Aspects of Biochemical Engineering
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Lecture – 45
Scale up of Bioreactor- I

Welcome back to my course aspects of biochemical engineering. In the last couple of lectures we I try to discuss the microbial cell growth kinetics with respect to substrate degradation and product formation. We discuss the different batch processes continuous process as for example, CSTR and plug flow reactor, and fed batch reactor, then we discuss several problems numerical problems related to the microbial growth kinetics or product formation.

Now, on this present lecture we are going to discuss a very special aspects of the biochemical engineering. I told you at the beginning the purpose of engineering it is kind of a application, application of the science am I right? That scientifically we can develop some kind of special thing in the lab and when you applied to the for the use of the society the engineering application is required; how we can transfer that information from the lab scale to the commercial scales.

So, the present topic that I am going to discuss today that is the scale up of bioreactor; because you know that suppose as for example, suppose somebody is walking with penicilium chrysogenum for the production of penicillin, and he developed one particular good microbial strain and also did some kind of produces the optimization for maximization of the penicillin production. But you might have carried out the experiment in the test tube or the conical flux then there is a small fermenters maybe to the extent of 2 liter or 10 liters that is look at it in the lab.

But when you go for the industrial scale it is very high, this is might be a 100 cubic meter, 100 cubic meter means 100000 liters or 200 cubic meter means 200000 liters. So, it is very big. Now question comes whatever when you do the scale up one thing we shall have to take into account that whatever environmental condition, whatever condition prevailing in the small reactor similar condition should prevail in the bigger reactor. This is the main purpose of scaling up and so that your organism should work in a similar manner and to give the product.

So, for doing so that what we are going to analyze, how the different operational parameters changes to maintain the identical situation. So, this particular lecture will deal with that and let us start with the definition of scale up.

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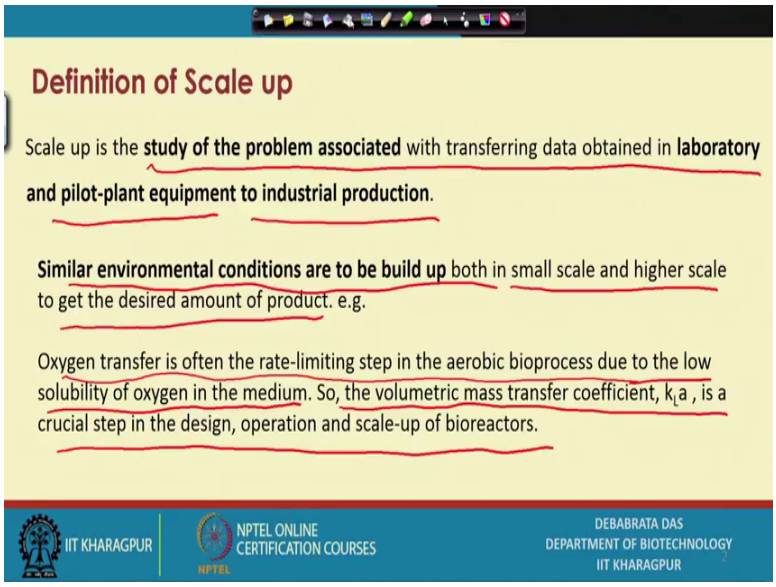

Now if you look at the definition of scale up, scale up is the study of the problem associated transferring data from the laboratory to pilot equipment to the industrial world production. So, what I want to tell you that, we cannot transfer we cannot use whatever conditions that we have operating operational conditions we have in the smaller reactor, similar conditions the will be applicable in the bigger fermenter.

So, you know that the operation conditions will be changed; so to maintain the similar type of environment. So, this particular scale up deals with that. Now the main purpose that similar environmental conditions are to build up both for the small and the higher scale to get the desired product. This is the main purpose obvious we doing the scale up as for example, oxygen transfer is of the rate limiting step in the aerobic bioprocess due to low solubility of oxygen in the media because we know that microorganism can take the oxygen which is dissolved in the liquid not like human beings. We take the oxygen which present in the air so, and seen the oxygen is sparingly soluble in water.

So, major bottlenecks of major or major limitations we have with an aerobic fermentation processes is the dissolve oxygen concentration. So, that is considered as the rate limiting cells. So, the volumetric mass transfer coefficient k L a is a crucial step in

the design and operation and scale up of bioreactor. So, when you do the scale up we will keep it in mind the k L a that we have in the small reactor and k L a that we have bigger reactor there should be more or less same. So, that we can build up we can give the similar we can fulfill the similar requirement for the microorganism.

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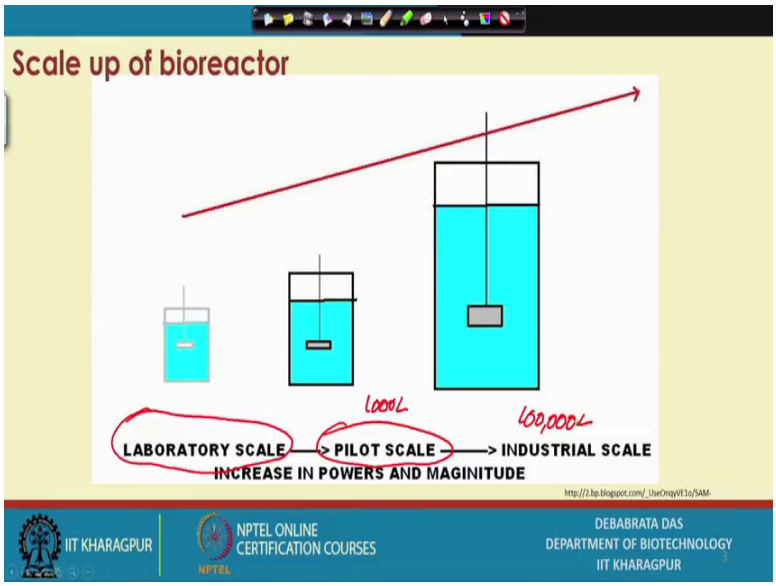

Now let us you consider the scale up how do they scale up that first we do in the laboratory scale, that is whatever we develop in the lab scale then it comes to the pilot scale because just to we elaborate just for example, suppose here we may start with conical flux of capacity 100 milliliter, then 500 milliliter, then 2 liter, then 10 liters, but after that we go for pilot scale maybe pilot scale, may be as high as maybe 1000 liters or so, and then we go for the industrial scale maybe 100000 liters or you know maybe 200000 liters of the industrial scale.

So, we want to find out that how the operational parameters keep on changing during the scaling up of the process.

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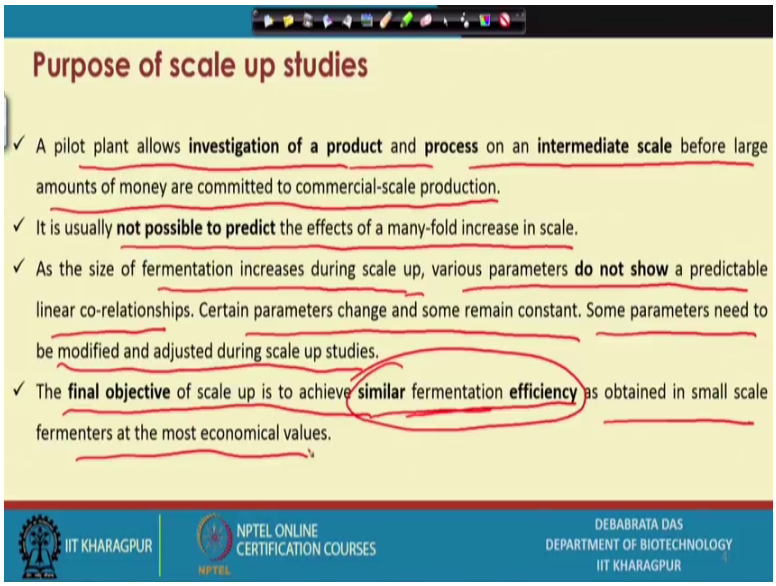

Now, purpose of the scale up, purpose of the scale up is the pilots plant allow the investigation of a product and the process of a intermediate scale before large amount of money are committed to the commercial scale. So, we do agree that when you run any kind of process that the small scale, the monetary involvement of the process will be very less am I right,? Now when you go to the bigger scale, then a monetary involvement will be very high. So, naturally when we go for the high investment they there should be confident on the investor that whatever be report we get in the small scale same should be available in the bigger scale.

So, it is the usually not possible to predict the effect of many fold increase in the scale. Suppose whatever data we have in the small scale, we cannot just multiply and find out that this might be suitable for this this not possible. As the size of the fermentation increases during scale up, various parameters do not show predictable linear co relationship that is the major problem there is no linear co relationship certain parameter change, certain parameter remain constant, some parameter need to be modified adjusted during the scale up studies.

So, these are the couple of things that we should have to keep in mind and final objective of the scale up is to achieve the similar fermentation efficiency this is very important; this is very very important that whatever efficiency we get in the small scale same

efficiency we should get in the bigger scale obtained in the small scale to the most at the most economical values. So, this way this is the very important aspects of scale up.

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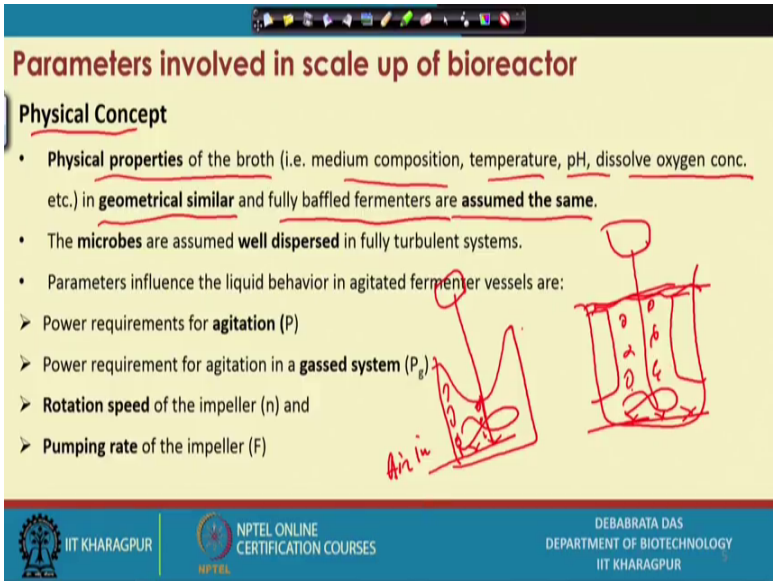

Now, parameters involve now question come, how you do the scale up? Naturally when we do the scale up we shall have to consider certain parameters and what are the parameters we should consider during the scaling up of the process.

So, first we have the physical concept that the physical property of the broth medium composition, temperature, pH, dissolve oxygen concentration etcetera in geometrically similar and fully baffled fermenters are assumed to be same. I told you can remember that most of the fermenter we require baffled why you require baffled? Because if you do not have baffled, then there will be vortex formation here you there will be no vortex formation, but if you have this stirrer here then you will find this kind of vortex formation.

Now, if you have vortex formation, now when you do kind of variation here you look at the air that is suppose this is air in. So, here the air will get less the will less the retention time as compared to here. So, when a bubble goes like this here it will take more time here it will. So, mass transfer that depends on the retention time the here since the level is the liquid level is the almost constant even your bubbles goes out the retention time of the bubbles will be more or less same.

So, this is one of the important aspects.

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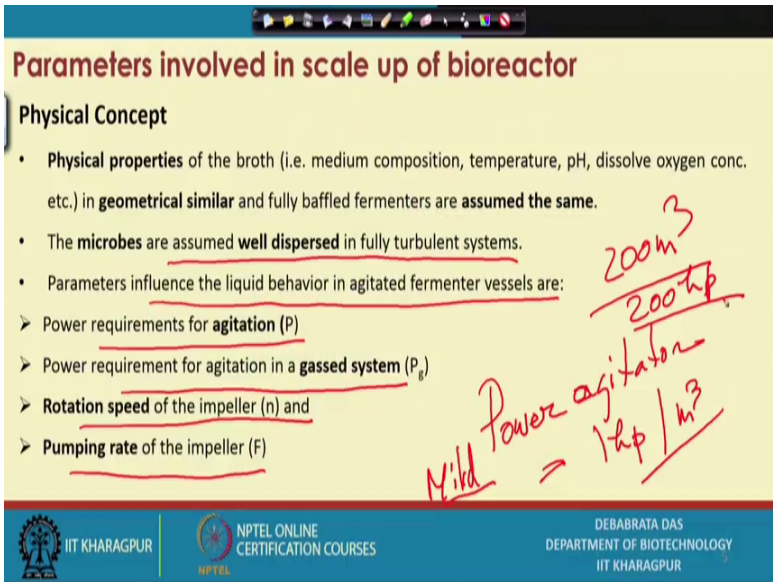

The microbes are assumed to be well dispersed in fully turbulent system. So, we know the microorganism they are in soluble mass and they should be well dispersed. So, that the substrate can freely interact with the microorganism and give the product. Now parameters influence the liquid behavior of the agitated vessel are one is the power requirement by the agitator, power requirement agitator with the gassed system rotational speed of the impeller and pumping rate of the impeller.

So, there are several parameters that you know plays the important role during this process one is the power. Now what is the power requirement? I told you that in a power requirement power most of the power is consumed by the agitator how much is power required for mild agitation if you consider mild agitation mild, then power requirement is about 1 hp horsepower per cubic meter volume of the reactor.

Now, suppose somebody is wanted to operate 200 cubic meter reactor. So, power drawn by the agitator will be as high as 200 hp the huge power that as to. So, you know that. So, more power that more monetary invest investment is there. So, our purpose of the scale up also we shall have to look into what should be the minimum power requirement in the agitator to get the maximum amount of product this is also another very important things.

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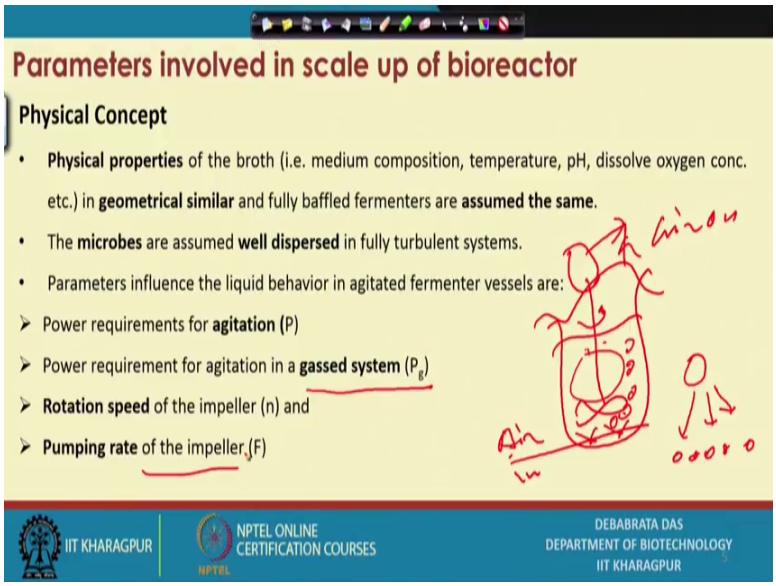

Now, another important thing is the gas system and non-gas systems. Suppose this is a stirrer now when it is stirring like this here, the naturally power drawn by the agitator will be more. Now here if you have some kind of air that you flow in the system air in and air out, this is the air out then the due to the aeration there will be the kind of turbulence the kind of movement of the water. And due to this that you know that a power requirement of the stirrer will be less as compared to the un gassed system.

So, this is the gassed system power requirement, a rotational speed of the stirrer that also plays a very important role because the as the bubble going out then if we increase the rotational speed then one bubble will disintegrate into the smaller bubbles these are all smaller bubble and more smaller bubbles; that means, more surface area. So, if the surface area is increases then what will happen, there will be more mass transfer. Now is the is pumping rate that is the what do you call the emission rate and that you know how more how this is usually explained that VVm, what is VVm?

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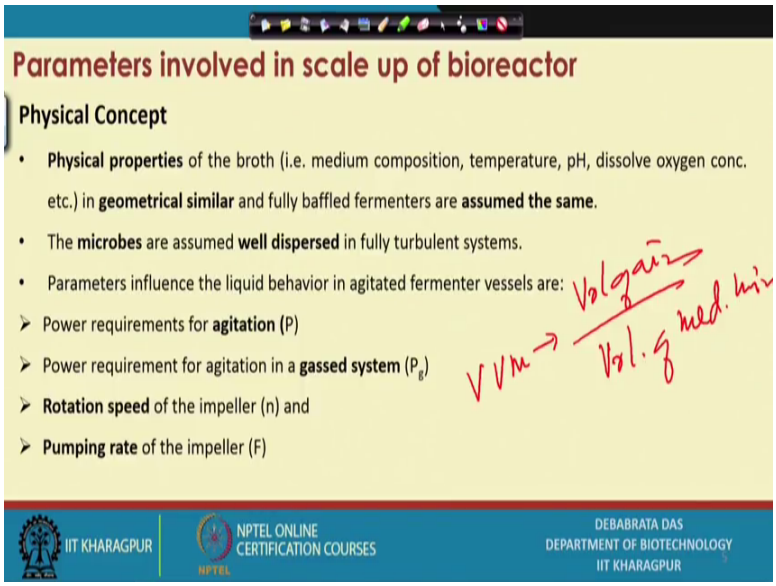

VVm is the, I told you this is volume of air per volume of media per minute.

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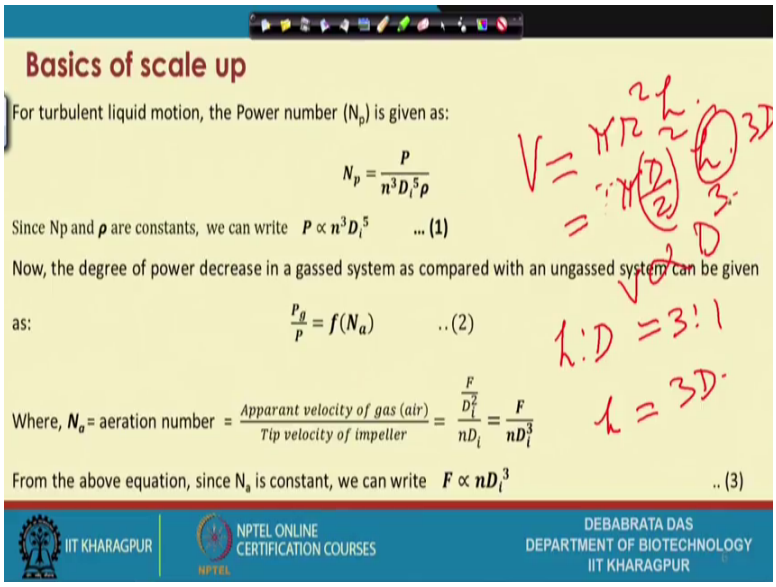

Now, let us see how you can calculate the power requirement by the agitator. Now this is the, this is what do you call, this is the power number, power number equal to P is the power drawn by the agitator, n is the excitational speed, Di is the diameter of the impeller and rho is the density. Now for a particular the type of there are different types of the agitator am I right and for different type of agitator at different Reynolds, the

Reynolds number they have, what is a Reynolds numbers? Reynolds number that indicate the flow characteristics of the fluid.

Now, we have different this power number. So, power number basically constant for the particular agitator at the particular Reynolds number. So, what we can write that if this is constant. So, then we can write power is proportional to n cube Di to the power 5. Now another thing I want to point out that suppose volume of the reactor how we can calculate? This is pi r square h am I right, what is r? R equal to I can write r equal to D by 2 whole square am I right.

Now, for a particular fermenter there is the fix h by D ratio. This is usually maybe 3 is to 1 1 2 is to 1 or you know some fix ratio is there. Now if you like this then I can write h equal to 3D. So, I can replaced by 3 D am I right. So, this is basically if you look at that the D V is usually proportional to D cubed.

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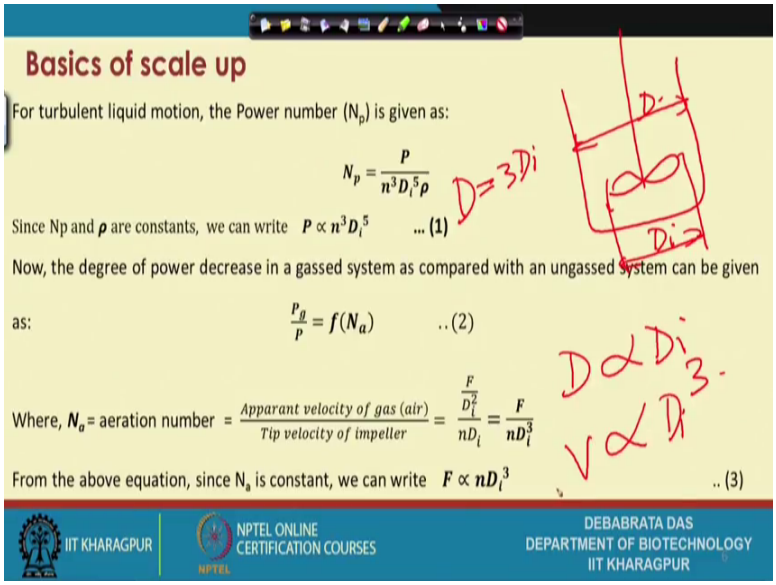

Now in a particular fermenter if you look at the, this is the fermenter now this is the agitator this is called diameter of the agitator and this is called diameter of the tank. So, there is the ratio between D and Di; may be D equal to that 3 into Di whatever may be 2 into Di whatever is there.

So, what I want to say tell the D is proportional to Di, if Di is proportional to I can write V is promotional to Di to the power cubed am I right. Now if it is Di to the power cubed then if we here if you write P by V.

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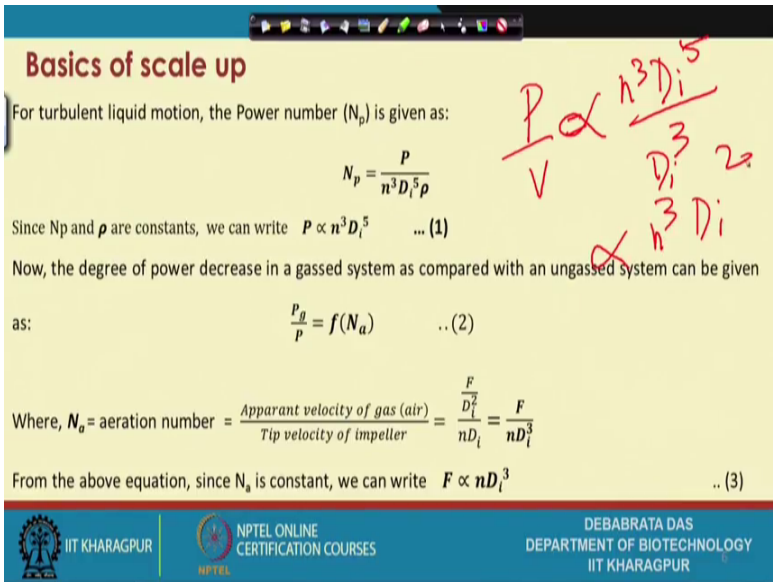

P by V if you write then what you can write? This is proportional to n cubed Di to the power 5 divided by Di cubed. So, this will be n cubed Di squared am I right. So, we can easily find out we can find in the next case it is there. Now I was talking about the gas system and un gas system.

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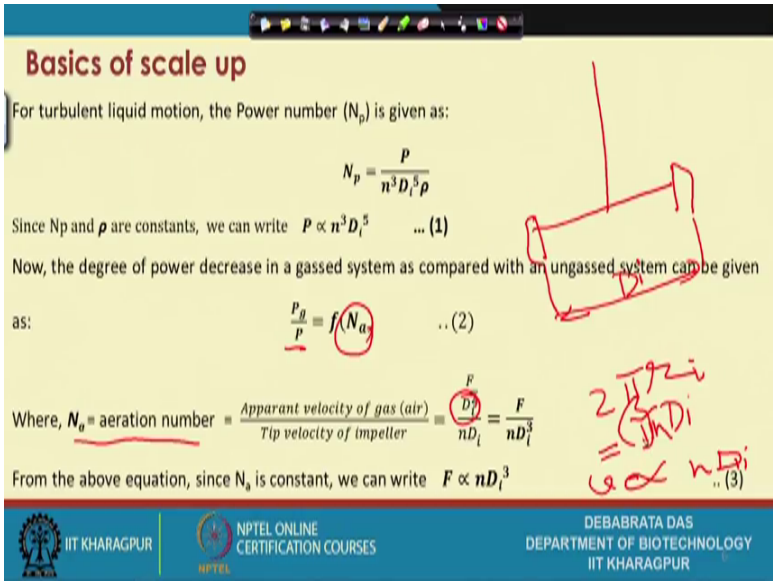

This is the ratio this is proportional to aeration number.

Now, what is the aeration number? Aeration number is the apparent velocity of the gas per unit surface area this is the surface area, surface area what is the unit per unit length? So, Di square I can easily write and this is the tip velocity of the impeller, the tip velocity of the impeller how we can determine? This is like this suppose this is Di am I right. So, what is the perimeter of that twice pi r, this is equal to pi into Di am I right, this is i. Now suppose n number of rotation per unit is there. So, you multiplied by n. So, we can write that rotation of that is tip velocity of the impeller is proportional to n into Di because the now pi is constant.

Now if we do solve this equation, then we find F the aeration rate that is equal to proportional to n Di cubed.

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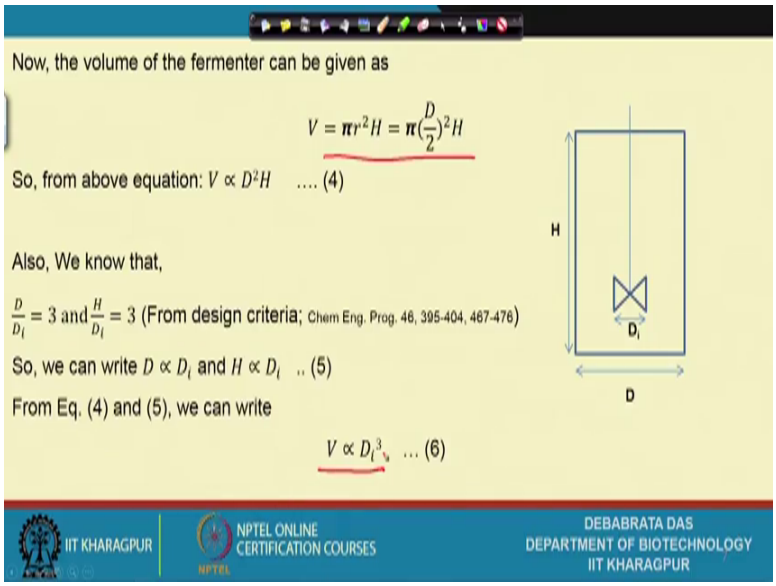

Now, this I have already shown you I do not like to discuss again this is how this is equal to Di cubed and now this is V equal to Di cubed that I have already shown you.

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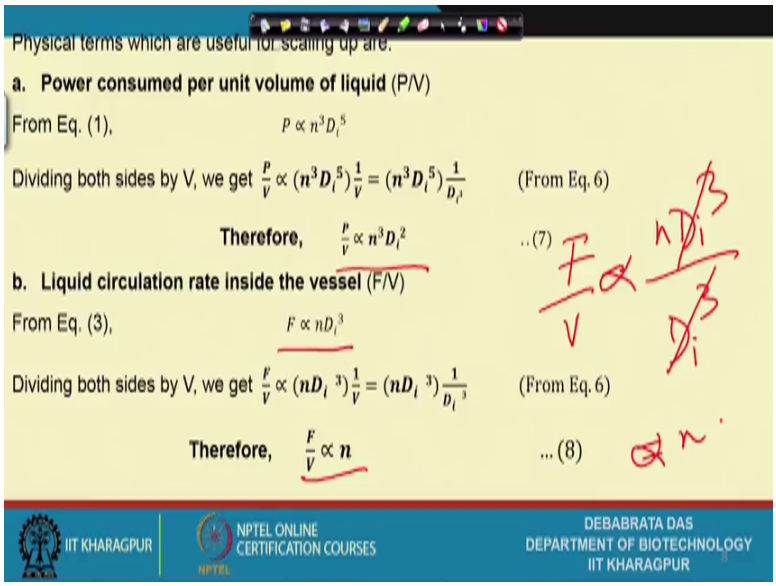

Now, here I also shown you that, how the P by V the ratio is this. Now if this also I have shown you. Now F by V that F is what? F by V will be, what F by V is proportional to n Di cubed am I right and this is Di volume is proportional to Di cubed. So, this, this will cancel, this will be equal to n. So, this is for given this is what is given here.

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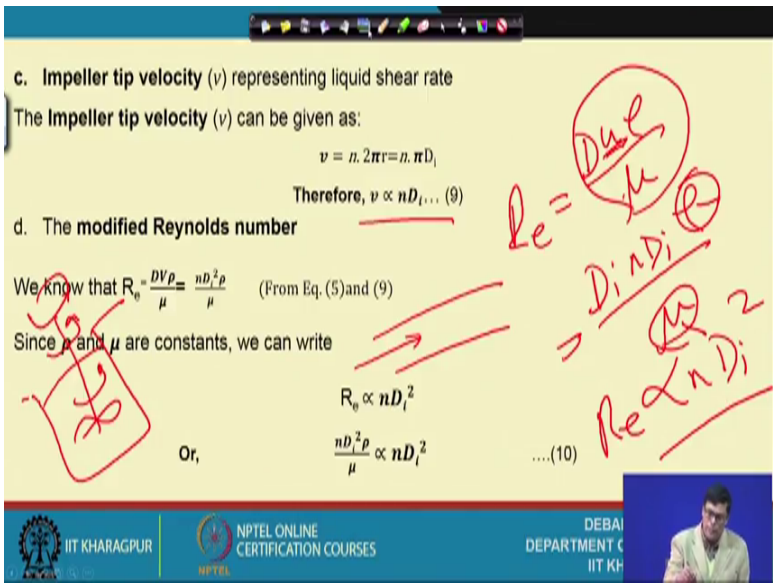

Now, this is the tip velocity I have already shown you how it has come and the Reynolds number, what is the Reynolds number? Reynolds number is the Re Du rho by mu am I

right or D is the diameter of the impeller because the one thing we should remember in case of any kind of vessel, the agitation we call it that agitation Reynolds number.

This is not the normal Reynolds number what is the normal Reynolds number? When suppose liquid is passing through a pipeline that Reynolds number is this, but when you have a vessel this is a vessel and this is a this is your stirrer. So, with the when this stirrer is moving will be the movement of the stirrer, what is happening that a liquid also moving am I right. So, this is the flow a characteristic of the liquid is due to the movement of the stirrer. So, since they due to the movement of the stirrer, we considered as agitator Reynolds number we should remember that.

Now this is equal to Di and what is the tip velocity of the air? The velocity this is the already we have find out n into Di this is rho into mu. So, I can write Re equal to is proportional to these are constant for a particular liquid this is the viscosity this is the rho is the density. So, we can write n Di square this we can write this is exactly what we have written here. So, the Reynolds number equal to nDi.

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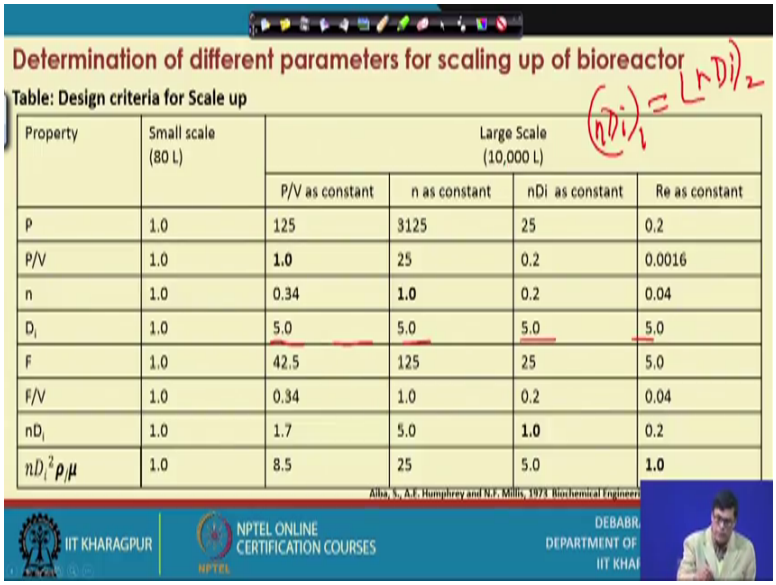

because now let me show you that how the different parameters we can calculate during the scale up. Now, here we have 3, 4 different instances we can find out that the one case P by V ratio is constant and that is a n is the constant, another is nDi is constant, another Reynolds number is constant. So, P by V is the power per unit volume of the reactor that is constant, n is the rotational speed of the stirrer is constant, another is the nDi, nDi is

that the tip velocity of the stirrer that is constant and Re is the Reynolds number now the first case P by V is constant.

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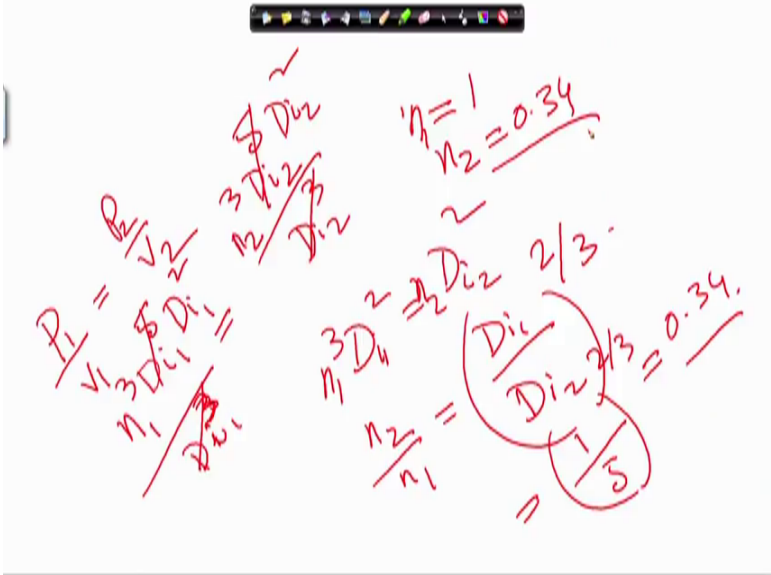

Now let me show you that if I keep P by V constant that what will happen? This is P 1 V 1 equal to P 2 V 2, I can write it like this. Now, this is the n 1 cubed Di to the power 5 divided by Di to the power cube, this is equal to I can write n 2 D 3 Di, this is Di 1 this is Di 2 to the power 5 and this is Di 2 cubed. So, if you this will you can cut and this will be Di 1 squared and this will be Di 2 square. So, what is the equation you will get? N 1 cubed Di 1 squared equal to n 2 Di 2 square. So, I can write n 2 by n 1 equal to Di 1 by Di 2 to the power 2 by 3, am I right that we can write like this.

So, what is the Di value 1, what is Di 2 value is 5. So, we can write this is 2 by 3 and it will come around about 0.34. So, what does it indicate that, in a small scale here what is the rotational speed do we have? This is that if it is 1 and then in the n 2 in the bigger scale is coming 0.34, am I right. So, I can give another instance now, how that other parameter has come that Di parameter has come.

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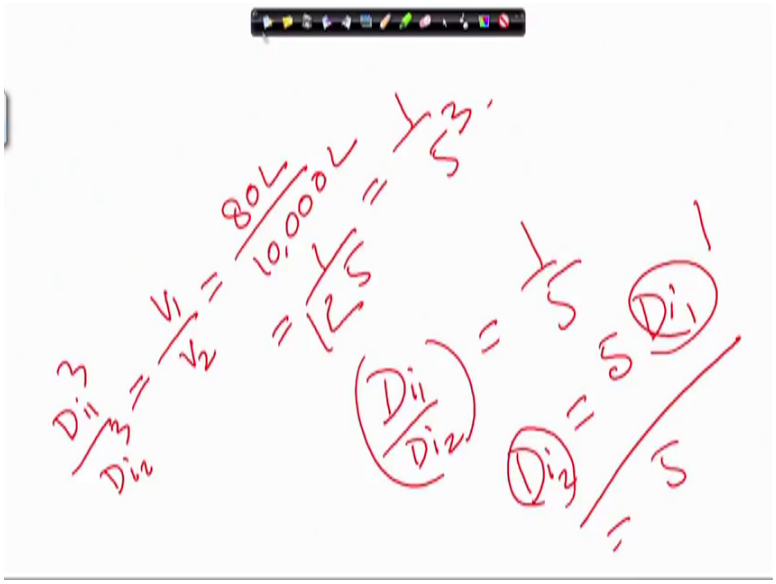

So, if you write V 1 by V 2 what is having V 1, what is the capacity 80 liters am I right this is 10000 liters.

Now, this is equal to I can write Di 1 cubed and this is Di 2 cubed am I right and this is equal to 1 by 125 then what is 1 2 5 it is 5 cubed. So, I can write Di 1 Di 2 this is equal to 1 by 5. So, Di here 2 will be what? Di 2 will be equal to 5 into Di 1. So, this is why this is Di 1 is 1. So, that is why we put Di value is 5.

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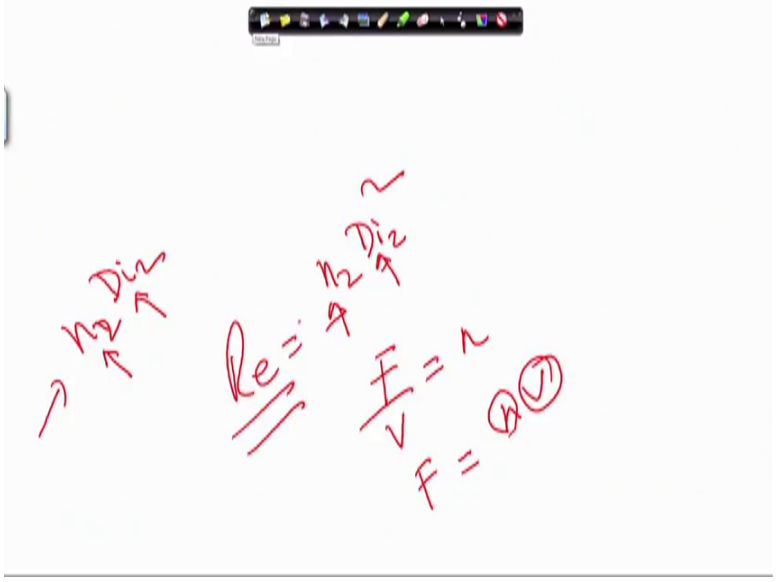

Similarly we can calculate the other parameters like n 2 Di 2 because we know now you know the value of n 2, and we are now we know the value of a Di 2. So, we can easily find out the a speed of the that we know in the rotational speed of the tip velocity of the stirrer. Now Reynolds number, Reynolds number is equal to what the Reynolds number is equal to n 2 of the bigger reactor a Di 2 squared. So, this is proportional to that. So, that we know n 2 value Di 2 value. So, we can easily calculate the value of Reynolds number. Now F by V ratio that what is equal to this is n. So, n value already we calculated. So, we can already report.

Now, F equal to what n into V we know the, what is the volume of the reactor? What is the n value? So, we can easily find out the F value. So, like this we can calculate all the values that we during the scaling up of the process, we can calculate all the values. So, next case is that n equal to n 1 equal to n 2 and second case Di 2 this is n Di 1 is equal to n Di 2. So, now, one thing I want to stress here that Di 2 value in all cases should be same because scale is same. So, we assume the geometrical configuration is remain almost constant.

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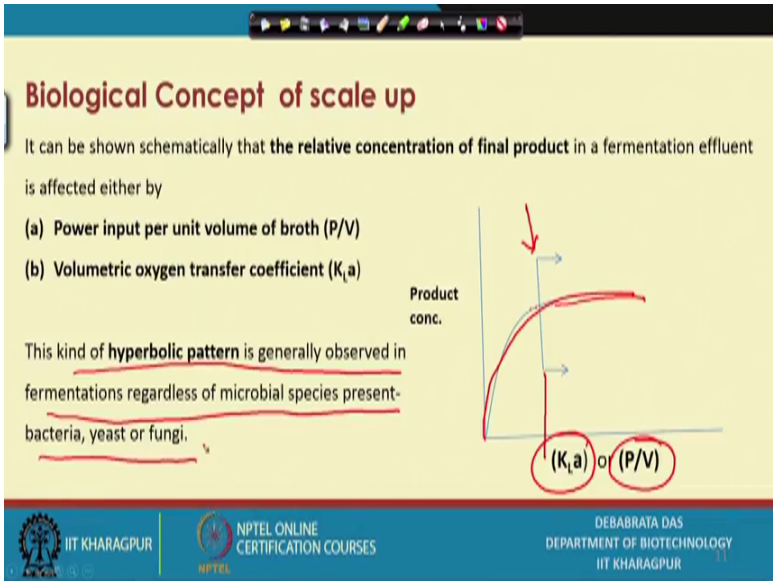

Now the another very important factor that we have the biological concept of the of this scaling up of the process. Now in the what is the biological concept that as the your power you input power increases per unit volume it increases the K La value, what is K La value? K La value is the volumetric mass transfer now here we want to a we have

shown here that here you see that K La value volumetric mass transfer this is P by V ratio. Now as it is increases your product concentration increases, then it attend the plato. So, why what I conclude that if you use this power after this power, this we have put a concentration remain constant. So, we know more you spend power more money we shall have to spend the process, it will be more expensive. So, biological concept is that what is the minimum power is required to get the maximum amount of product. So, here this kind of hyperbolic pattern is generally observed fermentation regardless the microbial species present in bacteria yeast and fungi.

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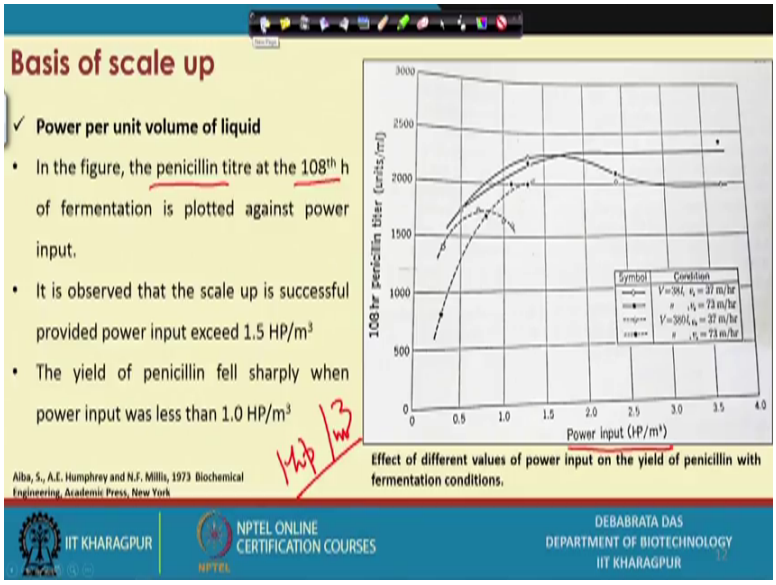

Now, I have given some typical example one is then the penicillin fermentation process, now if I carried out border 108 hours of fermentation and when we plot plotted the power input in the stirrer I told you, that a power drawn by the agitator in the fermentation industries much high because with a 1 hp that per cubic meter volume of the reactor this is usually the case.

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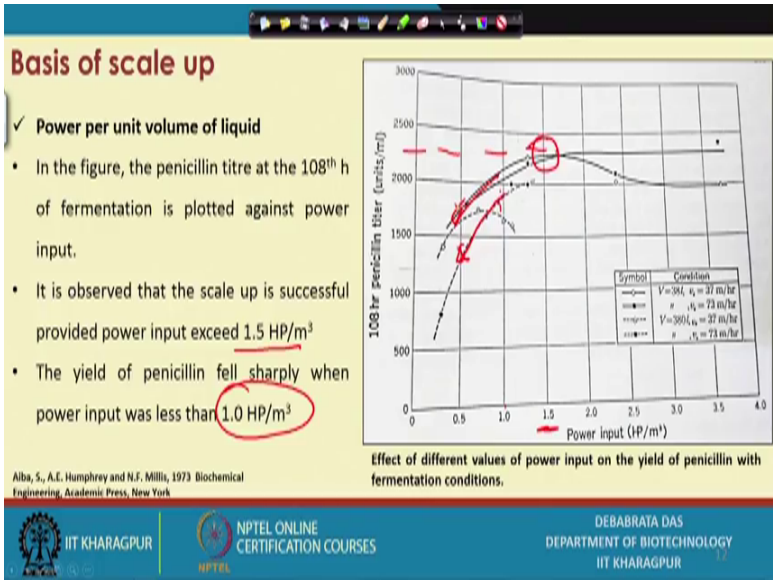

Now, here we will find in case of penicillin fermentation process, that if the power drawn by the agitator 1.5 here you can see 1.5, then we will get the maximum amount of product. But if we if it is less than 1 HP per this here that you there is a trend is less than that, then power that you know product concentration that is decreases.

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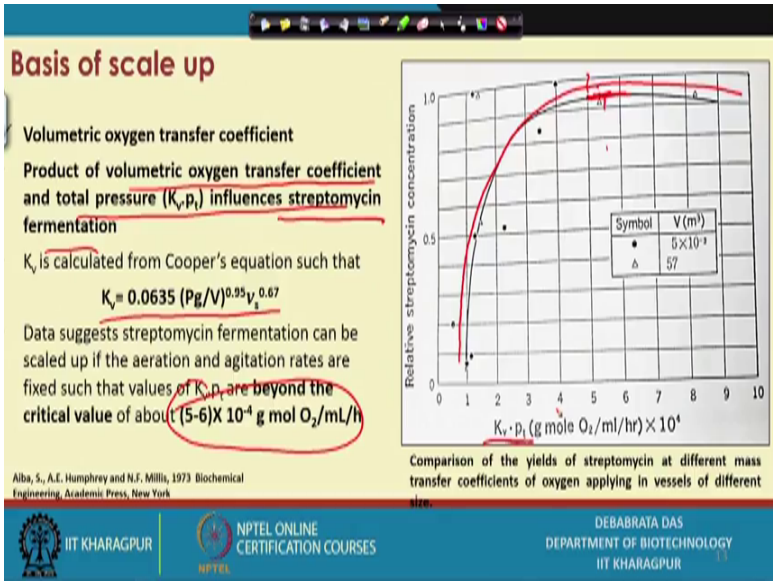

The next example we have with the streptomycin fermentation process. Now here I try to correlate this volumetric mass transfer coefficient. The product of volumetric oxygen transfer coefficient and total pressure influences the streptomycin fermentation process.

Now, this is the volumetric that the oxygen transfer rate and that the Pt is the total pressure. Now as it is the changes the relative concentration of the streptomycin changes like this. So, after sometimes it access the pluto am I right. So, here we get the maximum amount of streptomycin production. So, what is the written that you know 5 to 6 10 to the power minus 4 gram mol oxygen per millimeter per hour will give the maximum amount of product formation.

So, in this particular lecture, I try to discuss that during the scale up of the bioreactor how the different operational parameter changes. And I told you when you do the scaling up of the any kind of reactor will take into account whatever conditions we have in the small scale similar conditions should prevail in the bigger scale of fermentation process, that our product concentration even unaltered.

Thank you very much.