Bioreactor Design and Analysis
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Lecture - 31
Heat Transfer Operations in Bioreactors – Part 4

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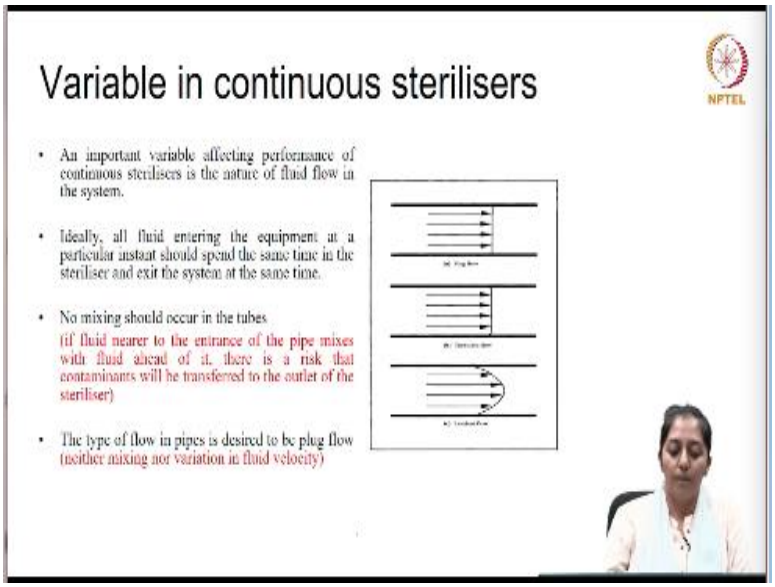

One important variable which may affect the performance of continuous sterilisers is the nature of the fluid flow in the system, as it has to go through the section for the holding period at sterilisation temperature. Now, ideally, all fluid which is entering the equipment at a particular instant should spend the same time in the steriliser and exit the system at the same time, which would be the case of plug flow. No mixing should occur in the tubes.

Now, if the fluid near to the entrance of the pipe mixes with the fluid ahead of it. So, if there are back mixing happening, then there will always be a risk that the contaminants will be transferred to the outlet of the steriliser. So, the type of flow in the pipes is desired to be plug flow. So, there is neither mixing nor variation in the fluid velocity.

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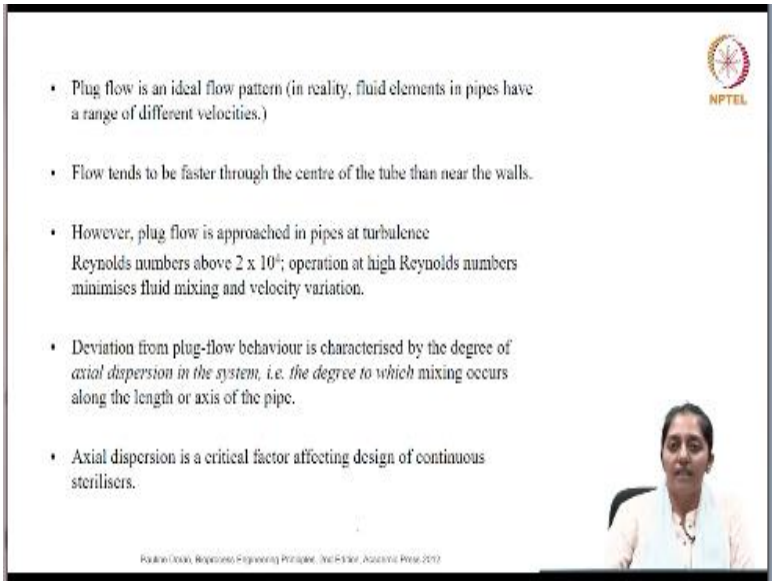

So, we know that the plug flow is an ideal flow pattern. In reality, the fluid elements in pipe have a range of different velocities. Now, flow tends to be faster through the centre of the tube than near the walls. However, the plug flow is approached in pipes at turbulence. Now, Reynolds numbers above 2 into 10 to the power of 4; operation at such high Reynolds number can minimise fluid mixing and the velocity variations.

So, deviation from the plug flow behaviour is to be characterised by the degree of axial dispersion in the system. So, if we have to characterise the non-ideal behaviour of the fluid flow, we must be able to characterise the degree of axial dispersion in this system that is the degree to which the mixing is occurring along the length or the axis of the pipe. Now, this axial dispersion therefore becomes a critical factor affecting the design of the continuous steriliser.

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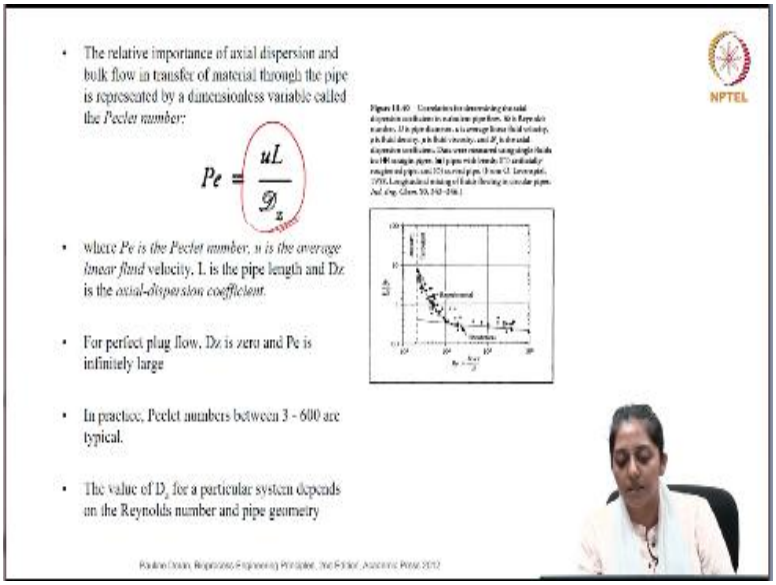

Now, in order to find the relative effect of axial dispersion in this process called as Peclet number, which talks about the relative importance of axial dispersion and bulk flow motion during the transfer of the material through the pipe. Now, if you see here, the Peclet number is given here as u times L divided by the dispersion coefficient. Now, u stands for the average fluid velocity; L stands for the length of the pipe of the holding section and the denominator here is your axial dispersion coefficient.

Now, for perfect plug flow the dispersion is 0. So, therefore, the Peclet number would be infinitely high. Now, in practical situations, the Peclet numbers are found to vary from within a big range from very small values, single values like 3 to 600. The value of the dispersion coefficient for particular systems, it further depends on the Reynolds number and the pipe geometry.

So, here for example, you can see a plot has been given between the Peclet number and the Reynolds number where, how the Peclet number changes with the change in the fluid flow shown here with the Reynolds number. And for different geometries like here, it is given for straight pipes, pipes with bends or artificially roughened pipes or curved pipes.

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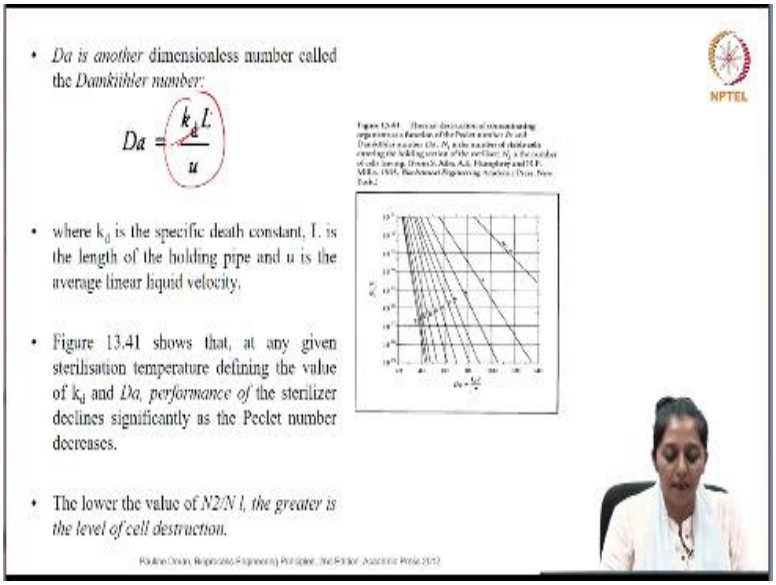

Now, there is another dimensionless number, which we call as Damkiihler number. Now, this dimensionless number, you can see the expression, it is given as k d L by u. So, L, we know is the length of the holding pipe, u was the average linear liquid velocity and k d was the death rate constant. So, if you see the plot given here, here the thermal distraction of the contaminating organisms has been defined as a function of the Peclet number and the Damkiihler number.

So, with the change in Peclet numbers, the thermal destruction as a ratio given here and N2 by N1 in the holding section is being plotted against the Damkiihler number; where N2 is the number of cells leaving the holding pipe holding section and N1is the number of viable cells entering the holding section of the steriliser. So, this figure shows that at any given sterilisation temperature, which would then define the Damkiihler number, the performance of the steriliser declines significantly as the Peclet number decreases.

You can see from here, the ratio of N2 by N1, it is going up as the Peclet number decreases. And the Peclet number decreases means, there is higher axial dispersion at a given steriliser temperature. Sterilisation temperature would define your Damkiihler number. As k d would be a function of temperature given the length of the holding section and the linear liquid velocity. And this N2 by N1 will be lower which means better sterilisation, greater level of cell destruction with higher Peclet numbers, which means lesser exhale dispersion.

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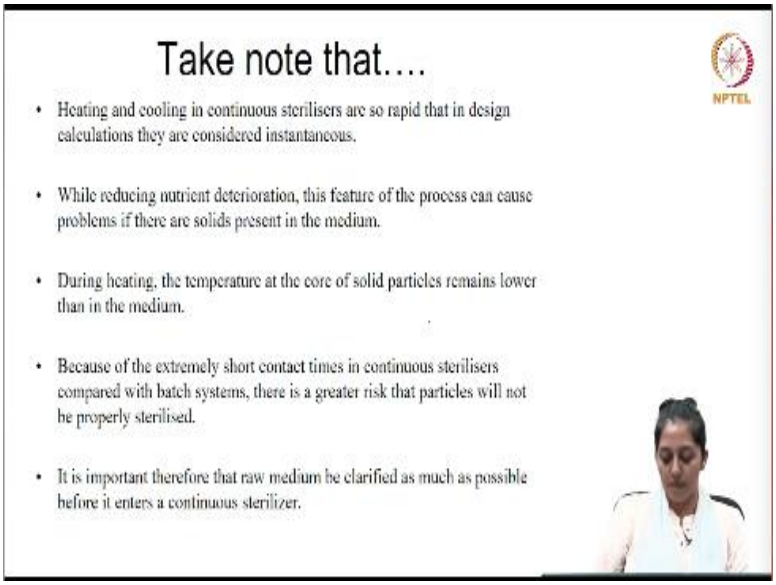

So, what is to be noted here is that heating and cooling in continuous sterilisers are, so, rapid that in design calculations, they are considered instantaneous. So, while reducing nutrient deterioration, this feature of the process can cause problems if there are solids present in the medium. Now, during heating, the temperature at the core of the solid particles will remain lower than in the medium.

So, because of the extremely short contact times in the continuous sterilisers compared with the batch systems, there is a greater risk that these particles if present, will not be properly sterilised. So, it is important that the raw medium is clarified as much as possible from such particles before it enters the continuous sterilizer.

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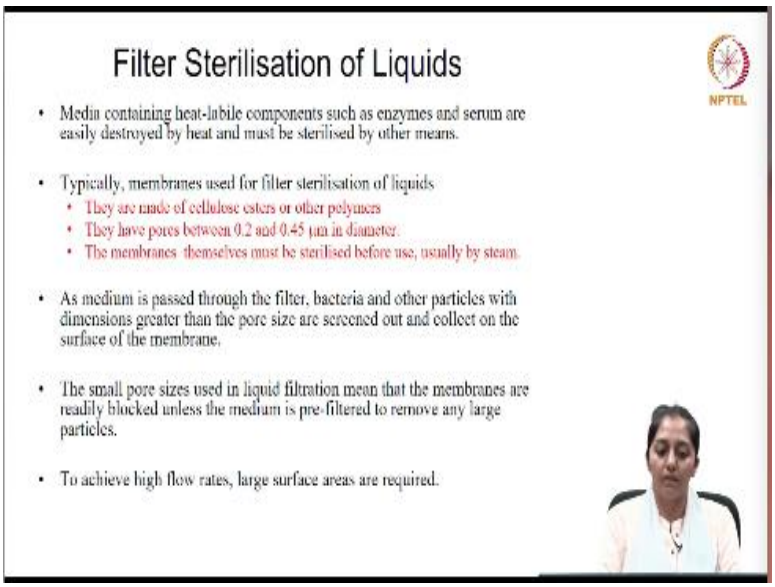

So, now, let us talk about, how filter sterilisation or where it is used? We have been talking about steam sterilisation. So, media containing heat-labile components such as enzymes or serum, they are can be easily destroyed by heat and therefore must be sterilised by other means. So, typically, membranes are used for filter sterilisation of liquids. Sometimes, they are made of cellulose, esters or other polymers.

They have pores between 0.2 to 0.45 microns in diameter depending on the use. The membranes themselves must be sterilised before use and sometimes, they are one time use membranes. As medium as pass through the filter, the bacteria and the other particles with dimensions greater than the pore size will be screened out and will get collected on the surface of the membrane.

Now, smaller the pore sizes used in liquid filtration would mean that the membranes can readily be blocked, unless the medium is pre-filtered to remove any large particles. So, to achieve high flow rates, large surface areas will be required.

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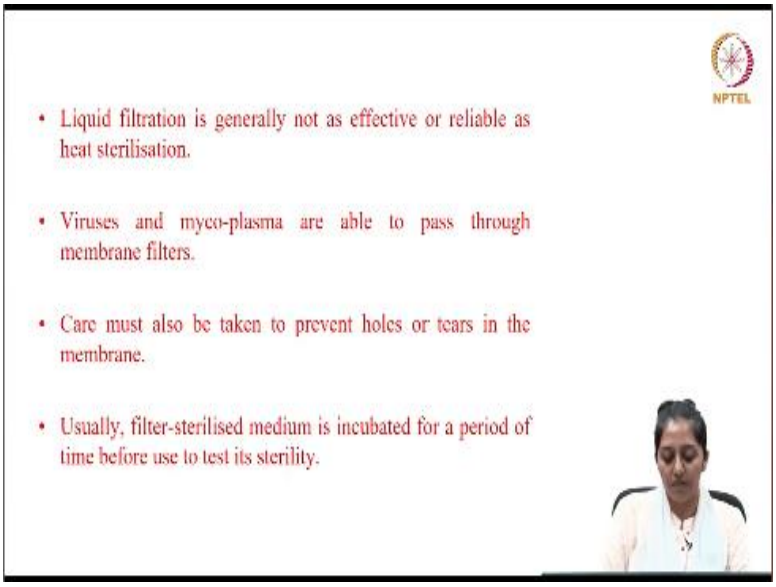

So, liquid filtration is generally not as effective and reliable as heat sterilisation. Because, viruses or myco-plasmas, they are able to pass through the membrane filters. So, care must also be taken to prevent any formations of holes or tears in the membrane due to high pressure. Usually filter sterilised medium is incubated for a period of time before using it in order to test it sterility levels.

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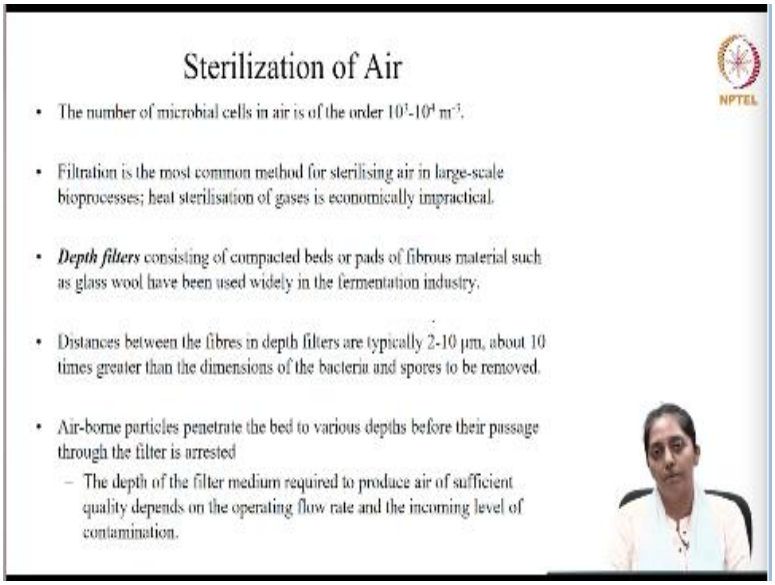

So, after talking about the filtration of liquid medium or sterile liquid using steam sparging, even the air is being sparked in the fermenter. Now, this air which is being continuously sparked inside the fermenter, also must be made sterile to avoid any contaminations during fermentation process. So, the number of microbial cells generally present in the air are of the order of 10 to the power of 3 to 10 to the power of 4 per metre cube.

Filtration is the most common method for sterilising air in large scale bioprocesses. Heat sterilisation of gases is economically impractical. So, for sterilising air generally, depth filters are used, which consist of compacted beds or pads of fibrous material, such as glass wool, which have been used widely in the fermentation industry. Now, the distances between the fibres in depth filters, they are typically in the range of 2 to 10 microns and about 10 times greater than the dimensions of the bacteria or spores which are required to be removed.

So, it is very interesting to note that this kind of a setup is used to get rid of much smaller size bacteria present in the air. So, airborne particles, they penetrate the bed to various depth before their passage through the filter is arrested. The depth of the filter medium required to produce air of sufficient quality would depend on the operating flow rate and the incoming level of the contaminants.

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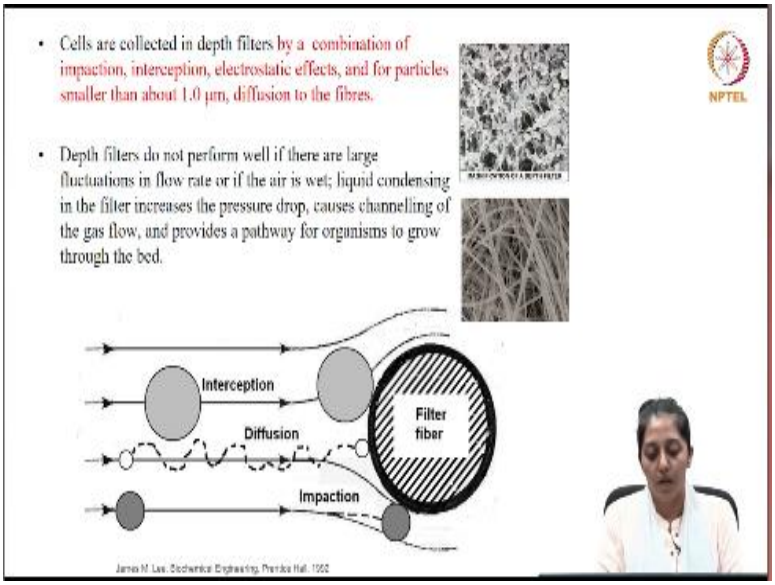

So, cells, they get collected in depth filters by a combination of processes including impaction, interception, electrostatic effects, for particles which are smaller than 1.0 micron. So, cells get collected in these depth filters by a combination of processes including impaction, interception and electrostatic effects and for particles which are smaller than 1.0 microns, diffusion through the fibres.

The depth filters, they do not perform well, if there are large fluctuations in the flow rate or if the air is humid or wet. The liquid condensing in the filter will increase the pressure drop causing channelling of the gas flow and provides a path for the organisms to escape or growing the bed. So, you can see the pictures of the depth filters shown here. And that is the magnification of the depth filter where you can see the pores and the fibres here and see such a complex network of fibres through which the air passes through for filtration.

So, here in the schematic, the 3 processes are shown here, interception, diffusion, the impaction. You can also make note that the size of the particles is different for different process by which they are getting removed or getting held in the filter.

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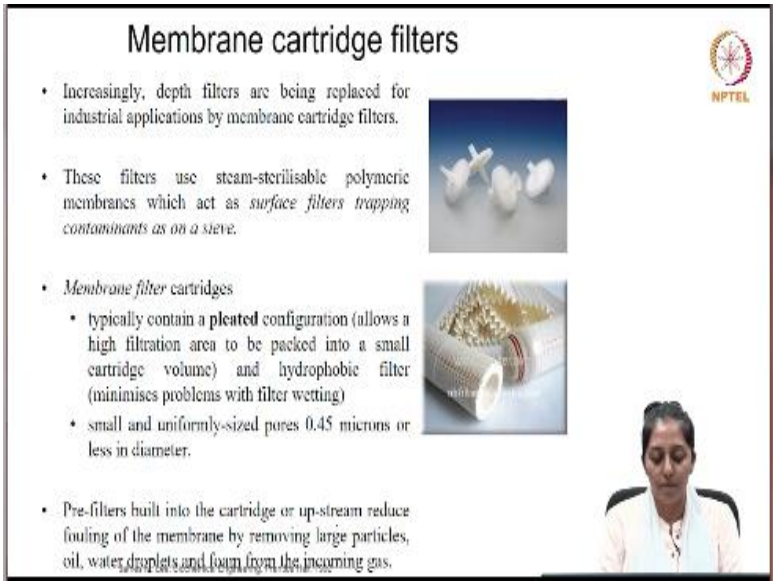

So, increasingly depth filters are being replaced for industrial applications by membrane cartridge filters. These filters, they are steam-sterilisable polymeric membranes, which act as surface filters, trapping the contaminants as on a sieve. So, membrane filter cartridges, they typically contain a pleated configuration as shown in the picture here, which will allow of high filtration area to be packed into a small cartridge volume.

And hydrophobic filters will minimise problems with the filter getting wet. Small and uniformly sized pores which is nearly 0.45 microns or less in diameter are present on these membrane filter cartridges. Pre-filters can be built in these cartridges or up-stream which can reduce the fouling of the membrane by removing the large particles. Like for example, air or water droplets or foam in the incoming gas.

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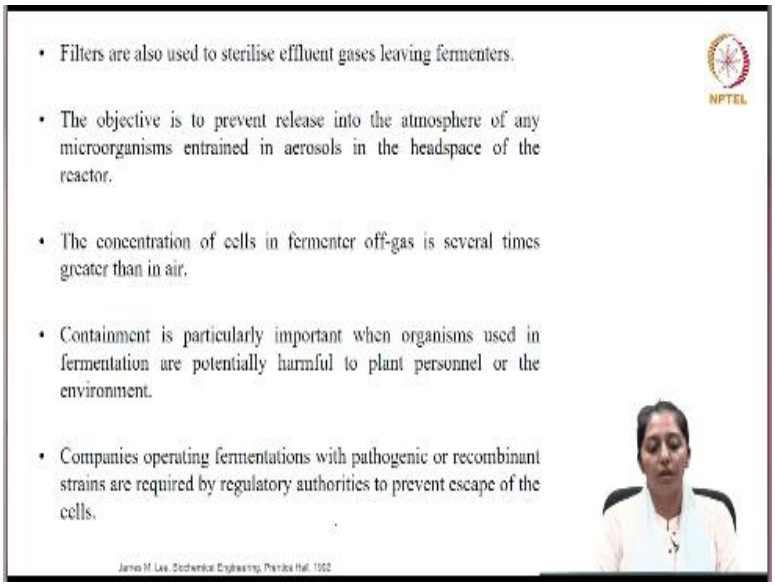

Filters, they are used to sterilise also the effluent gases leaving the fermenters. Apart from the sterile air which is being (()) (15:52), there is a continuous outlet of air from the headspace to release pressure. So, that effluent gas is also sterilised passes through these filters before it moves out of the fermenter. The objective is to prevent release into the atmosphere of any microorganisms, which gets entrained in the aerosols through the headspace of the reactor.

The concentration of cells in the fermenter off-gas is several times greater than in the air, which is coming inside. So, containment becomes particularly important when organisms used in fermentation are potentially harmful to the human personnels, which are working or the environment. Companies operating fermentations with pathogenic or recombinant strains, they are required by the regulatory authorities to prevent the escape of the cells.

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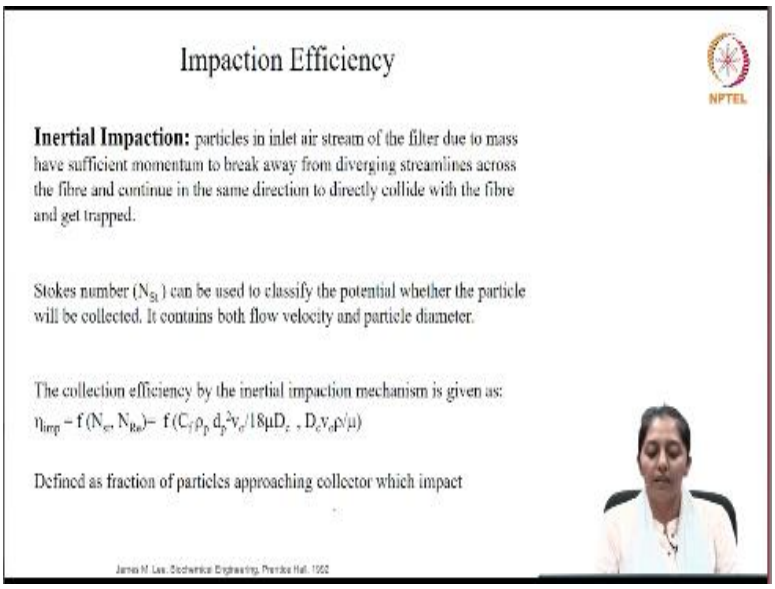

So, if we need to characterise the efficiency of the air filtration process, we must first see how the 3 process impact the removal of the organisms. So, inertial impaction, this is the particles in the inlet air stream of the filter can get impacted due to mass being sufficient due to sufficient particles in inlet air stream of the filter. If they have enough mass, then they will have sufficient momentum to break away from the diverging streamlines across the fibre and they will continue in the same direction to directly collide with the fibre and get trapped.

So, if you see the schematic here, you can see the impaction process shown here. If it has enough mass due to the momentum it gains, it can continue to move in the same direction deviating from the streamlines and can get stuck in the fibre. Now, Stokes number is

generally used to classify the potential whether the particle will be collected by inertial impaction or not. This would be dependent on the flow velocity and the particle diameter.

So, the collection efficiency by the inertial impaction mechanism is given as a function of the Stokes number and Reynolds number.

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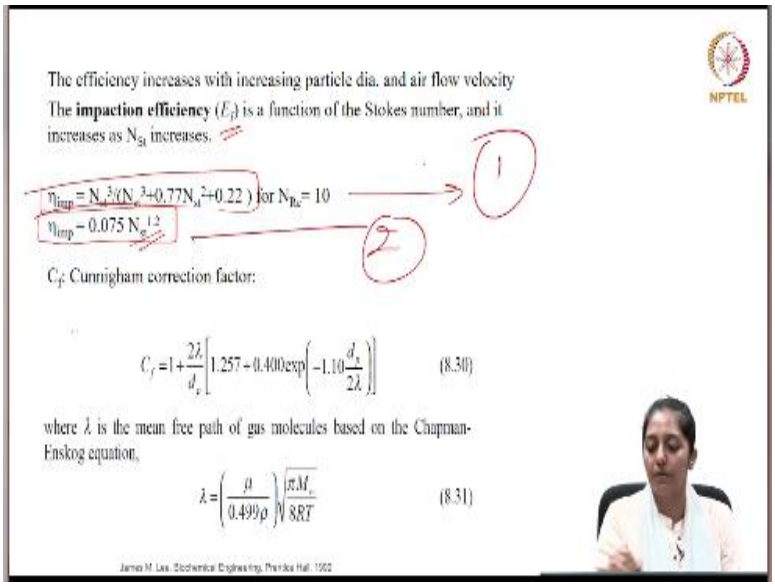

Efficiency would increase with the increasing particle diameter and the airflow velocity. So, impaction efficiency if it is defined as E I, it is a function of Stokes number and it increases as the Stokes number increases. So, here, for a Reynolds number equal to 10; an empirical relationship for the inertial impaction efficiency is given here in terms of Stokes number. And for other than 10, the efficiency of impaction is being defined by the second empirical equation.

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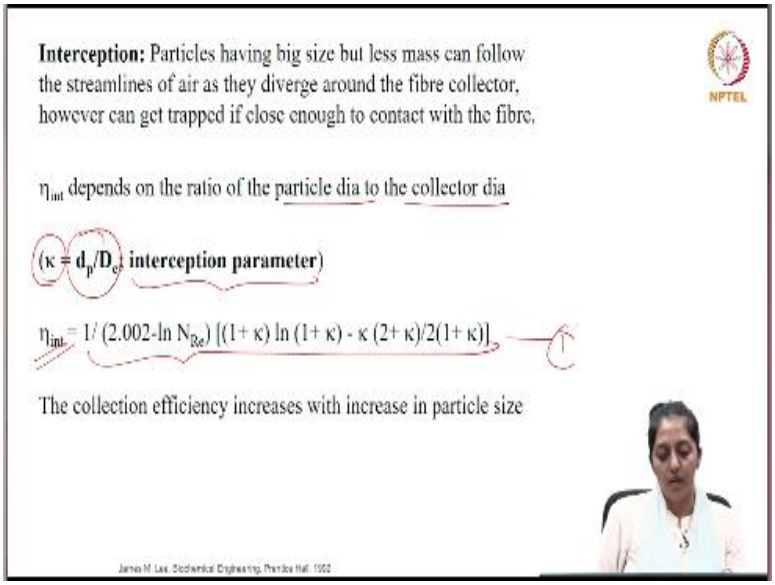

Similarly, if the particle is getting trapped by the interception process, what does that mean? It means that the particles having big size but less mass, they will follow the streamline of air as they diverged around the fibre collector. However, they can get trapped if they are close enough to contact with the fibre. So, if you see the schematic, here, it is shown for a interception, the particle is large in size, but the mass is not heavy. So, it is being carried by the streamline of air and because of its size, it may interact with the fibre and get stuck.

So, the efficiency of interception would depend on the ratio of the particle diameter to the collector diameter, the fibre diameter. So, interception parameter has been defined here as the ratio of the diameter of the particle to the diameter of the collector and in turn, it can be a function of the Reynolds number and the interception parameter. So, this is one empirical relationship shown how to define the efficiency due to interception.

Efficiency means the collection efficiency. So, one can make out the collection efficiency would increase with the increase in the particle size.

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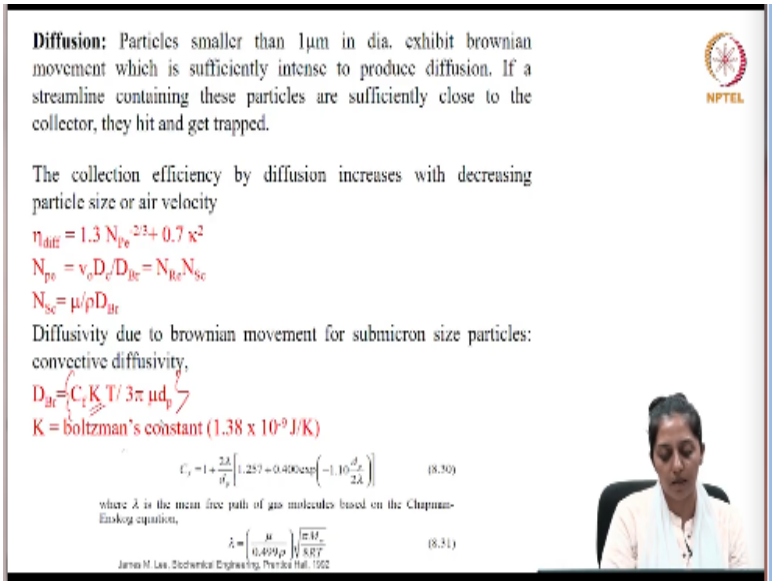

Now, the particle size is very small, then smaller than 1 micron in diameter, they will exhibit Brownian movement, which will be sufficiently intense to produce diffusion. Now, if a streamline containing these particles, they are sufficiently close to the collector, the particle might hit and then get trapped. So, the collection efficiency by diffusion will increase with decrease in particle size or the air velocity, the bulk flow.

So, here the efficiency due to diffusion has been found to be a function of the Peclet number and the interception parameter. So, here, the Peclet number in turn is made a function of the Reynolds number and the Schmitz number. The diffusivity due to Brownian movement is your DBR for sub micron sized particles. So, you may call it as convective diffusivity. So, the efficiency due to diffusion is a function of the Peclet number here has been defined as an empirical relationship.

Being a function of Peclet number and the Boltzmann's constant, the Peclet number in turn being a function of Reynolds number and Schmitz number. The Schmitz number is being defined by the convective diffusivity due to Brownian movement, which would depend on the diameter of the particle. And the Boltzmann's constant K in the diffusivity function is the Boltzmann constant, C f is the correction factor in turn being given by this function shown here.

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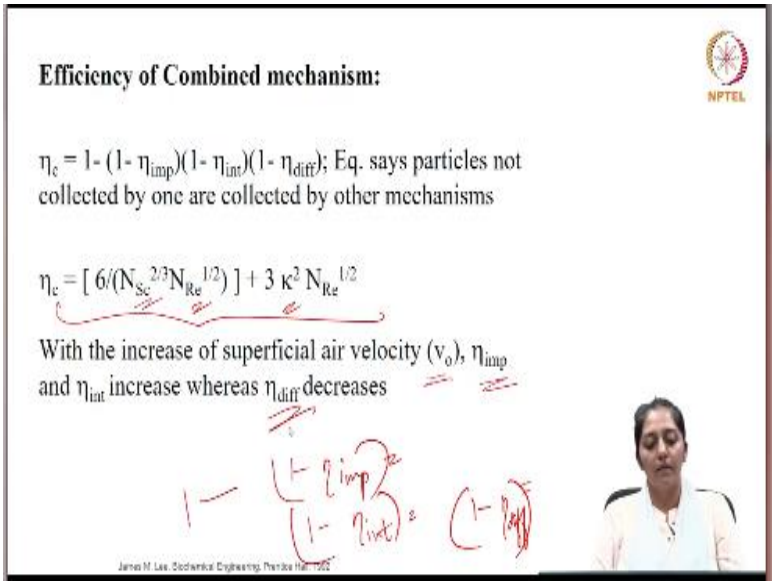

Now, if we need to calculate the overall efficiency of impaction or interception or by diffusion, the efficiency for collection of the particle by the filter can be obtained, if we know the individual efficiencies of impaction, interception and diffusion. So, the probability of successfully collecting the particle by one or more of the mechanisms, then we first calculate the probability of particles not getting collected by one, but getting collected by any other mechanisms.

So, 1 minus eta imp would be the probability of not getting collected by impaction. 1 minus eta int would be the probability of not getting collected by interception. Similarly, 1 minus eta diff would be the probability of not getting collected by diffusion process and the overall probability of not getting collected by any of these processes will be multiplication of all these probabilities.

And if, we reduce this by one, then it will be the probability of being able to collect by one or more of these mechanisms. So, your overall collection efficiency here is being given by an empirical co-relationship defined by the Schmitz number and the Reynolds number and the interception parameter. So, with the increase in the superficial air velocity, the efficiency due to impaction and efficiency due to interception would increase, whereas the efficiency due to diffusion might decrease.