrate consumption rate. So, we have all equations for the bioreactor modeling.

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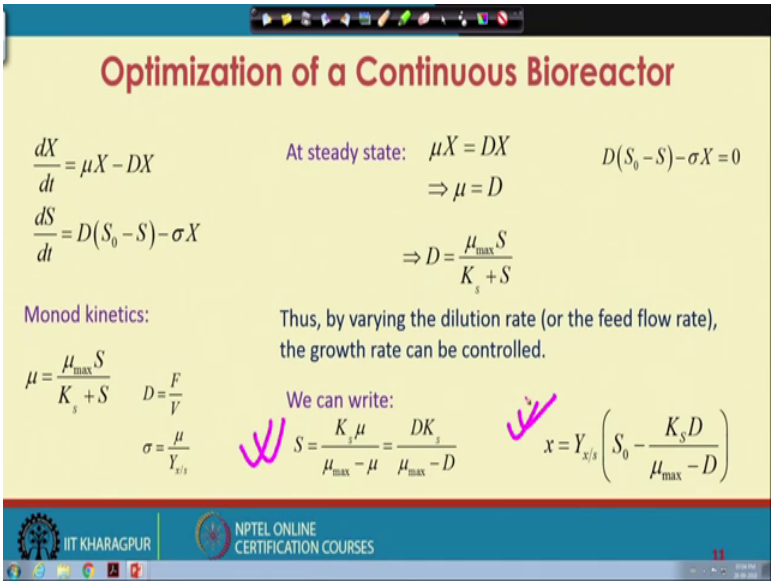

There are several kinetics Monod kinetics is the simplest one. There is substrate in addition kinetics, you can assume that if we give more substrate, the microorganisms will happily consume substrate and grow more, but sometimes more amount of substrate may

inhibit the growth of the microorganisms and to account for this we have substrate inhibition kinetics. But let us talk about only Monod kinetics. So, this is the modeling equations now at steady state D S D t equal to 0 dS dt equal to 0.

So, we get mu equal to D; dilution rate equal to the growth rate. Similarly, the second equation leads to D into S 0 minus S minus sigma S equal to 0. So, mu for Monod kinetics is mu mas into S into K S plus S. So, D is equal to mu max S by K S plus S at steady state. So, by wearing the dilution rate or the feed slow rate the growth rate can be controlled. Now, you can write for substrate concentration, you can also write for cell mass concentration.

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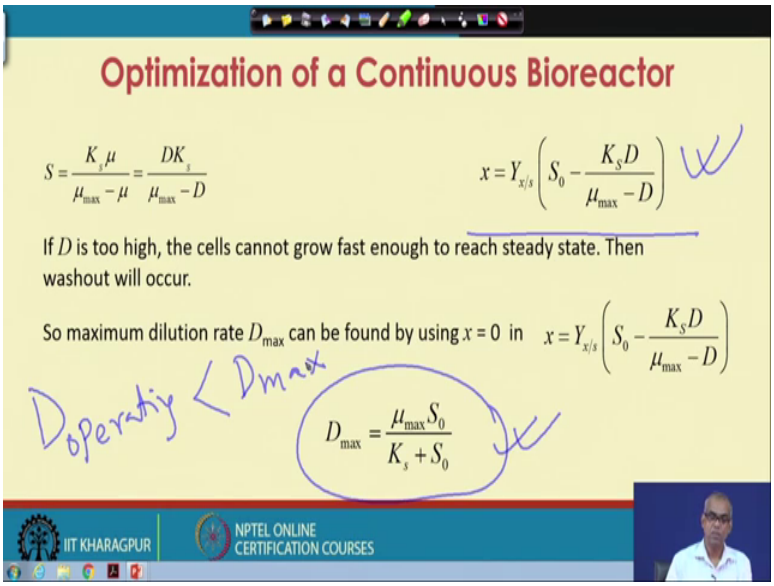

So, we have now obtain the substrate concentration expression as well as cell mass expression for a given dilution rate. So, for a given dilution rate you can rearrange these equations and can obtain closed form expression for substrate concentration as well as cell mass or biomass concentration. Note that, the D influences both biomass concentration X as well as substrate concentration S. If the dilution that D is too high the cells cannot grow fast enough to reach steady state.

Suppose the dilution rate is very high so in that case, the cells will not stay for long time within the reactor, and will not be able to grow fast enough to reach steady state. Then all the cells will soon be out of the reactor, this is known as washout condition. So, if D is too high the cells cannot grow fast enough to reach steady state, then wash out will

occur, this is highly undesirable, because in your bioreactor, there will not be any biomass or cell mass. It will only be filled with the feed stream that you are entering. So, this happens only when D is very, very high. So, how high is very high.

So, the maximum dilution rate then can be found by putting X equal to 0 in this equation, because our I now have an expression for X. And I know that X equal to 0 in washout condition. So, I can put X equal to 0, and solve for the D to get the maximum dilution rate at which the washout will occur. So, the maximum dilution rate D max, we obtain as mu max S 0 divided by K S plus S 0. So, your dilution rate must be lower than this. If the dilution date is more than this you will get wash out condition.

So, operating D must be less than the maximum dilution rate at which wash out will occur. So now, we ask the question what should be the optimal dilution rate then.

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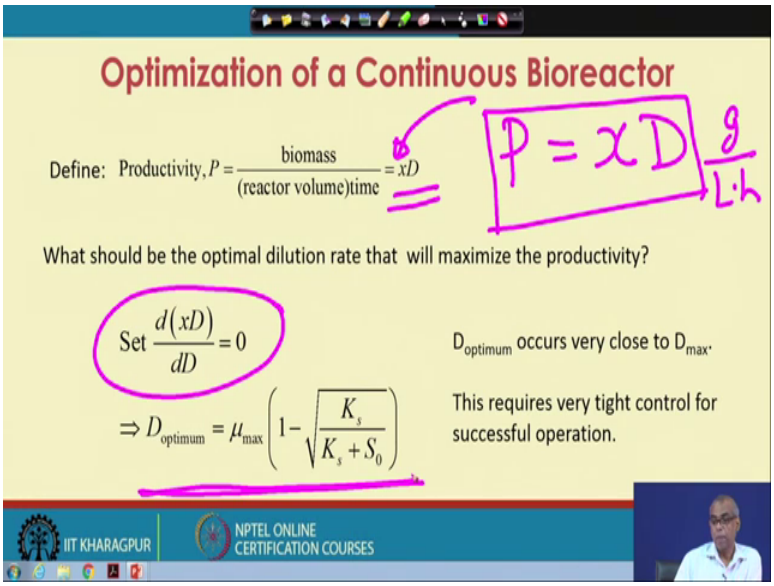

So, to answer this question first I have to define an objective function, what is it that I want? Let us define the productivity P as biomass divided by reactor volume into time; that means, biomass reactor volume is nothing but cell mass concentration, and dilution rate has unique per time. So, xD gives me a quantity which is amount of biomass per unit reactor volume per unit time.

So, this is a measure of productivity. So, the measure of productivity for continuous bioreactor P is biomass concentration x in to dilution rate. So, the productivity or x D or

D x will have unit, biomass per reactor volume into time. So, something like gram per liter into hour. So now, we ask the question what should be the optimal dilution rate, such that the productivity P will be maximum? What should be the optimal dilution rate so that we will obtain the maximum productivity?

So, xD will be maximum for what D. Note that you can go you cannot go on increasing D, because if you go to D equal to D max wash out will take place and there will not be any cell in the bioreactors, so X will be 0 the productivity will be 0. So, to obtain the optimal dilution rate, you can take the derivative of the productivity that is xD with respect to the dilution rate and set it equal to 0, and can obtain a closed form solution for the optimal dilution rate. These optimum dilution rate occurs, not very far from the maximum dilution rate. The optimum dilution rate occurs close to the maximum dilution rate.

So, immediately can conclude that a successful operation for a continuous bioreactor will require very tight control so that you are operating in the specified dilution rate, you are operating with the specified dilution rate and not going very close to the maximum dilution rate leading to washout condition. So now, let us see how do we numerically find out the optimal dilution rate?

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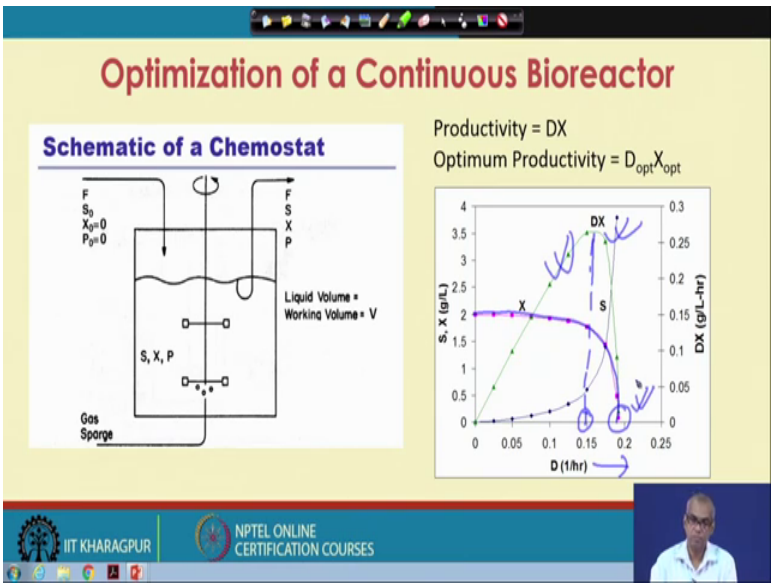

So, productivity equal to dx or X D optimum productivity will be D optimum into X optimum.

So, this is a typical figure for the concentration of the cell mass substrate with respect to dilution rate, and also how the productivity D X change with the dilution rate. Look at this figure, this is for cell mass. Note that as the dilution rate increases, here you reach the maximum dilution rate and the cell mass becomes 0. In that case the substrate concentration becomes very high, in fact the substrate concentration will be same as the concentration in the feed stream. And this is for the variation of the productivity D X with dilution rate. You see it reaches a maximum and then decreases shortly with increasing dilution rate, and you see that the optimal dilution rate is not very far from the maximum dilution rate that is corresponding to wash out condition.

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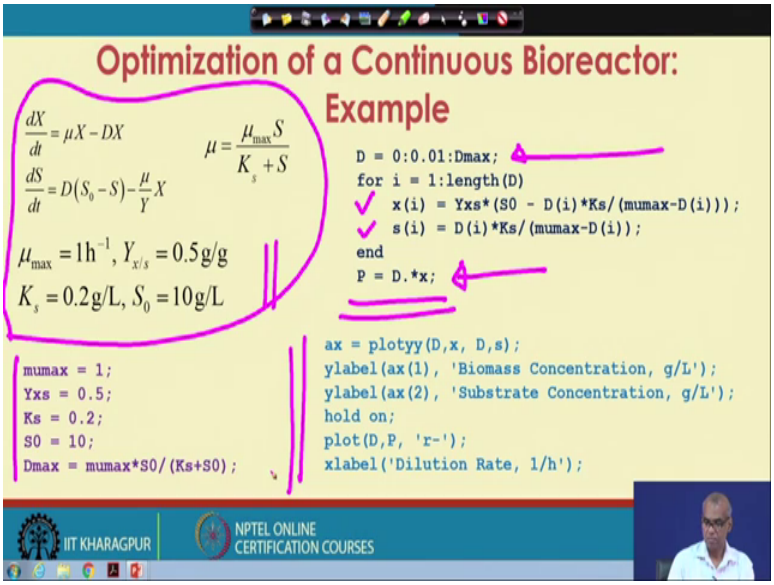

So, now let us take help of MATLAB optimization toolbox to solve this problem. In fact, you can also solve this problem by simply making use of the equations for cell mass and the substrate concentration you define dilution rate from 0 to say the maximum dilution rate. And for each dilution rate you just solve for X and for S. Then they take product of D and X, and then just plot DX versus D, so you will get the optimal dilution rate, as simple as that, so let us first demonstrate that.

So, we are taking this example we have biomass equation we have substrate consumption equation. And the data are given, mu max equal to 1 hour inverse, yield is 0.5 gram per gram per gram means gram biomass per gram substrate. K S is 0.2 gram per liter and the substrate concentration in the feed stream is 10 gram per liter. So, in the

MATLAB to write a on the MATLAB environment, you write an m 5 to define these quantities. Then let us create a D vector, which grows from 0 to D max, let us say with an increment of 0.01. So, like 0 then 0.01, then 0.02 up to D max.

So, for each of these D, I can calculate x and s, and then just take the product of D into x. So, this is how you can use the vector product. In one state you can multiply all the elements in the D vector with all the elements in the x vector and then just plot so you get this plot.

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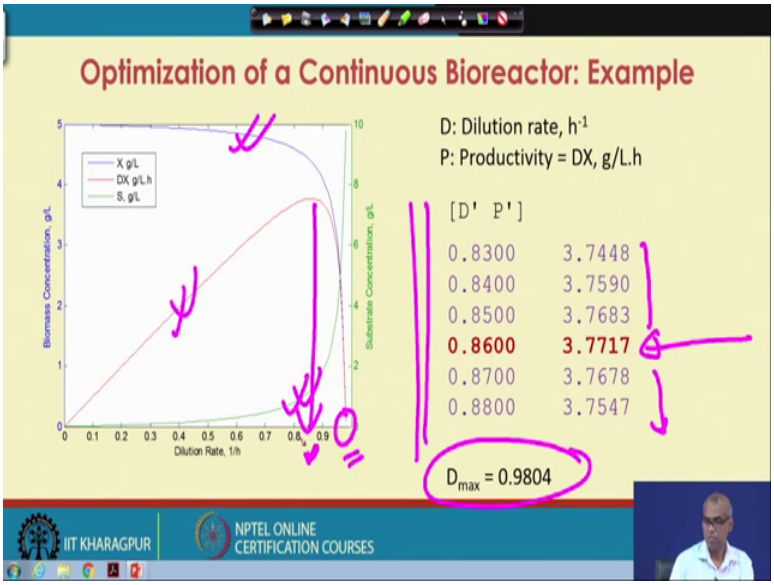

So, this is how the biomass changes with change in increasing dilution rate, this is how the substrate increases with increasing dilution rate. Both make sense, because as you increase the dilution rate, you are sending out the biomass from the reactor and when you reach wash out condition. Your cell mass becomes 0 in the bio reactor.

And as you increase the dilution rate we increase the substrate concentration in the reactor. And this is how the productivity changes with change in the dilution rate. So, this is the optimal dilution rate. So, you just list the values D versus D X and you look at here that how the dilute how with dilution rate that the productivity changes. And we get an optimum solution rate of 0.86 and the productivity is 0.37717.

Note that dilution rate goes on increasing reaches the maximum and then again decreases. You can use the equation for D max and the D max takes place at 0.9804, so

this is 0.9804. And the optimal dilution rate is 0.86 so, not very far from the washout condition.

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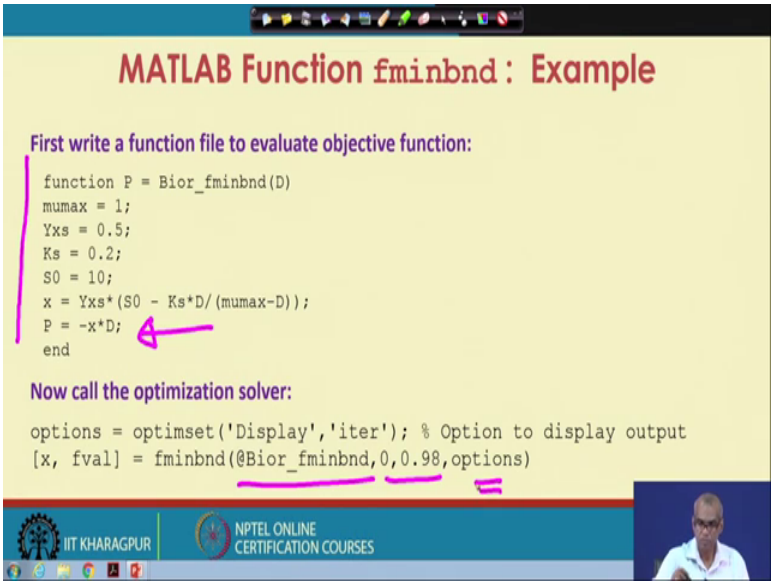

Of course you can also use say F min search or fminbnd. So, to use fminbnd I first define the function. Then I call the fminbnd solver, note that it requires the function which will calculate the objective function, I am maximizing it, but the fminbnd will find the minimum of a function.

So, that is why the objective function is being taken as P equal to minus of the productivity. And then the lower bound and upper bound I am supplying as 0 and 0.98. So, we have just seen that 0.98 corresponds to maximum dilution rate. You can also send options.

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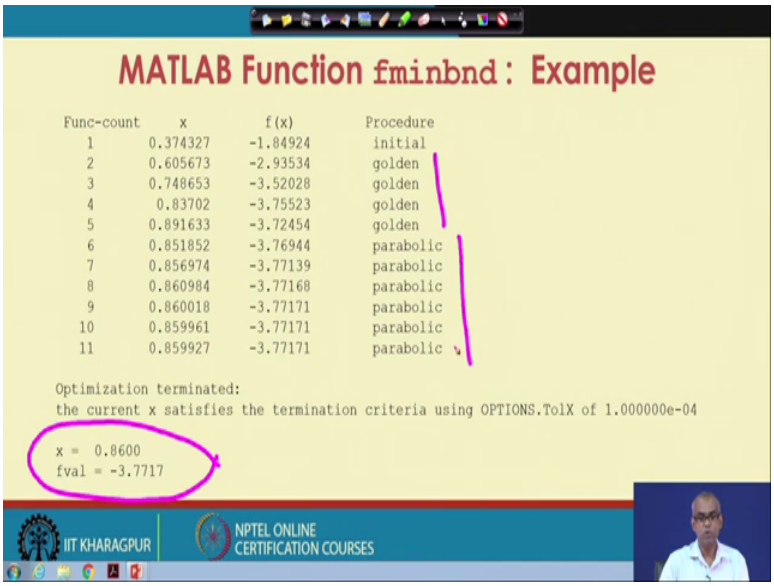

So, if you run this program you get the solution; x is 0.8600, and the objective function values 3.7717, note that the minus sign due to the maximization problem is converted as minimization problem.

So, fminbnd initially use as golden section search and then uses parabolic interpellation. So, you obtain the same solution as expected. So, this is how you can solve an optimization problem related to microbial growth in a chemostate or in a continuous bioreactor. So, with this we will stop lecture 55 here. In this week 11 we talked about various applications of optimizations. We learn various MATLAB functions, tools from the MATLAB optimization toolbox. And we formulated the optimization problems, and solved using the MATLAB tools that are available.