Aspects of Biochemical Engineering
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Lecture – 46
Scale up of Bioreactor – II

Welcome back to my new course Aspects of Biochemical Engineering. Now in the last lecture I tried to discuss the Scale up of Bioreactor and the, I told you that this is very important part of this course because, main part was of the course of biochemical engineering that that we want to applied, that whatever things we develop in the lab in the bigger scales.

So, now question comes whatever through the research work in the lab day to day lab, we develop some kind of product. Now that we might have developed in a very tiny scale may be in the test tube may be in the chemical flux may be in the 2 liter or 10 liter reactor, but that is not good enough for marketing the product am I right.

So, we shall have to we shall have to go for the higher scale, when you go for the higher scale that we should remember the monetary involvement of the process includes drastically. So, so in naturally that when we any investor when invested money, he should have 100 percent confidence that whatever things, we get in the small scale the same thing we should get in the bigger scale of operation and, that is why scaling of the bioreactor is very much essential any kind of process of first we scale it up and, try to find out that you know that whether under what circumstances, we can have we can develop the similar environment that we have small reactor and the big reactor.

And so you know for doing so, we there is certain operational parameters as for example, power drown by the agitator I told you this plays very important role and mild hesitation because, we know in the microbial fermentation process, that when you do the agitation and as we increase the speed of the agitator, there will be sign come shear effect. And do the shear effect the growth of the organism will be hampered.

So, naturally that should be optimization of the of the power that that to be to be applied in agitator and, that is why we have a thing that is called biological concept of the of the process for scale up, and this tell that under at what scale a or p that p by V ratio powered

per unit volume of the reactor that we will get the maximum amount of product formation.

But because we say when we scale it up we shall have to find out what is the minimum, that you know power required for getting the maximum amount of product because, industry when we work with any kind of process main concern is the money and the operation. That that monitory involvement because, I told you that you know more power you applied, more power more current will be drown and the that you know you the electrical explain electrical power is expenditure, for the process increases drastically.

So, and I try to give a 2 different instances like many penicillin fermentation and streptomycin fermentation, how the p by V ratio and the volumetric mass transfer coefficient, how that influence the product formation.

Now, this particular lecture I want to discuss say two different problem of this scaling up of the bio process and at the end, I want to discuss the scale down of the bioprocess. Now first let me start with that with this problem.

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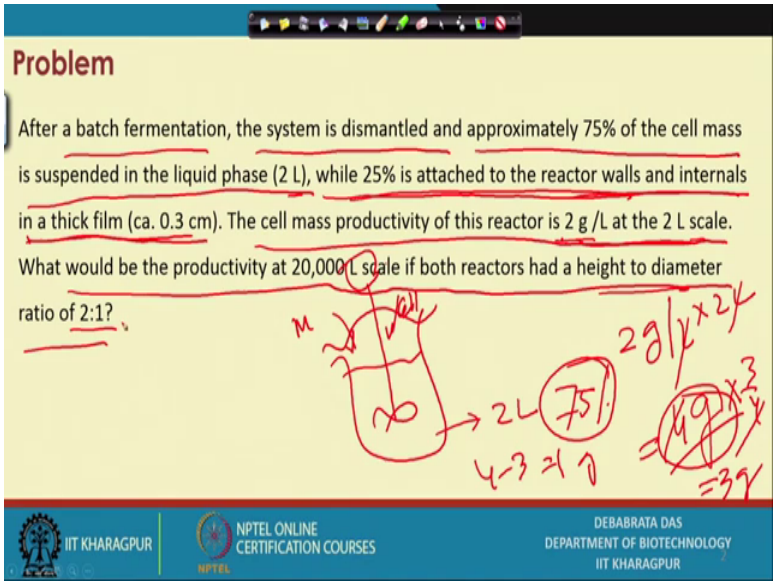

Now the problem says after a batch fermentation the system is dismantled, dismantled means the you just open it up and approximately 75 of the cell mass is suspended in the liquid phase that is the 2 liters, and while 2 percent attached to the reactor wall and internal with a thickness of calculated 0.3 centimeter.

Cell mass productivity of the reactor is 2 gram per liter at 2 liter scale, what will be the productivity of 20000 liter scale, if both the reactor have high diameter ratio is 2 2 is to 1. So, this is the problem that so, I can explain little bit, what is the problem is that this is the reactor am I right, and after the suppose you put the media here and you put the cell here.

So, then after the fermentation you open the things and, initially this is 2 liter capacity. And if you say 75 percent you take the liquid out and 75 percent approximately 70 percent of the cell mass suspended in the liquid. So, what is the total amount of cell mass we have, that is 2 gram per liter mass is cell mass producted 2 gram per liter at 2 liter scale that means, how much is the cell mass 2 gram per liter into 2 liter am I right, the liter the liter will cancel. So, this will be 4 gram.

So, you will get the 4 gram of cell in 2 liter fermentation, out of 4 gram 75 percent goes in the solution am I right, I hope I hope you have understand that that means this is multiply by 3.4th that is 4 4 will cancel. So, 3 gram will go to the solution that you know suspended liquid and, 1 gram remaining 4 minus 1 3 equal to 1 1 gram 25 percent attached to the reactor wall and, internally the thickness of 0.3 centimeter and high diameter ratio is given here 2 is to 1.

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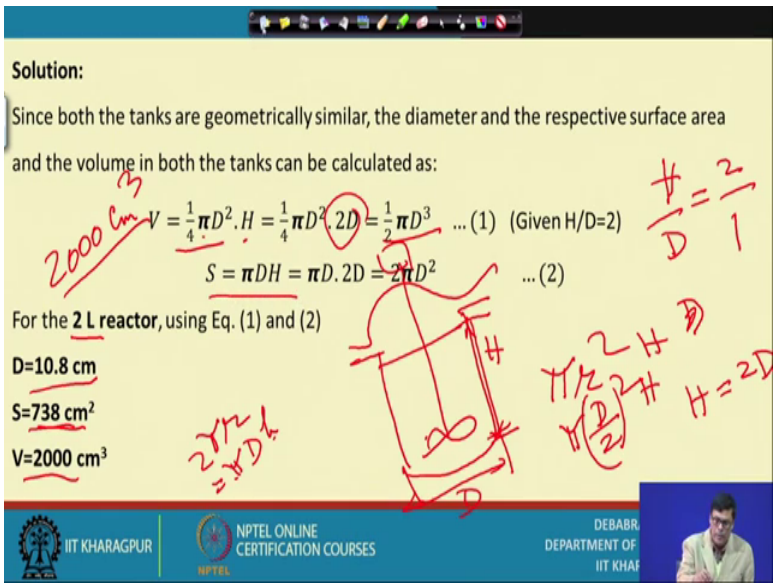

Now, you see that the how we can solve this problem that in volume of the reactor how we can write, this is that you know that this is pi r square H am I right, this is the

cylindrical fermented. So, V is like this, we do not assume diameter is D pi r square will be what this is the cross sectional area, this is the liquid height undefined H.

Now, r will be what r will be D by 2 whole square into H. So, that is why we have write to 1 by 4 pi b I square in to H now H by b ratio is what is 2 is to one. So, if 2 is to 1 I can write H equal to H equal to 2 D so, this is exactly what we have written, then this is like this.

Now, this is equal to 2 liters and one case this is 2 liters 2 liter means 2000 centimeter cubed. So, you can we can easily find out what is the diameter, what is the surface area, what are the volume, that we can we can easily find out surface area is equal to I can calculate the surface here peri what is the periphery peri twice pi r am I right. So, 2 r equal to dimeter am I right, this is 2 a equal to pi D and height is H this surface area we will be 2 pi D into H, this is how we can calculate the surface area.

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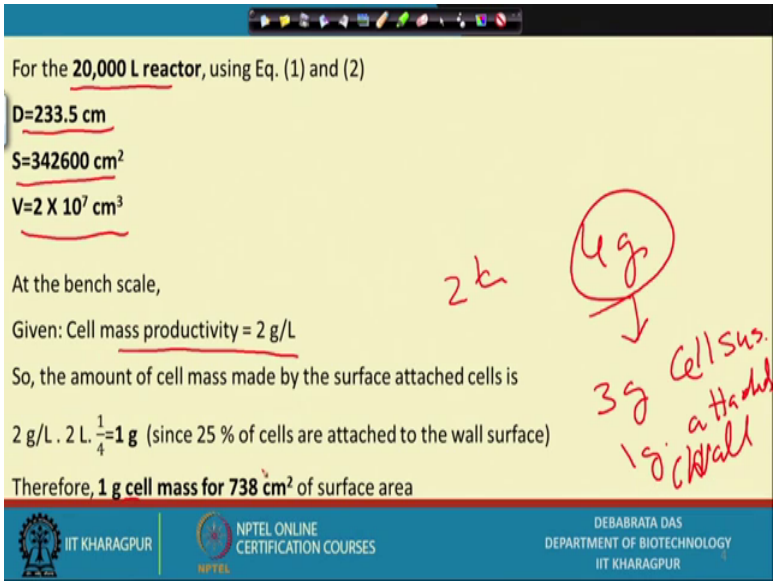

Now, similarly in case of 20000 liter reactor, we can calculate the diameter this is 233.5 centimeters surface area is this and volume is this ok. Now let us see how you can solve this problem, what is cell mass productivity 2 gram per liter.

And what is the what is the volume of this small scale 2 liter, the it will be I told you that how much cell will get 4 4 grams out of 4 gram 3 grams remain in cell suspension, suspension and 1 gram the attached with the attached with the cell wall with the with the

wall it is wall it is that you know fermented wall that will be the 1 gram biomass is attached with the now, if you if you look at, now here we already calculated what is the surface area in 2 liter reactor, this is 7 730 4 gram am I right 38, the 1 gram of cell; that means, 1 gram of cell is for 173 square meter surface area.

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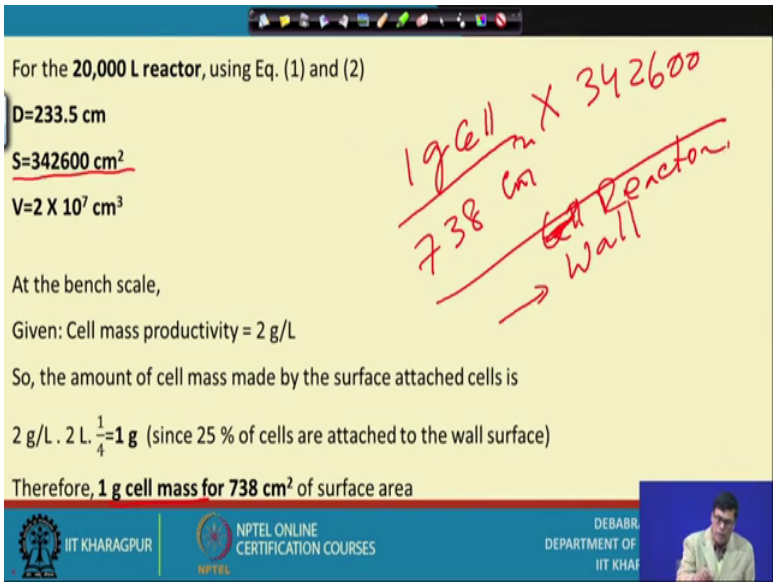

So, so 1 gram cell present in 7 centimeters square that you, we have already find out and so, here in the bigger scale how much cell will be there in the cell wall, this is 3 4 2 6 0 0, this is the amount of cell will be present with the as a cell wall, in the reactor wall not cell wall, it is reactor wall.

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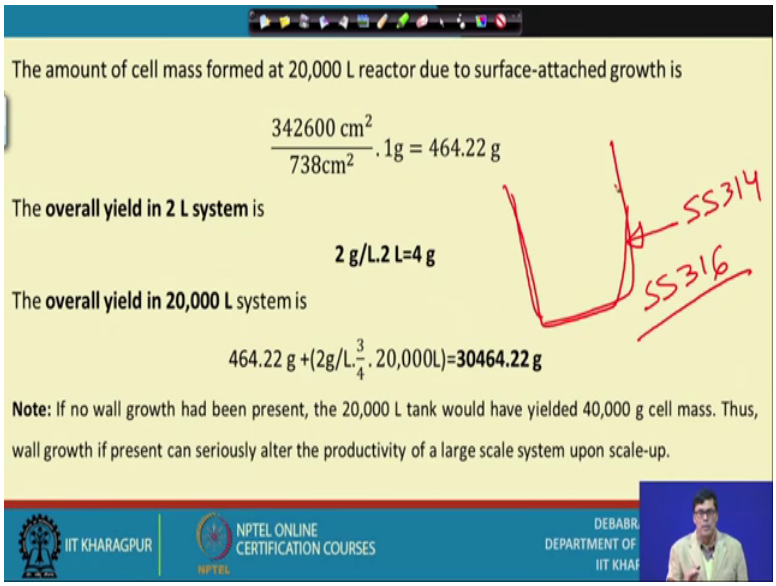

So, this is exactly how we have calculated here you can see how we calculate, we find out that how much gram of that how much gram of cell, remain in the surface attached growth that we find out. Now 2 liters we have this much the now in that 2 20000 liters how much will be there, now here we can we can we can we can find out like this, that this is 2 liter per this is 75 percent is the new suspension.

So, I can I can in the, you the concentration was 2 gram per liter. So, 3 by 4 into 20000 and the plus this is due to the attached growth. So, total gram of cell mass, you can get that is about 30464.22 gram.

The if your cell growth has been present in the 20000, liter then 400, 400 cell gram cell mass thus cell wall, if present can seriously altered the productivity the large scale upon the scale up. So, that is the that is the that is one very interesting thing that we have that you material of construction of the fermented place very important role particularly that that usually the fermented, the material construction should be stainless steel.

Now, as we as we know the stainless steel may be of a different types, that in the chemical industry we use this is 314 and in fermentation industry, we use one this is 316 sometimes we want some kind of special type of stainless steel. Now we add some kind of in varied metal here, that is that will show that that you know that the smoothness of the surface increases. So, the attach the same should not attach with the surface of the of the reactor too much.

So, this is so this a, this is a kind of analysis that has been performed just to find out that, how much cell may attach with the with the with the with the surface of the reactor.

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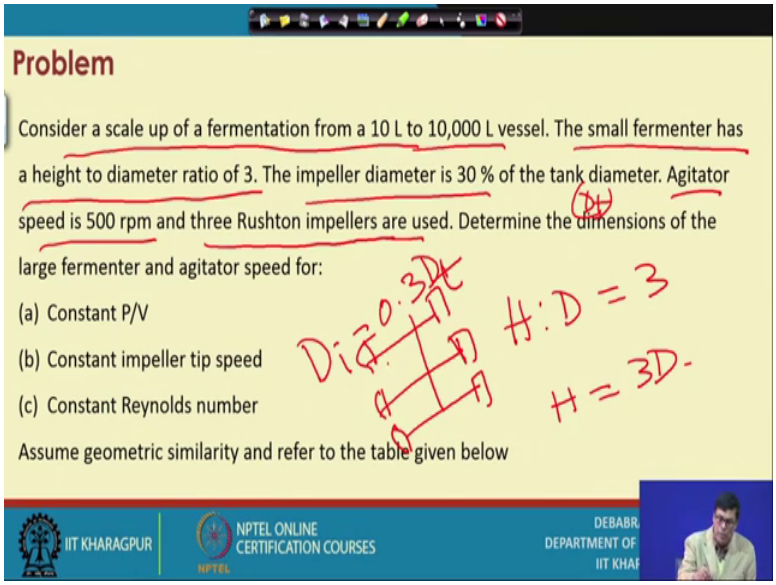

Now, next problem that we have this is simple scale up problem considered as scale up of fermented, from 10 liter to 10000 liter vessel, small fermented has the height to diameter ratio 3 is a 3 that means H is to D this is equal to 3 though, I can write H equal to 3 D am I write, we can write the impeller diameter is 30 percent of the tank diameter; that means, I D I impeller diameter a 30 percent 30 percent means point 3.

That D i D t D t if you say the D t is the tank diameter this is equal to D t, then we can write point 3 into D t, the agitator speed is 500 RPM and 3 Rushton Rushton impeller are used and, and this Rushton impeller looks like this is like this, because you might be knowing that why we use the multiple starter let me explain again.

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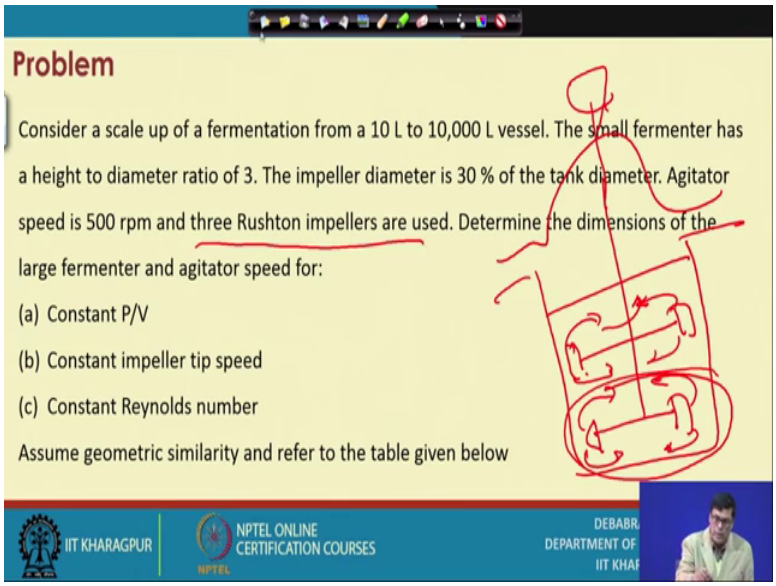

That the suppose you have one starter like this. Now in case of double liquid the liquid will go like this.

So, when it was rotate so, more you can see that most of the stirring will be occur at the bottom part of the liquid not upper part of the liquid, but you want to have the homogeneity in the reaction mixture. So, we shall have to have another impeller here, another so, that you know that here there will be started like this.

So, that is why they have written the 3 Rushton impeller are used determine, the dimensions of the large scale and agitated speed for by a considering constant P by V ratio and P by V means power per unit volume constant impeller tip velocity and, constant Reynolds number assume geometrical say similarity, referred to the given below. The geometrical similarity let us assume that with geometrical. So, let us remove that, we let us assume the geometry similarity of the reactor that means, both are cylindrical reactor. So, now let us see how we can solve this.

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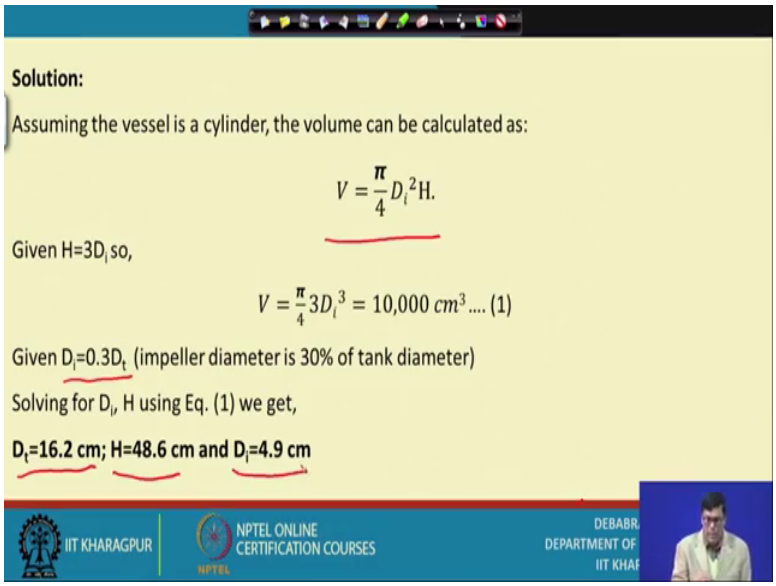

So, here what we what we have in this problem, the initially, we have 10 liter and that is to be scale it up to 10000 liter am I right. So, so this is this is the equation that we have this is a volume of the cylindrical vessel equal to V equal to pi by 4 D i this is square into H.

And we know that H equal to 3 D i, then we can we can write this is the equation and, then we can we can find out that what is the value of D i; D i, because D i equal to point 3 D t that is 3 to 30 percent of the tank, I already explained and then we can find out what is the D t value, what is the H value, what is D i value.

So, in the small reactor the dimensions of the dimensions of the reactor, we can easily find out now what is the height, what is the dimeter and what is the impeller diameter tank diameter all these thing we can we can easily find it out.

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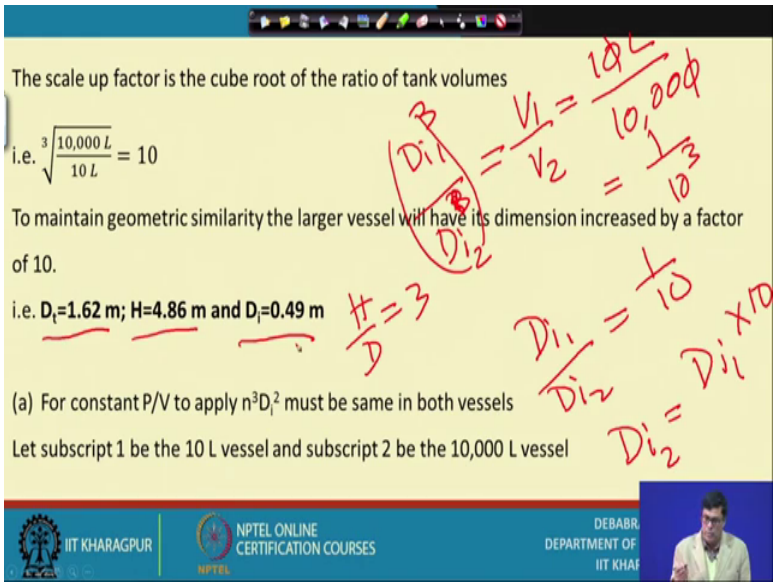

Now, next is the 10000 liter reactor am I right, 10000 reactor so, you know that the scale up,. So, how you can how you can find out that I told you that V 1 by V 2 is equal to what this is V is 10 liters and V 2 is the 10000 liters am I write.

So, I can I can cancel it so, it is 1000. So, this is 1 by 10 to the power 3, this is this is what this is equal to D i 1 cubed by D i 2 cubed am I right. Now then I can write D i 1 by D i 2 this will be 1 by 10, because this is 3 this is also 3 this is a whole to the power 3 if we remove it and, then D i 2 is equal to D i 1 into 1 10 times.

So, we can easily find out the dimeter of the of the vessel if you know the diameter we can easily find out the height of the vessel because, we know where H D i H by D ratio that is equal to 3 and, then also impeller diameter you can 30 percent of the tank diameter is the impeller diameter that we can easily find out it out.

So, this is this is how you can calculate, now let a let us come to the problem.

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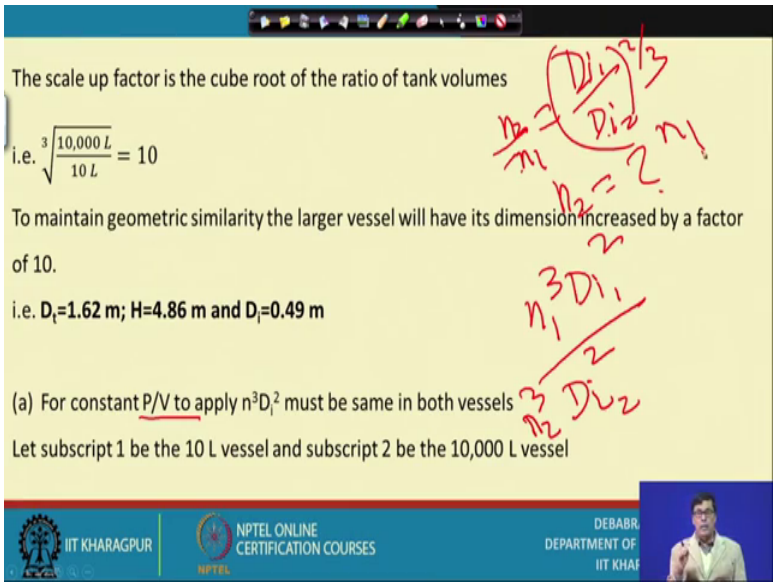

Now the problem is that there are saying at constant P by V ratio, then what will be the, what will the agitator speed; that means, n value we have to calculate. Now P by V I I already mentioned that n 1 cubed D i 1 square into cubed D i 2 square, this is constant am I right if this is constant, then we similarly previously we have already done, that we have seen n 2 by n 1 is equal to what D i 1 by D i 2 to the power 2 by 3 am I right.

So, we know this is one this is a, this is ratio is 1 is to 10. So, we can easily find out the we know n 2 value. So, we can find n 1 value, we know so, n 2 value we can easily find it out. Now if we assume now question comes that if n 1 value is not given, then we can write a this is this in to n 1.

Now, if you if you assume n 1 value is 1, then you can easily write this n 2 value will be the time, or as compared to the small reactor.

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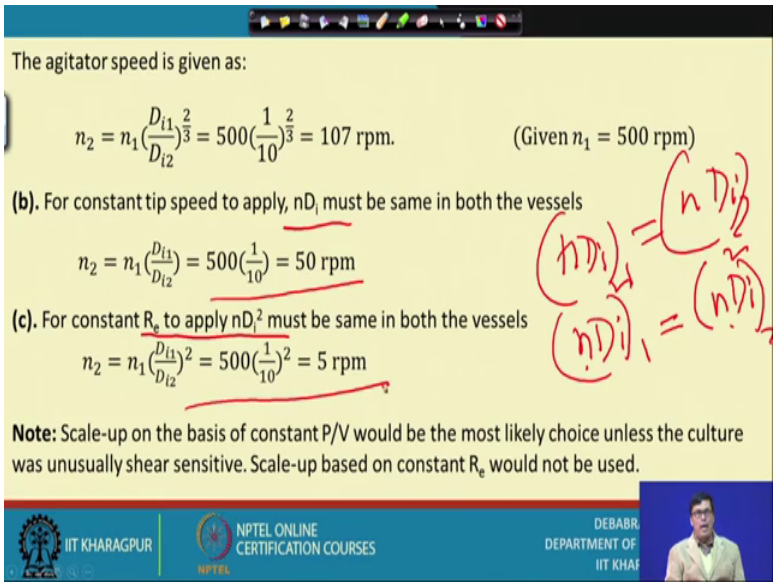

Now next problem that we have that is if when that tip for the constants tip velocity, constant tip velocity means n D i 1 is equal to n D i 2.

So, so if this is this then what will be the n value then you can easily find it out because, this is n 2 equal to n 1 into D i 1 by D i 2 we put this value you can easily find it out. Now next is the Reynolds number Reynolds number what is that the n D i square 1, this should be used in D i D i square 2 am I right. So, this is first case this is second case if it is equal to this, then we can easily find it out this n 2 value is a.

So, it is very simple to calculate that you know what will be the value, during the scaling up of the bio reactor different we can easily solve this you know that, how we can solve the different operation diameter during scaling up of the bio reactor.

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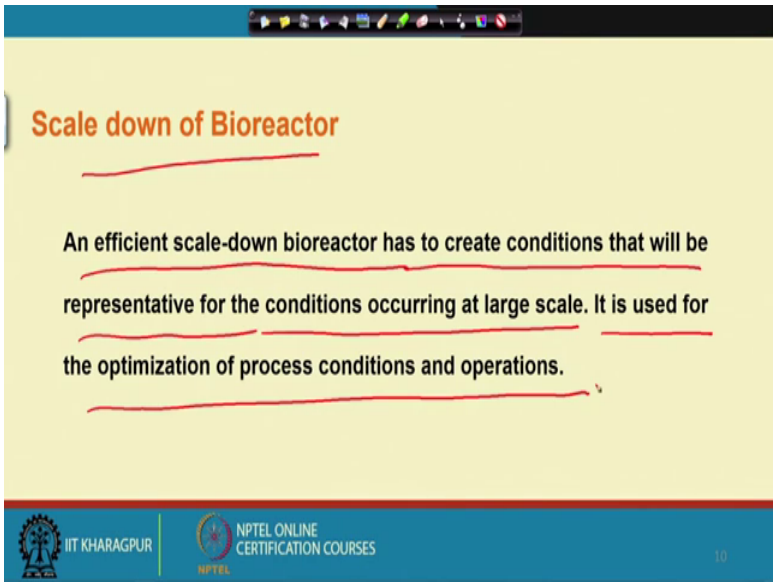

Now next thing that, I am going to going to discuss that scale down of bio reactor up till now, we are discussing about the scale up of bioreactor.

Now, question comes why the scale down of bioreactor is required, because very simple because suppose I am I have been working with a some 200 meter to 200 cubic meter reactor and, we found that we want to form a study, the effect of certain parameters on the productivity of the process. Now if we if we want to study that you know that effect of that parameter, that not necessarily always this should be positive sometime it may be negative also.

So, we cannot pick disk of for studying any parameter in the bigger scale. So, what is required we required at you know that that you we shall have to scale down that, we shall have to that you know if you want to study, some parameter of in the bigger scale first, we shall have to steady that in the smaller scale, I can tell very simple instantaneous.

I work with citric acid industry, and citric acid industry we know that that you know that that we see some kind of industrial strain. And industrial strain as we know that the is considered as a very stable strength and, the productivity of the of the of the particular organism remains unaltered, where do have after generation to generation it does not depends on the generation of the organism.

But still for the operation form of when we go for the full scale trail, full scale operation production parameter, we always run that same generation of the organism. In the small scale just to find out, what are the productivity of the parameter is will be same or it will be going to change and, if it is same then and only then we form the same generation, we prepare the culture and do that.

Similarly, that suppose if we if we want to study, any kind of parameters for these find out that you know whether, this parameter is suitable can enhance the productivity of the of the process. What is the productivity? Productivity means amount of product that is produced per time, I know that that is called I know what is the volumetric productivity, volumetric products is the amount of product permission, per unit time by per volume of the reactor that is called volumetric productivity.

Now, this productivity if we find the if you want to study the effect of certain parameters on the productivity particular on the particular system, then first we shall have to go with in the small scale, that is that is we call scale down, we cannot we cannot study in the be that the high bigger scale. So, this is this is considered the scale down of bioreactor and, efficient this scale down bioreactor has to create the condition, that will be represented in for the conditions occurring in the large scale and, it use for the optimization of the process condition and the operation.

This is the main part for sub scale down, then we want to want to find out the, what is the optimum conditions that we have for this particular process, that you know that will be that we cannot do in the big scale. We can we shall have to be always in the in the in the in the small scale and that a, that we call we always consider as the scale down.

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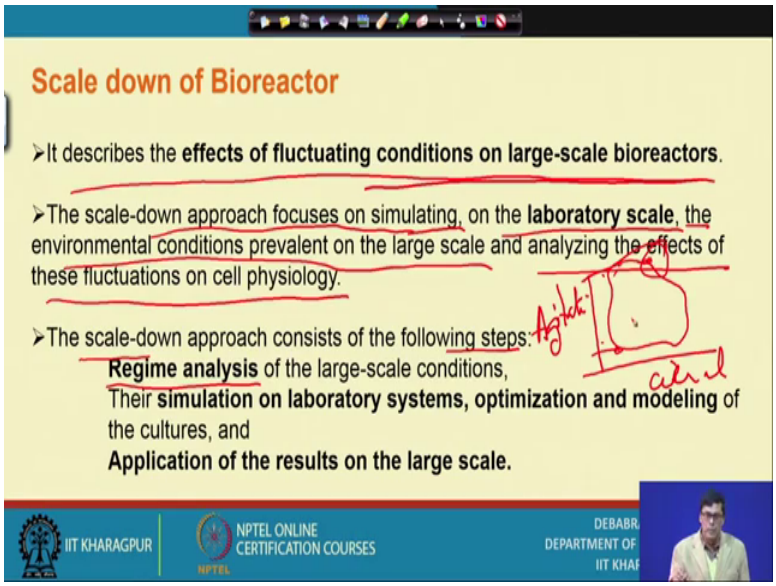

Now, in the scale down what happens is described scale down is when you describe effect of fluctuating condition on the large scale bioreactor because, you know that that a you know when we operate any kind of fermenter it may so, happen that you know operational condition may change you know the although, I can give their it simple example that power failure power failure is a common issue, of any kind of industry as per India is concerned.

So, though it is connected with a (Refer Time: 25:06) set the that you know what will be that you know that you know power generation system, but it may required some kind of time you know some kind of the time is required for start up the process again. So, you know that kind of a fluctuation, whether it affects the productivity of the system that we can study in the small scale also. And find out whether it is there or not.

So, we describe the effect of fluctuation condition on the large scale bioreactor, the scale down approach focuses on simulating, the large scale laboratory scale and the environmental condition prevalent on the large scale and analyzing, the effects of this fluctuation on self physiology, that we can do it very easily in the small this cannot be done in the big scale big scale it will be very difficult.

Now, since scale down operation consist of following steps, one is the regime analysis regime analysis is very important, regime analysis means. Suppose I can tell you suppose this is a agitation am I right, this is agitation and this is aeration. The Google analysis

something like this that means, we shall have to we shall have try to do this do this operation within this regime, we cannot go beyond as for example, if you if you go for this you know if you go for this situation, what is this situation a agitation is maximum aeration is maximum.

So, here you can expect more shear forces, now here you see here agitation is less aeration is the also less. So, here, you have agitation and aeration both are less than that is the permutation processed to a great extent. So, so you have to this a regime analysis. So, while you are going to operate your system, that you can easily do in the in the small scale.

Then their simulation of laboratory system optimization and modeling of the culture that we can I have already mentioned. And application of the results on the large scale this whatever we find out in the small scale, then we can apply into the we whatever good results, we if have then we can test within the larger scale. So, for before you go for the large scale operation it is always advisable to keep the run in the smaller scales.

So, in this particular presentation, I try to discuss some problem related with the scaling up and, when you scale up of the any kind of bio process I have given one example, that when you produce the cell mass by the particularly I can I can give the example of (Refer Time: 27:54) fermentation process. Now there that if cell produce in the cell that you know reacted well, it is very difficult to separate it out.

So, so that that we shall have to find out, that the how much how much productive of the process will be lost, how much cell concentration will be in attached below, then with that we then change the material of construction so, that you can have more smoothness on the surface of the material of construction. So, that you are less attached growth will be there and, second problem we have discuss the combination of the scale up problem, that how different the other parameters can be monitored and finally, I discuss that the what is the purpose of scale down.

Scale down process usually we adopt, when we operate any kind of a bigger scale of fermenter, we want to study the effect of any parameters on the productivity of the process. That we cannot do in the big scale, we shall have to do in the small small scale and, when you when you do that kind of study, we call it scale down. We shall have to

scale down to optimization any kind of optimization study usually carry out in the so, in the in the smaller scale not in the bigger scale.

Thank you very much.