**Principles of downstream techniques in Bioprocess – a short course**
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**Lecture – 6**
**Filters, Centrifuges, Filter Aids**

Last class we talked about solid-liquid separation, several different types of solid-liquid separation and now we will talk about filters, centrifuges and what it means by filter aids. Okay so if you look at a material that needs to be filtered, so there are different problems that material can come into, the viscosity could be very high, the solids that is getting removed may have problem because it may form a compressible bed and so on actually.

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So we need to do some sort of a pretreatment in order to make the filtration process easier. So the pretreatment can be different types of pretreatment. It could be heat, the slurry, so that it becomes easy for filtration or you can add a coagulating or a flocculating agent, so that the filtration is very easy or we can use something called filter aids, which will prevent the compression of the bed or improve the porosity of the bed, so that the filtration process is fast and reasonably good.

So these are the three different approaches by which one could perform the or improve the process of filtration.

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So heating, this is the simplest and easiest method, least expensive of all these methods, it improves the broth handling because when you heat it up a little bit, the filtration process is simplified because the viscosity comes down and the problem is, it is not suitable for thermally labile product, that is the biggest problem with the heating. It can also be used as a pasteurizing, especially if you are talking about milk or milk products, which need to be quickly heated up and cooled so that the bacteria dies, then this type of heating method is very good actually okay.

So for example if you look at downstream processing of pullulan from certain pullalanase type of organism, so when you heat it up, what happens is, all the proteins get denatured, so the precipitate down but pullulan, nothing happens to the pullulan. So generally we can go up to 80 degree centigrade for 20 minutes, so all the proteins as you know are very thermally sensitive, so they get degraded or deactivated, then they precipitate down except pullulan.

So if you know the stability of the protein at a certain temperature, then we can heat up slightly below that value, so that the proteins which are more thermally sensitive may precipitate down.

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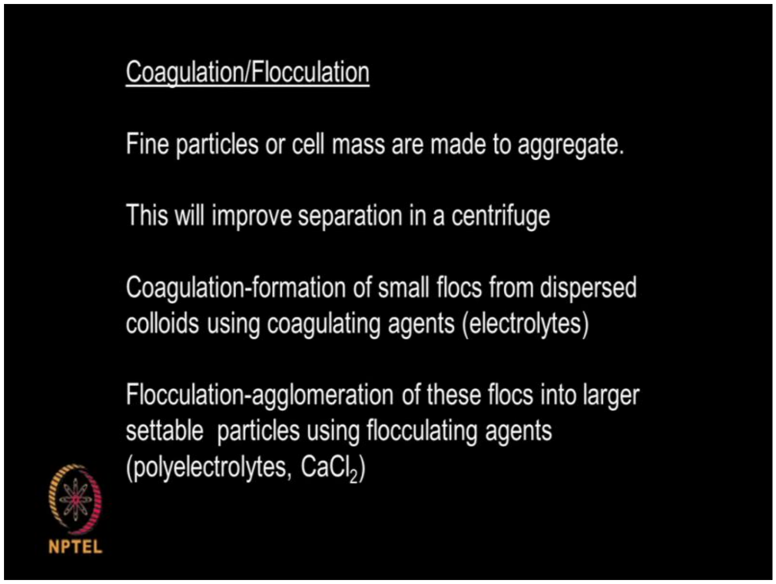


Next one is coagulation or flocculation, so we did mention about coagulation, flocculation in the previous class, where we are trying to disrupt the electrostatic forces that are present on the surface of fine particles because of that the particles are not coming together and forming larger flocks. So we can add some coagulating agents or flocculating agents, so as soon as you add this, the particles become slightly larger and then it becomes easy for you to filter.

Otherwise the particles are so fine, it may be difficult for you to filter or you may have, you may require a nano filter type of a setup. So in order to avoid that we can add a coagulating agent or a flocculating agent, make the particles to come together, so the particles become larger and then it can be resort to an ordinary filtration techniques.

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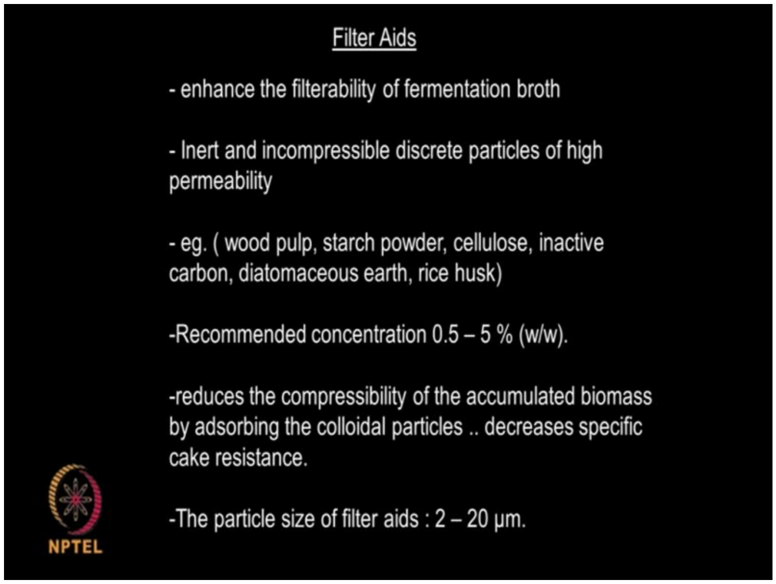


Filter aids, what are these filter aids? Filter aids help in increasing the porosity of the bed. It prevents the bed from compression, as you know if the bed gets compressed as the pressure increases, then the flow of liquid through the bed becomes impossible and so at some point of filtration, the entire process stops. So we can add filter aids which will increase the porosity as well as it prevents the compression of the bed. So there are natural materials which are added, there are synthetic materials that which are added as filter aids.

So they are basically inert incompressible particles, it could be wood pulp, starch powder, cellulose, inactive carbon, diatomaceous earth, rice husk and so on actually. You can have almost 5 % of that can be added into that actually.

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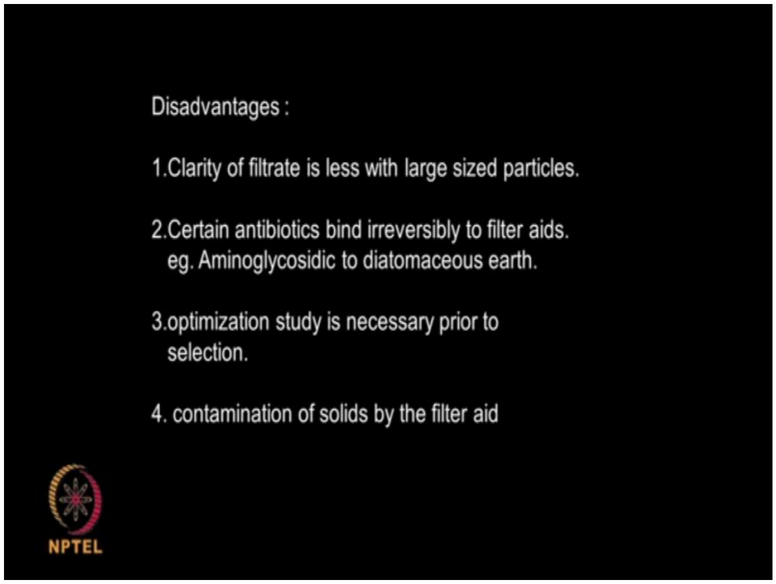


But then it has got disadvantages. Many disadvantages because the clarity of the filtrate is less in large size particles, certain antibiotics may bind to the filtrates, okay so when it binds to the filtrate for losing the product, you need to do some optimization. That means we need to perform few experiments at different concentrations of filtrate and then see which is best concentration, then you are going to have contamination of the filtrate in the solid.

So if solid is the desired product then obviously this type of approach is not advised. If the liquid is desired product then it is okay.

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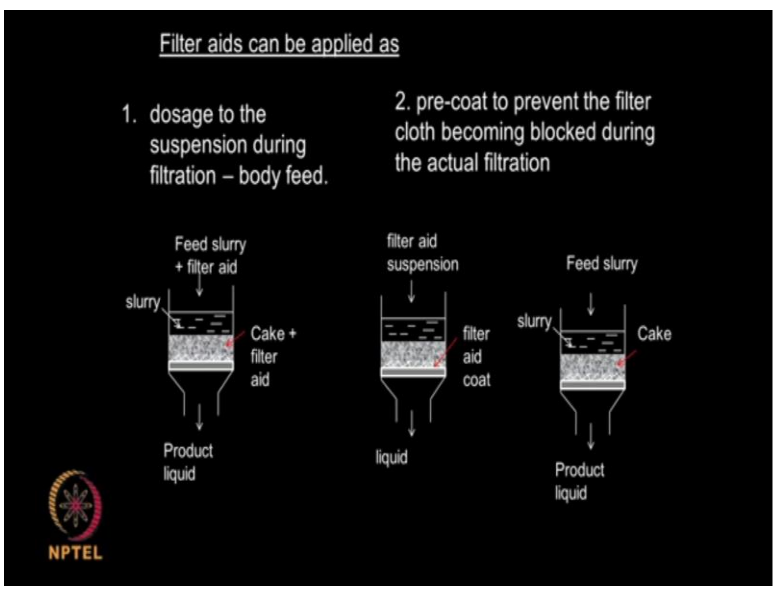


So you can add filtrate in two different approaches, one is first we can add filtrate so that there is a pre-coat that is formed, that is one approach. Other approach is we can add filtrate and the slurry together, so that the cake contains the filtrate is deposited on the surface. So if you are adding that, so we can add the feed slurry to the filtrate and the cake will contain both the solid as well as the filtrate. The other approach is you first add the filtrate suspension, so it forms a pre-coat here and after that you add your feed slurry.

So the filtrate prevents the blockage of the holes in the filter medium, so that he liquid flows nicely. So both the approaches are carried out in industrial scale actually.

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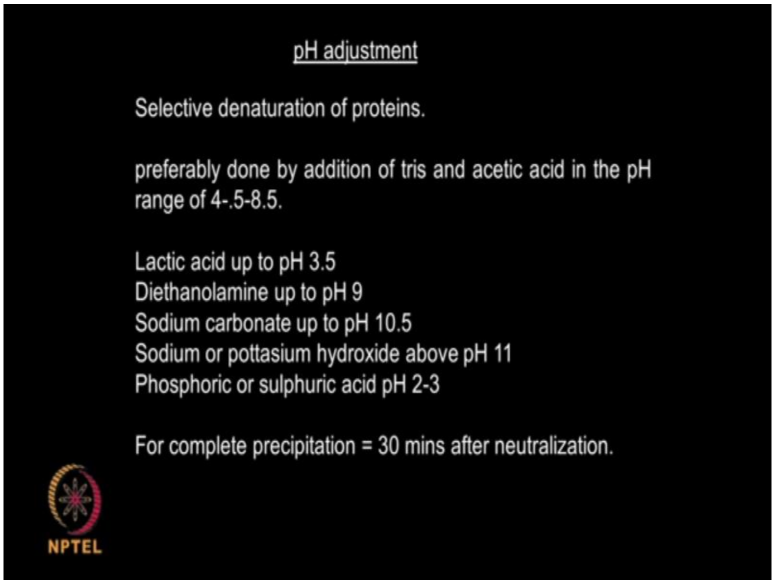


pH adjustment that is another approach by which we can improve the filtration. Sometimes we can adjust the pH so that selectively you are denaturing some proteins and once the protein gets denatured, they may just precipitate down actually. So for each protein you may have certain pH at which it gets denatured, so we can add this for acetic acid, in the pH range of 4.5 to 8.5. For example lactic acid up to pH of 3.5 and so on actually.

So we change the pH or we adjust the pH so that unwanted proteins gets denatured and precipitate, so you give some time, so may be half an hour to 45 minutes. So that the neutralized protein aggregates, settle down and then you can take out your liquid or you can decide to normal filtration. So these are the different approaches by which one could improve the filtration process actually okay. Now let us look at some principles on which the filtration is based on.

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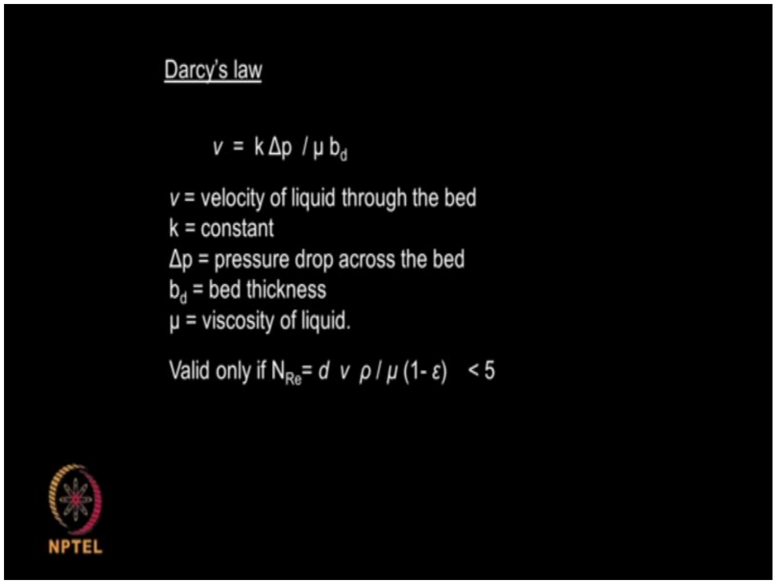


The most important principle I did mention in the previous class that is called the Darcy's law. Okay. Darcy's law tells you the velocity of liquid to the bed as a function of directly proportional to the pressure drop across the bed. So higher is the pressure drop, higher will be the velocity, inversely proportional to viscosity. If the viscosity of the liquid is high, obviously the velocity is going to be less and inversely proportional to the bed thickness.

The bed thickness is less, I mean if the bed thickness is more, the velocity is going to be less and it is valid when the Reynolds number is less than 5. So you need to always check that actually okay.

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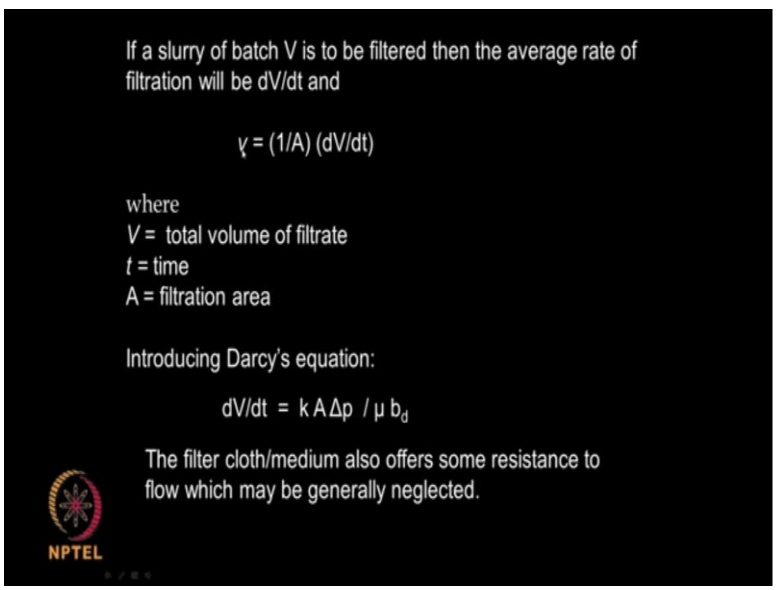


Now we can use Darcy's law for doing many things. Suppose I am doing a batch filtration and I have V volume of slurry which needs to be filtered in time t, so dV/dt /A will give you the velocity. Okay. So the velocity is equal to 1 /area, area of filtration dV/dt that is the rate of filtration. So now you can create this with the previous equation of Darcy's law and then do some adjustments and then we can get some very useful relationships.

Now there are situations, various situations the filter cloth or the filter medium can offer some resistance on the filter cloth or the filter medium did not offer any resistance. So we if we can have both types of situation.

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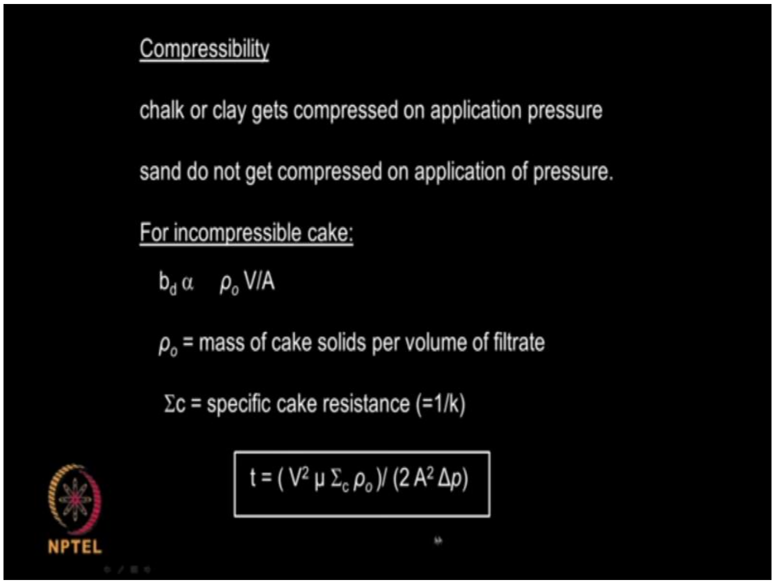


So if the another situation is, the solids that is getting removed may form a compressible cake of the solid, that may form an incompressible cake. So for example if you take chalk or clay, I may get compressed as you increase the pressure and it may form a compressible cake. So the liquid will not flow, so basically the flow through will be directly proportional to this packet. Incompressible cake, incompressible cake that will not be a problem. So if you have that sort of situation, then we get a very useful relationship.

Am not going into the mathematics of it, how to derive that but you get up with the equation for the new incompressible cake. If I have V volume of slurry to be filtered and if I am applying a pressure of delta p on a filter cloth of area A okay, this the sigma is the specific cake resistance and row not is mass of cake of solids per volume of filtrate. It is almost like density, right? Mass /volume, it gives you time, how long it will take for me to filter a slurry of volume V using a filter of area A, when I apply a pressure of delta p

And the viscosity of the liquid is mu and the slurry, mass / volume is row not okay sigma is the cake resistance actually. So it is a very useful relationship for a batch filtration and we can calculate how long it will take on the time here on the left hand side, this is for incompressible cake. You have to remember. So for compressible cake, you may, you will have one more term that may be coming, which will bring in the effect of pressure and similarly if the medium or the filter cloth offer some resistance, then the you will have one more term which will include that as well. So you need to remember that.

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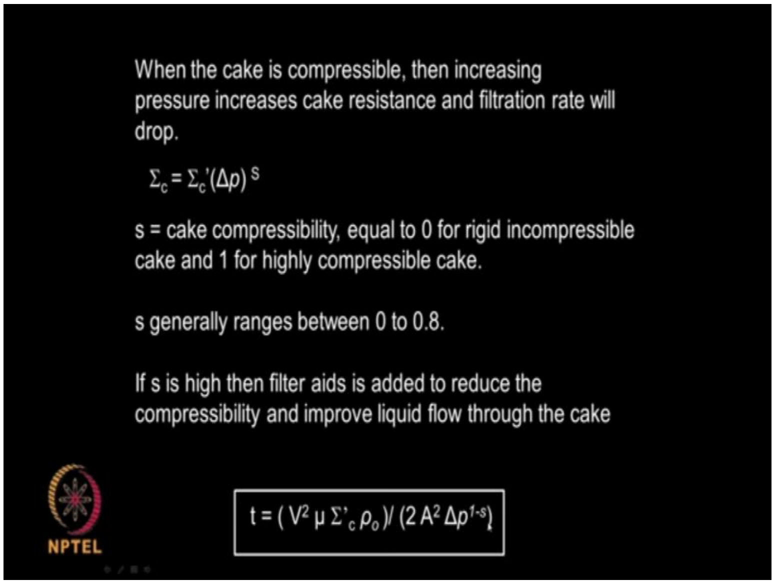


So then you have the compressible cake, this factor, okay the resistance will be modified to include delta p raised to the power S where S is the cake compressibility, it will vary between 0 to 1 okay. So 0 means it is not compressible, incompressible. So larger the number, there is more compressibility. So if you bring in that, then your time equation, that is time required for compare filtering will become like this. So you end up with delta p 1/1-S in the denominator here you understand. delta p 1-S. So if S = 0 then we are talking about incompressible cake, this term will go away.

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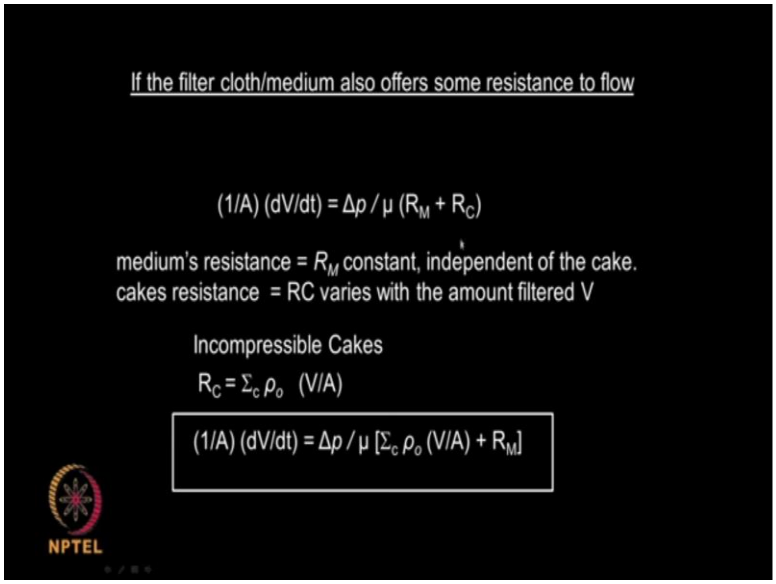


So we have this very useful relationship and we can do lot of mathematical calculations which we will see one or two examples here. Now if the filter clock or filter medium offer some resistance, then we term it gets introduced that is called rm. rm is the term which gives you the resistance offered by the filter cloth. Okay. If that is not, the filter cloth does not offer then this will go away and we will have the direct old relationship which we saw in the previous class. Okay so how do you find out whether the filter cloth offers any resistance or not? Okay.

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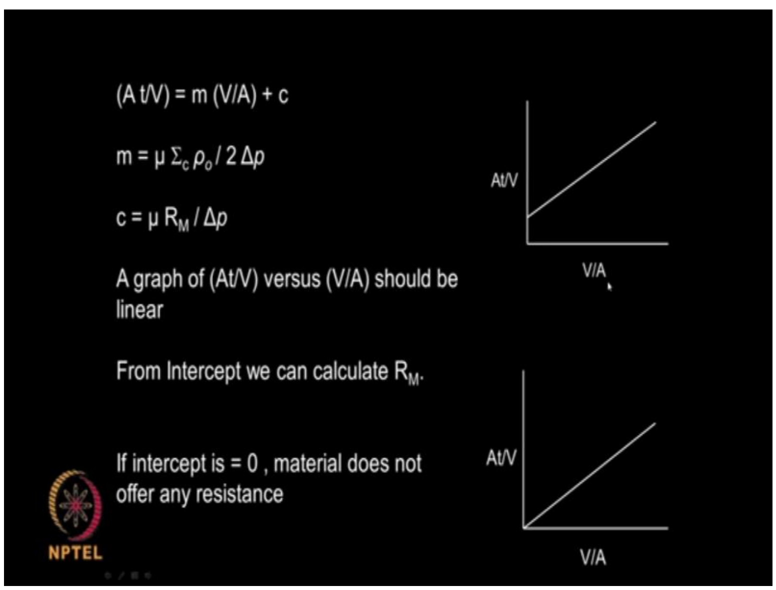


So if I plot relationship between volume of filtrate / area of the x axis as against area * time taken for filtration / the volume of the filtrate on the y axis. Okay so volume of filtrate / area in the x axis, volume of filtrate area and time here in the y axis and if the line the straight line passes through the origin or it does not pass through the origin. If it does not pass through the origin, we can say the filter cloth offers some resistance and this term will correspond to that resistance offered by the filter cloth.

If it passes through the origin and then we can say the filter cloth does not offer any resistance, so if we can do this type of graphical method to identify whether the filter cloth offers resistance or not okay.
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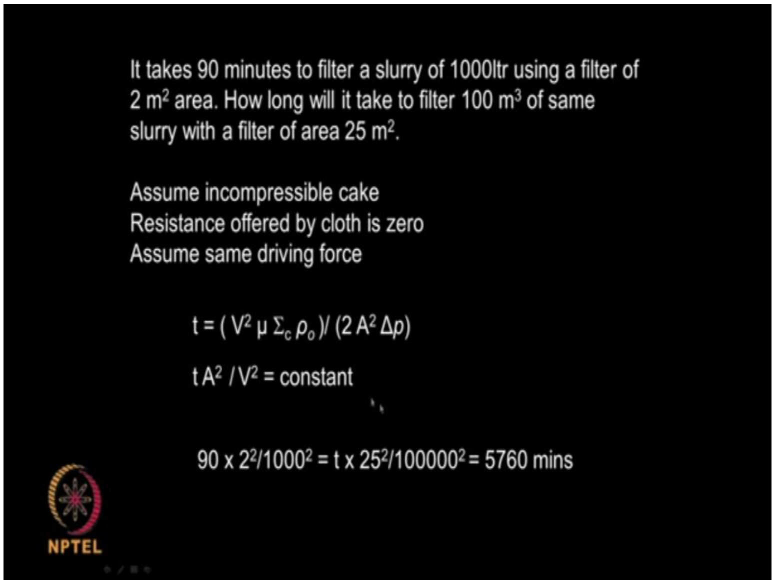


So let us look at a very simple problem. It takes 90 minutes to filter a slurry of 1000 liters using a filter of 2 meter square area, how long it will take to filter 100 meter cube of the same slurry with the filter area of 25 meter square. So we have increased the quantity that needs to be filtered, that means v has increased, we have increased the area from 2 meter to 25 meter square, so originally its 90 minutes. How long it will take so the cake properties of the same, it is an incompressible cake, okay the resistance offered by the cloth is also 0 and we will assume the same driving force.

So all you have to do is use the original equation, the time equation where there is no compressibility factor, where there is no resistance offered by the cloth, 1000 liters, 2 meter square area, so we can calculate the remaining factors like sigma and row not and then substitute that in the second equation and calculate the time. That is what you have to do. Okay so take this equation in the first case, you have 90 here, we have 1000 liters here, we have 2 meter square here okay.

So we can calculate the tA square /V square those remaining terms are going to be constant okay. And then use that in the second equation and we know V as 100 meter cube which is 100 *1000 and we know area is 25 meter square okay. So we substitute them and we calculate the time that is what we have to do in for the identifying what how long it will take to filter 100 meter square and that is what we are doing okay. So 90 minutes is the first case, 2 is the area, 1000 is your volume.

The second case we do not know the time, I know the area 25 meter square, I know the volume which is 100 meter cube, one meter cube is 1000 liters, so I put it. I get fine 5760, it is very useful way. When I am going scaling up, I want to find out how long it will take to filter larger volume. How long it will take if I increase the area and so on actually. So all I am using is this equation and then I am doing all the calculations okay.

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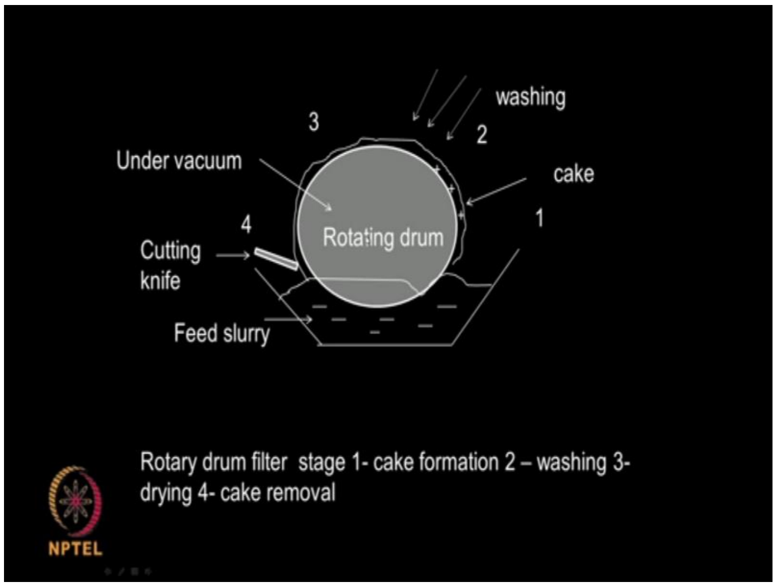


Now next one is rotary drum filter so I had talked about it here before also so the there is a vacuum so the slurry gets sucked that means the solids is coated outside because only the liquid flows through the drum is porous then there is a washing that is taking place here if there is any impurity which can dissolve in the solvent it gets dissolved and gets sucked in and then you are drying the material and then it is removing.

This is a very continuous process here so the filtration generally takes place when the when the drum is inside so otherwise there is no filtration the remaining level 2 3 4 there is no filtration only when the drum is inside the filtration takes place and we can use the same filtration equation for calculating all the terms here actually.

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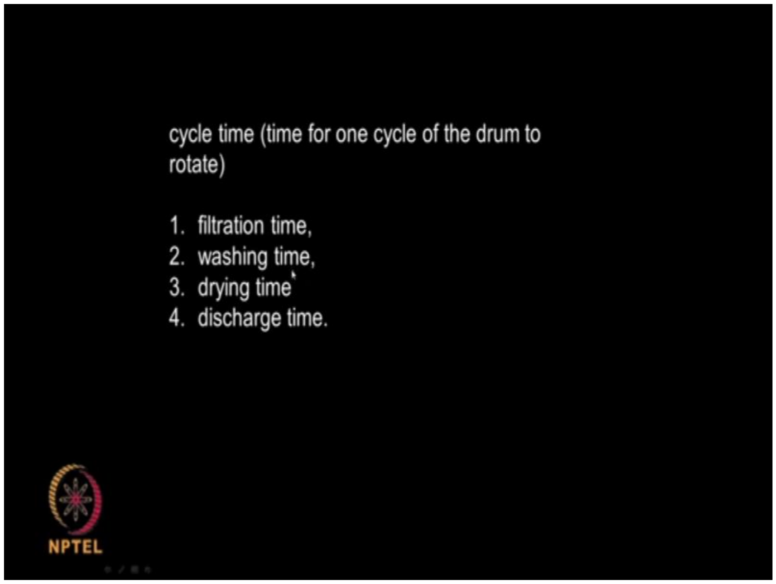


So there is filtration time, washing time, drying time and discharge time and only during the filtration time, we can use the same Darcy's law type of equation to calculate all the parameters. We want actually okay.

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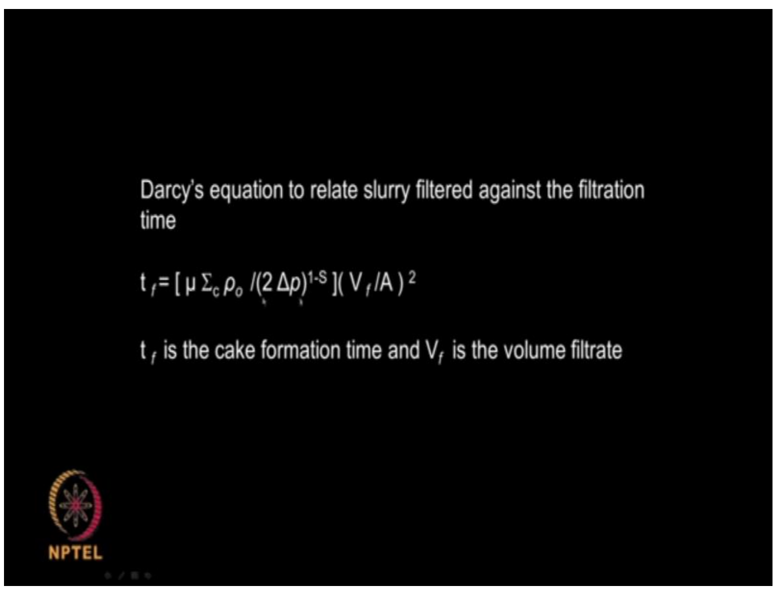


So during the filtration time, we can use the same Darcy's law, if it is a compressible, we use this 1-S in the exponent term okay.

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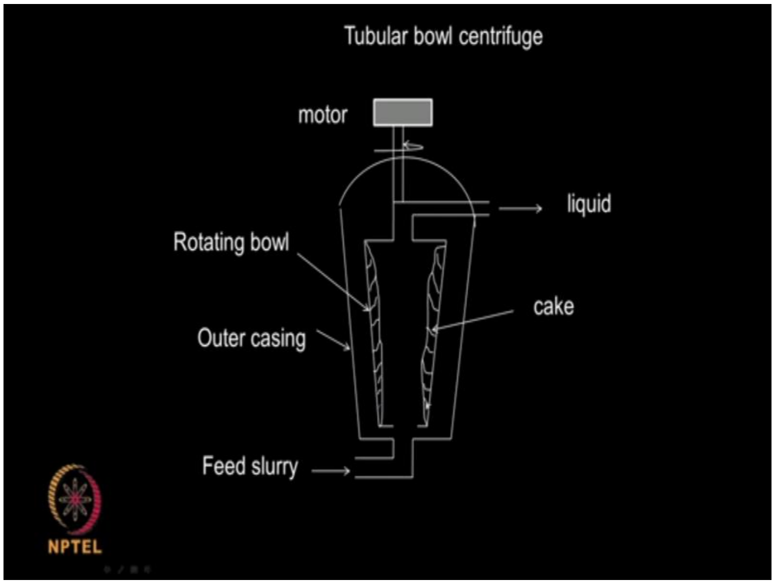


Then we have the centrifuges, there are different types of centrifuge. I mentioned there is tubular bowl centrifuge where the solids, the slurry comes from the bottom, the solids are thrown out and they form a coat on both sides and the pure liquid goes out.

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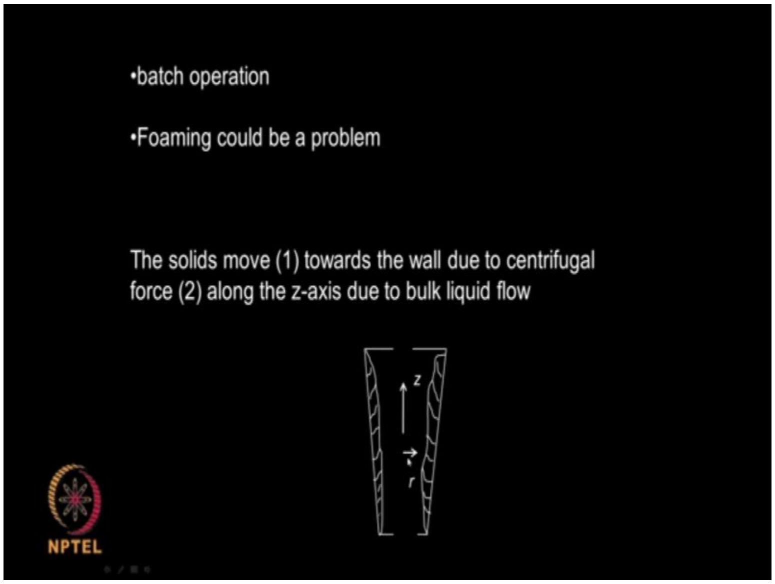


Generally this is used when the amount of solids are much less, whereas filter is preferred if the amount of solids are large quantities. Okay. So we can look and to modeling of this tubular bowl centrifuge also. So you have when the solids are moving up, you have 2 forces that are acting on the solids. One is the centrifugal force which is throwing the solid out and one is the force along the axis where the bulk of the liquid is flowing. So if we use these 2 terms and then write the model to end up with a very interesting equation like this.

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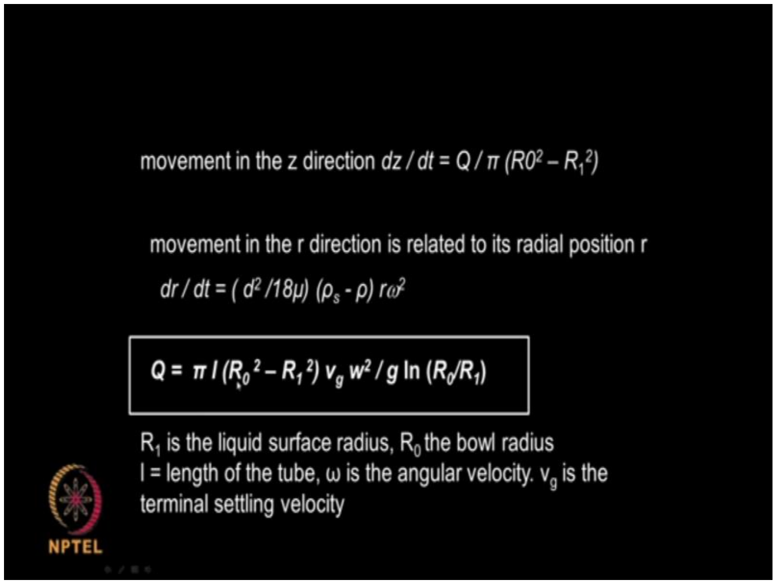


The throughput through the bowl centrifuge is made up of the radius, this is the radius of the bowl and then the omega, that is the angular velocity at which it is rotating g and v is the velocity, terminal settling velocity term comes in. So if I assume that r0 and r1 are almost the same that means it does not form a very thick cake. Then the equation becomes very simple.

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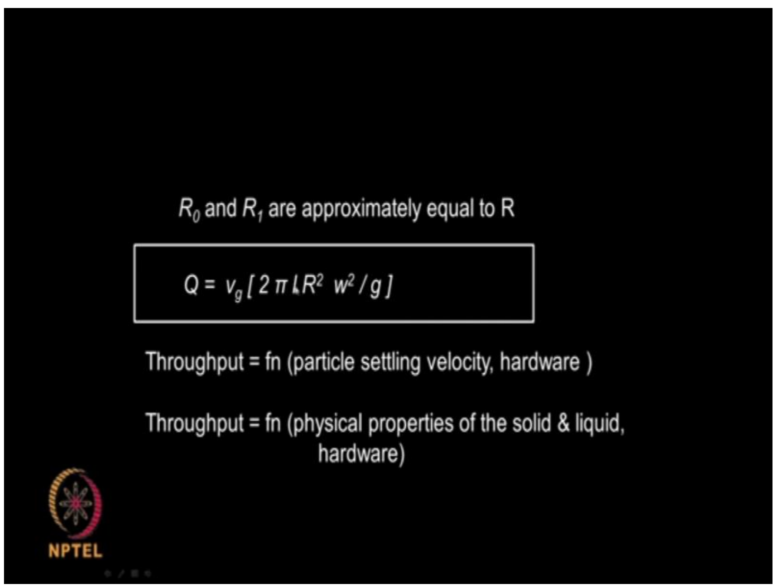


The throughput through the centrifuge is made up of the particle settling velocity v and these parameters are connected with the hardware details of your centrifuge. r is your radius, l is your length, omega is your angular velocity. So the throughput depends on 2 parameters, that particle settling velocity again particle settling velocity, if you remember terminal settling velocity depends on their physical properties of the solid and.

Liquid like the density of the solid, density of the liquid and viscosity of the liquid, diameter of the particle and the term inside the square bracket is all related to the hardware okay. So this is a very simple and useful relationship which you can use many problems using this I am going to do one problem soon for you on this actually okay.

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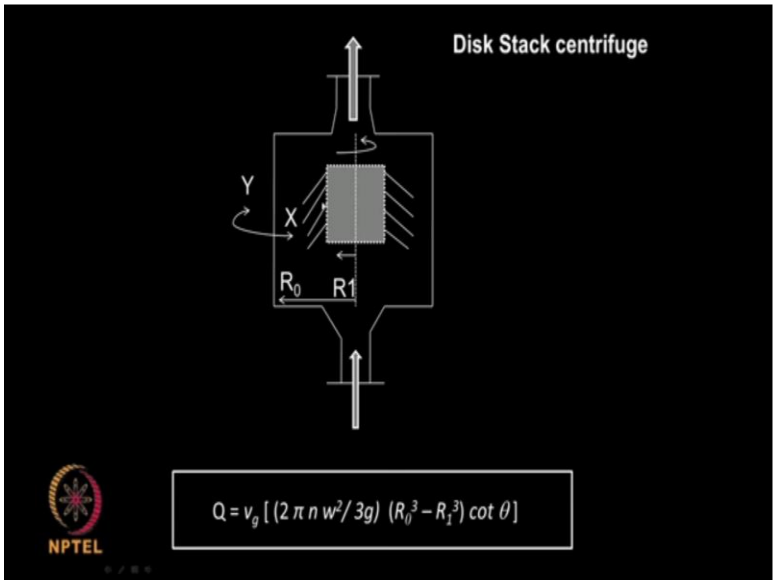


Same thing for the disk stack centrifuge, it is got lot of disks here. So the liquid, the slurry flows from the bottom, solids hits the disk and gets thrown out and so this walls will be full of solid which can be drained and central portion will be clear liquid, which is removed out. So here again you model this performance, you get throughput = velocity, that is the terminal settling velocity multiplied by the hardware details which takes care of radius and frequency and angle at which it is the disks are placed on and so on actually.

So the velocity here again will depend upon the physical properties of the solid and the liquid and then the hardware details.

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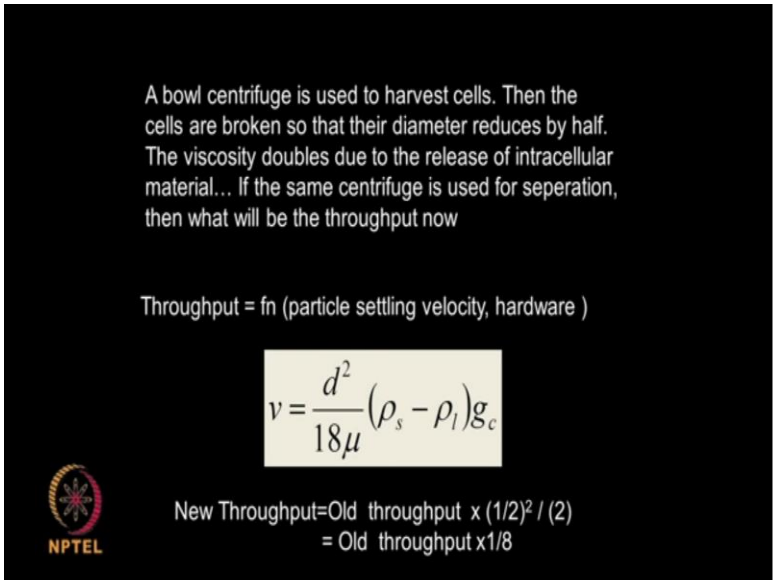


Okay so let us look at one simple problem. A bowl centrifuge used to harvest cells, the cells are broken. So the diameter reduces by half. So if the diameter was d it has become d half. The viscosity has become double that means the viscosity is mu, it has become 2 mu now. If the same centrifuge is used, then what will be the throughput? So now the diameter has come down, the viscosity has doubled, so only the velocity V has changed whereas the hardware of the centrifuge is the same.

So we have q = velocity * hardware details. Velocity is based on Stoke's law, so we put in these terms and we can calculate the mu cube and that it is what is requested here. What will the throughput? Okay so throughput is function of particle settling velocity and hardware okay particle settling velocity. If you remember Stoke's law couple of classes back I did, so d square 18 mu row s row l g. Now d has become half, so 1 /g will come here, mu has become 2 mu, so it becomes 1/8.

So throughput has become 1/8, so new throughput will be old throughput multiplied by 1 / 8 because your velocity has (())(21:20) 1/8 because so it is a very useful, if I am u using the same centrifuge for the larger particle, same centrifuge for smaller particle, I need to realize because particle size has come down, the terminal settling velocity will come down, so throughput will also come down okay. So if the viscosity changes, particle settling velocity will change. So throughput will come down.

So I cannot use the same centrifuge to do both the jobs, larger particles and smaller particles because the throughput will come down quite a lot. We can see just a simple equation, we get lot of information out of it.

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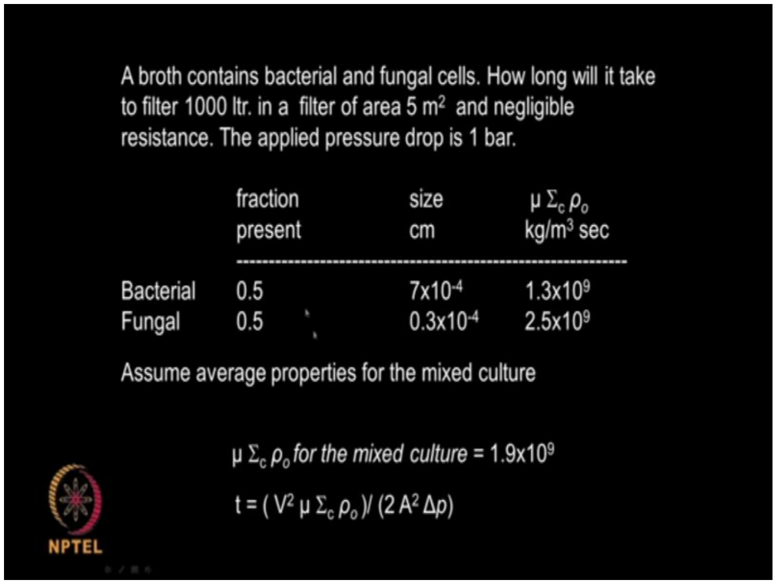


Okay so look at another problem. You have mixtures of bacteria 2 bacteria which you need turn them I It is at certain fraction fifty-fifty and these are the properties of these 2 bacteria given and I want to know, how long it will take for me to filter 1000 litres okay, using a 5 meter square filter cloth. There is no resistance and the filter cloth, there is the delta p is 1. So here what do you do? You have sigma c right, Mu sigma c row0 for bacteria 1 is given here, for bacteria 2 is given here and both are fifty-fifty.

We can take average of these 2 as the average mu row0 c, average mu sigma row substitute here and calculate time. So it is very simple. So we are taking average of the properties because we are taking fifty-fifty, so depending upon the concentration, we can take the particular weightage and do the calculation okay. If there are two or three or four, we will take correspondingly the mu sigma row0 in that particular ratio of concentration. Okay.

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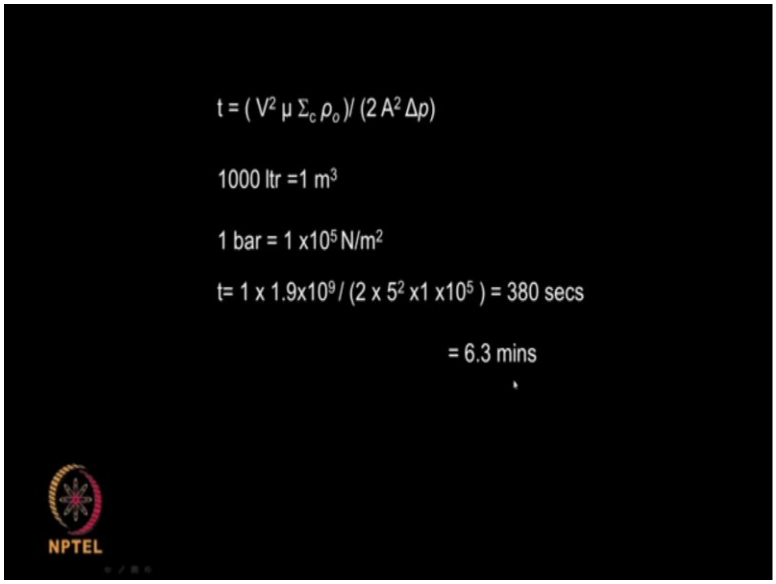


So we end up with 6.3 minutes for filtering the mixture of these 2 bacteria.

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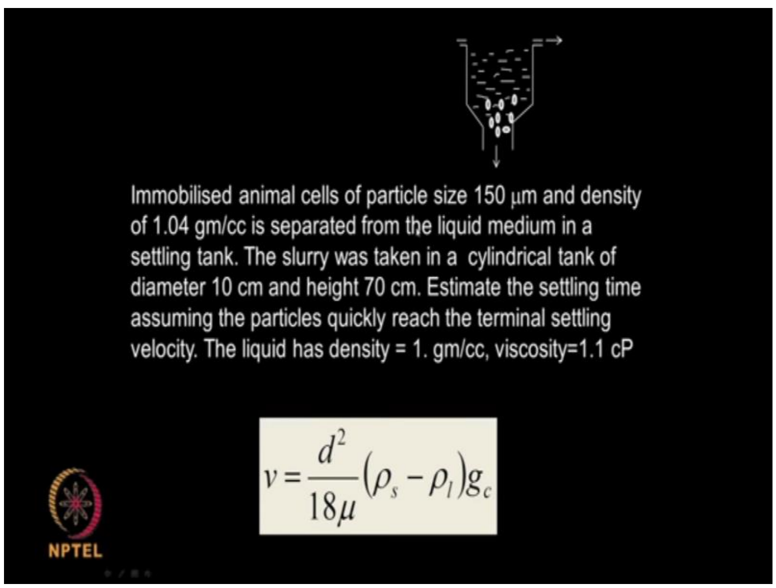


Okay let us look at another problem. We have immobilized animal cells, they are having certain particles here, 150 microns and it is got a density of 1.04 grams is separated from a liquid medium in a settling tank, so you must I talked about settling tank, you know lass last class right. So it is a cylindrical tank, it got a diameter of 10 cm and it is got a height of 70 cm. So you are supposed to calculate what will be the settling time?

Assuming the particle completely reach the terminal settling velocity, the liquid density is 1 viscosity 1.1 centipoise. So use Stoke's law, Stoke's law gives you the velocity = d square /18 mu row S - row l gc. So row S is given, that is the solid density 1.04, the liquid density is 1 and the mu is given 1.1

centipoise. The diameter is 1. 150 microns, so we convert all of them in proper units we get the velocity.

Once you calculate the velocity, the height is given as 70 cm okay. So the height/velocity will give you the time. So it will tell you how long it will take for that to settle from top to bottom. Okay so that is what you are doing here.

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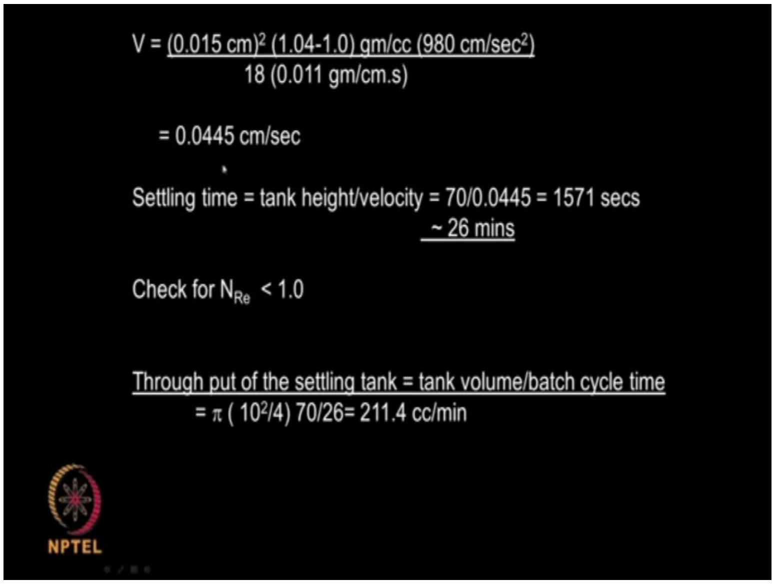


So you calculate the velocity using and then tank height by velocity, you cal, you get the time. So it takes 26 minutes actually, it will take much longer. We assume that the particles reach terminal settling velocity immediately but it will take some time. So normally if you are running an industry, if you calculate this settling time based on this 26 minutes, you will add about 20, 30% extra okay so you will add another 6, 7 minutes you will say about, it will take about 35 minutes for the solids to settle down.

So your tank height, you can redesign to assume about 35 minutes of you will leave much slightly longer so that the solids get settled okay. Of course there are some assumptions here because if the slurry is very thick that means the %age of solid is very high, we cannot use Stokes' law. Generally Stokes' law is valid when Reynolds number is less than 1, if it is much larger there is going to be solid-solid interaction. So there is simple terminal settling velocity, equation of Stokes' law is not valid in that situation.

So what you will do is, you can recheck to see whether your Reynolds number is really coming down to less than 1. You all know that Reynolds number is diameter of the particle velocity at which it is flowing density of the liquid divided by viscosity of the liquid and check whether Reynolds number is okay. If it is not okay then obviously the Stokes law is not really valid but even in industrial scale, you can add some extra safety margin at is as it is called and then we can give more time for it to settle.

Now what is the throughput? Throughput is nothing but the tank volume / the batch cycle time okay. The batch cycle time is actually 26 minutes right and what is the volume? Volume is nothing but it is a cylindrical vessel / square / 4 * height / time. Diameter is 10, so you are making it 10 square and the height of the tank is 70 cm. So you are multiplying 26 minutes is what you calculated, so it is coming down to 211.

But if you are assuming instead of 26 minutes settling time, 35 minutes settling time, you will divide by 35 not 26. So your throughput will come down, so you have to keep that in mind. So if you give some safety margin, you need to correspondingly reduce the throughput, so this is the ideal or this is the best you may think of achieving but if you are going to increase this particular time because of safety margin, then your throughput would come down.

So today we did some very useful problems using 2 simple equations, one is the Stokes law equation which tells you the velocity at which solid settle down in very dilute solutions. So it is dependent of the diameter of the particles, density of the liquid, density of the solid and viscosity of the liquid okay. That is very very useful in centrifuge type situation, its useful in settling in gravitational situation. Next one we used Darcy's law.

Darcy's law is very useful to look at filtration, we can calculate what is the time required for filtering a slurry of volume v, given a area a, you can have 2 situations, one is the compressible solid bed, other is incompressible solid bed. If you have compressible solid bed you bring in term called compressibility, if you remember S okay otherwise if it is incompressible you do not bring in that term, okay and then we said that the filter medium that is filter cloth or resistance rm, we said and filter cloth does not offer resistance, so we can bring in that also.

So by incorporating all these, we can get relationship for time in the left hand side, we can calculate how long it will take to filter a slurry of volume v, if given an area of filtration, a with certain properties of slurry and certain delta p and compressible or incompressible okay. Then in centrifuge, we looked at the throughput through a centrifuge is product of the settling velocity into hardware details. So if I use the same hardware that means if I use the same centrifuge, if I am having particles of d size and if I am using particle of d / 2, how will the throughput change?

If I have a viscosity of the medium mu, the viscosity of the medium doubles to mu, what will happen? So the settling velocity changes that Stokes law will change, hardware will not change. So that will affect the overall throughput. So simple equations but lot of useful knowledge we got from these simple equations okay.

Thank you very much.