Downstream Processing
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Lecture - 24
Membranes (Continued)

We will continue with the Membranes, we were talking about pervaporation, let me go slightly more in detail on pervaporation. Pervaporation is also a membrane process, it is a combination of permeation and evaporation; that means, the liquid changes into a vapor phase, it gets permeated through the membrane material; and then on the other side it gets again condense into a liquid.

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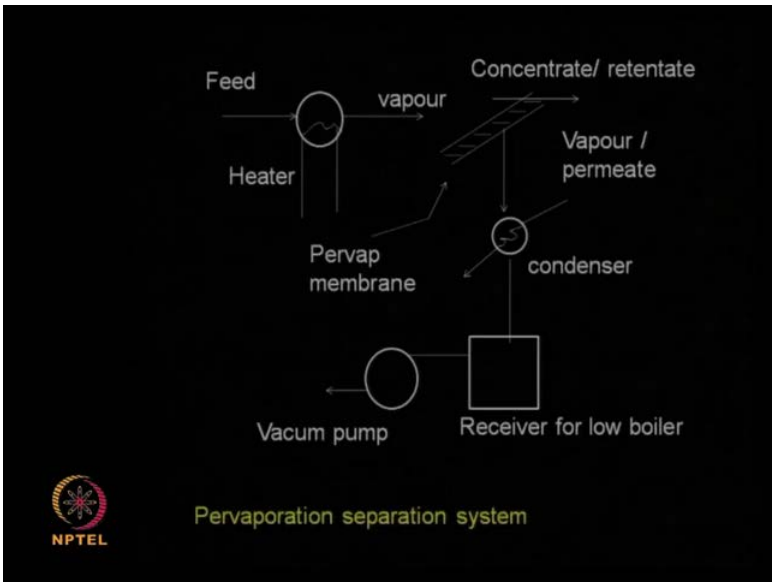

This is a typical flow sheet of a pervaporation process. So, you have feed it is a liquid feed, it gets a vaporized in a heater and then it comes in contact to the membrane. A membrane could be hydrophilic or a hydrophobic membrane, I mean hydrophilic membranes will be used if you are wanting to pullout water from a broth, especially in manufacture of say concentrated fruit juices or concentrated syrups. You do not want any water present inside or you can have a hydrophobic membrane; that means, if you interested in separating out hydrophobic hydrocarbons or solvents, then this type of a membranes are used.

So, the membrane could be a hydrophilic or a hydrophobic, once the feed is vaporized it gets dissolved inside the membrane and then there is a diffusion taking place. And on the other side the vapor comes and gets condense into the liquid. Now, what is the there is a driving here we are using a vacuum, so that the vapor travels through the membrane. So, you can use pervaporation for concentrating fruit juices for concentrating even say ethanol to almost 100 percent and removal of solvents and so on actually.

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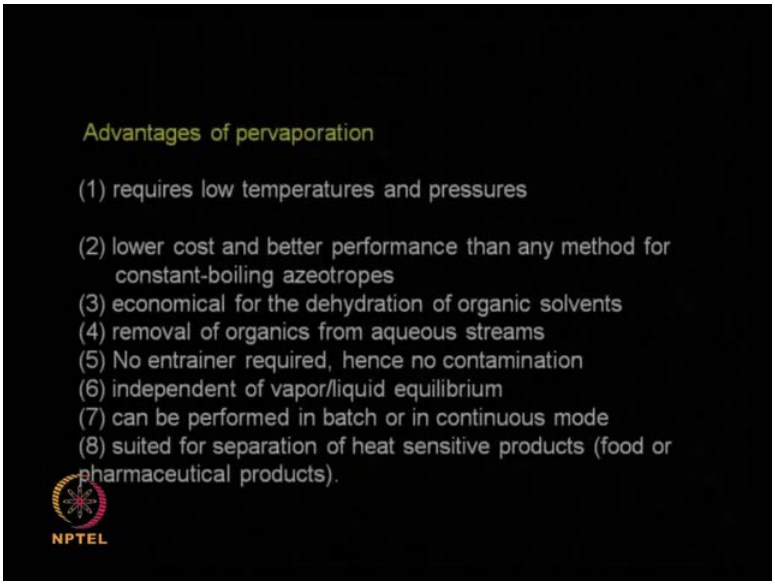

Many advantages are there it requires low temperature and pressure, because you are using a vacuum and you just need to put in some heat. So, that the liquid is vaporized so; obviously, the temperature of operation is very, very low. So, it can be used for temperature sensitive material the energy usage is less, so these are the advantages. Now, it is very good for separating out azeotropic mixtures, you know what is azeotrope? Azeotrope is called a constant boiling system for example, ethanol water is a typical azeotrope, so you cannot purify 200 percent ethanol.

So, normally what people use to do in the past 100 years they use to add entrainer, which will break the azeotrope then they will distilled out remove the water, then again they will distill to remove the entrainer from the water and the entrainer is recycle back. So, it will be a series of distillation column and you are adding an entrainer and so on. It cannot be done for a if you want a purify fruit juices, because you are talking about a

food product. So, in such situations pervaporation is very good, because it will separate the liquid very efficiently.

It is very economical for dehydration of organic solvents; that means, I want to completely remove all the water present in solvent. So, what else can I do, I may use a distillation that is energy intensive and sometimes you might not be able to get 100 percent dehydrated solvent. So, what else can you do, you can add some adsorbent, which will absorb water or moisture, then you have to filter out that adsorbent. And then the adsorbent have to be heated again, so that it gets regenerate and ready for further processing.

So, it is going to be two or three steps you will be adding an adsorbent like a silica gel or alumina or zeolite, it will absorb all the water present in a solvent and then you will do a filtration now this silica gel or alumina will contain water. So, you may have to take it to heater heat it, so the water gets vaporized the silica gel is again available you can take it back again for adsorption.

So, you see there are, so many extra steps it is are going to add to the cost; whereas, pervaporation is going to very economical for dehydrating organic solvents, all you are going to use is a vacuum pump and little bit of heating, so that the liquid gets vaporized.

So, we can also use it for organics from aqueous stream, so like if you are using a hydrophobic membrane and if the concentration of organic present in aqueous is very small, when the organics can be removed from aqueous stream. Especially we are talking about waste water you want to removed some traces amount of organics, so that the water can be used for other purposes.

Then pervaporation is very good you do not require entrainer, so there is no contamination I talked about entrainer in isotopic distillation. So, there is no contamination especially in pharmaceutical products or food and health care products, it is independent of vapor liquid equilibrium. I hope you all know what is vapor liquid equilibrium, you know it is a most important principle on which distillation columns are based on. So, distillation separation of two or three or multi componently quiz happen because of this vapor liquid equilibrium.

So, here liquid which has low boiling point will have more vapor present in the gas phase a liquid, which has higher boiling point will have less vapor present in the gas phase. So, because of this vapor liquid equilibrium you are able to separate out in the vapor phase the low boiling component and in the liquid phase the high boiling component that is what is called vapor liquid equilibrium. You are not bothered about vapor liquid equilibrium here, because the process is permeation and evaporation. So, vapor liquid equilibrium does not come into picture here.

It can be performed in batch or continuous mode; that means, we can do this operation by in a batch mode or continuously you may pass your mixture and continuously you may be purifying the mixture, it is very suited for heat sensitive products you know food pharmaceutical products. So, because as I mentioned in point number 1, we are not going to heated, so there no question of denaturalization or formation of tar caramel and so on actually. So, it is very good for food products and also pharmaceutical products, because you are not going to deactivate there are any proteins present you are not going to deactivate it here.

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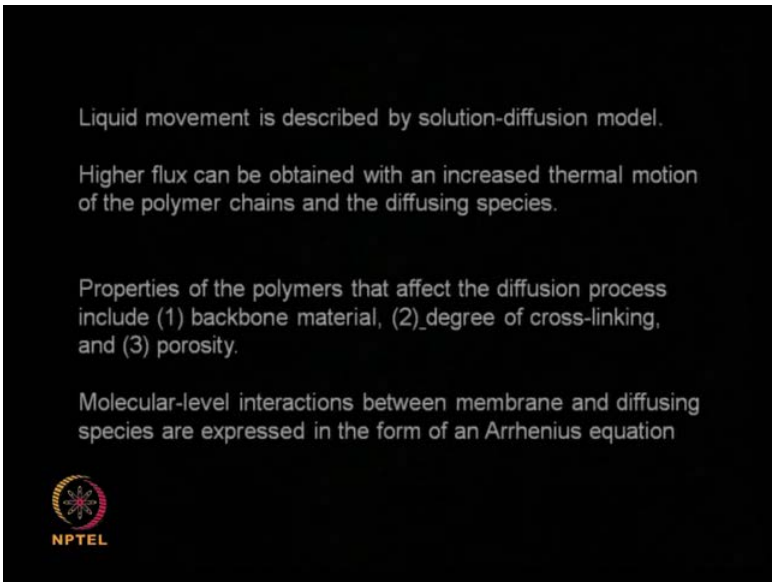

So, the liquid movement here is by the solution diffusion model. So, higher flux or higher movement of the solute can be obtained with an increased thermal motion of the polymer chains and the diffusing species. So, in the diffusion coefficient of the diffusing species is high it can travel faster through the membrane. And if the polymer on which

the membrane is made up of, if it is got better mobility when the diffusion of the solute is also going to be very good.

So, the polymer on which the pervaporation membrane is made up of has a very strong effect on the diffusion process. So, the polymer backbone makes lot of difference, the degree of cross linking of the polymer makes lot of difference, porosity makes lot of difference. So, there is molecular-level interaction between the membrane polymer and the diffusing species of a.

So, you can describe this interaction in terms of Arrhenius equation you must have all heard about Arrhenius equation long time back right. Arrhenius equation comes in kinetics, the kinetic rate constant is a function of temperature and the activation energy and that is where we might have studied Arrhenius equation, here to Arrhenius equation comes into play.

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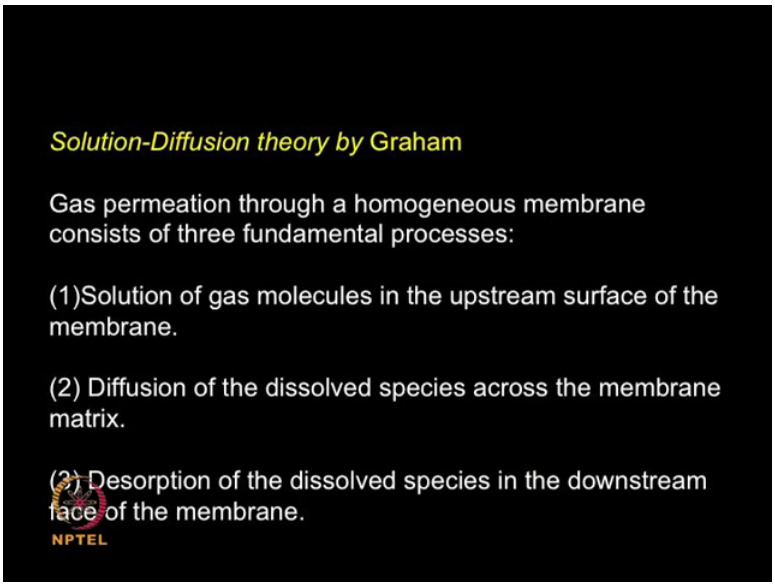

There is another theory it is called solution diffusion theory which is posted by Graham on which pervaporation system can be modeled or described. So, there is a gas permeation through a homogeneous membrane, this permeation is made up of three fundamental basic steps. So, the solute is permeating through a membrane. So, there are three things that is going to be happening. So, solution of gas molecules in the upstream surface of the membrane, so initially you have the solution of liquid, which goes into gas and that gas molecule is in contact to the membrane surface in the upstream.

Then you are going to have a diffusion of this dissolved species or solute through the membrane that is the diffusion and the third step is the desorption of this dissolved species, back into the downstream face of the membrane. So, it will be a desorption of the dissolved species as a vapor and then in the condenser this vapor is condensed into liquid, so these three things are happening.

So, you are going to have the gas molecules going into solution in the membrane, diffusion of the gas molecules through the membrane and finally the desorption of this dissolved species back into the vapor phase. So, all these parameters affect this pervaporation process and that is what Graham has proposed and that is why he called it as solution diffusion theory.

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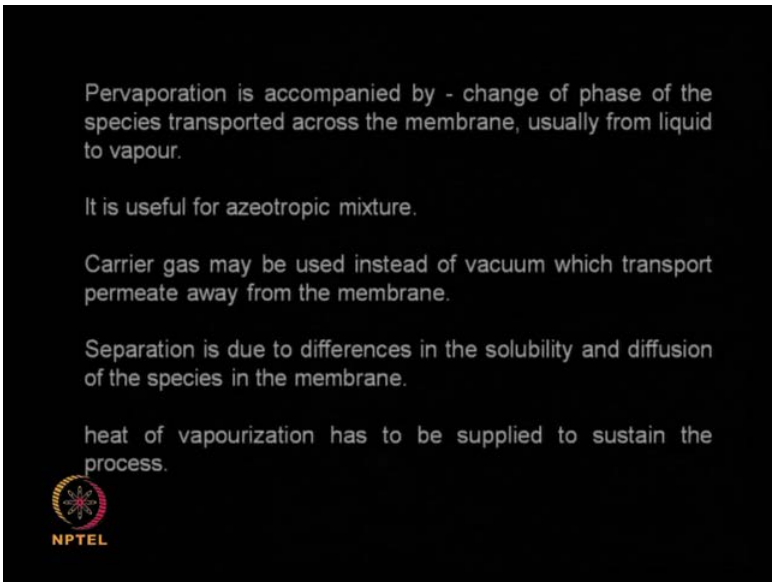

So, in pervaporation there is always a change of phase. So, initially you have the liquid then goes into vapor, this way then after diffusion this vapor again goes back into liquid. So, there is a change of phase, it is very useful for azeotropic mixtures, you can also use carrier gas instead of putting vacuum on the downstream, we can use carrier gas. So, the carrier gas can swipe the vapor that is diffusing out of the membrane. So, the separation is due to differences in the solubility and diffusion of the species of the membrane.

So, if some species diffuses very fast then it will be collected faster on that downstream, if there is another species which is very slow it will take much longer for it to be collected on the downstream. You need to of course, supply heat that is called the heat of

vaporization for converting the liquid into a gasses phase this is obvious. Now, the diffusion of this species through the membrane is also proportional to the size of this species.

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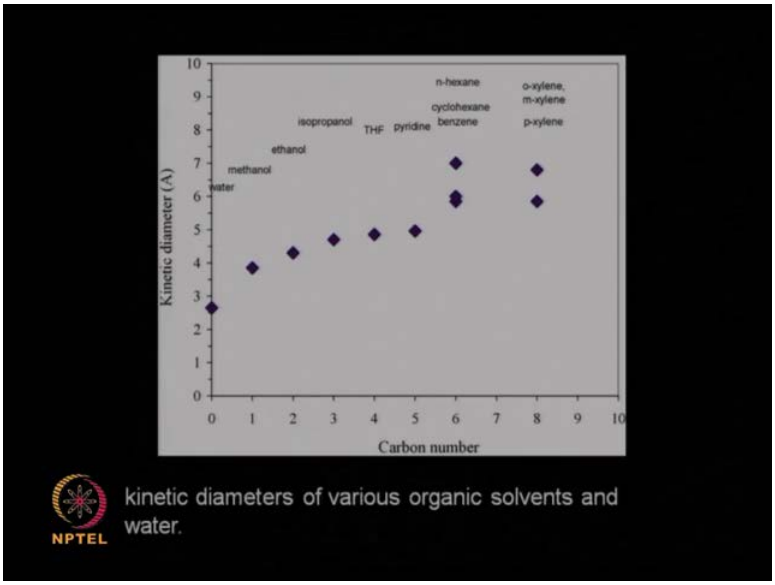

This picture has gives you an idea about the kinetic diameters of a various hydrocarbons, depending upon the carbon number, the kinetic diameter keeps increasing as you can see water is very, very low kinetic diameter is very small, because it does not have any carbon of course. Then you have methanol, ethanol, isopropanol, THF pyridine, n-hexene, paraxylene and so on.

So, you see the kinetic diameter increases from almost 2.5 to 7, so the diffusion of this species is a function of the kinetic diameter. So, a species like paraxylene as against isopropanol will be diffusing very, very slowly because of the size. Here ethanol will be diffusing much lower than methanol, because the kinetic diameters are different.

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Now, this is a very interesting book and it gives quite lot of information about a membrane pervaporation it is a review. So, some of these studies, which I am talking about or collected from this book kind, if one is interested to know more about pervaporation and polymers and the science on the principles one can look into this reference.

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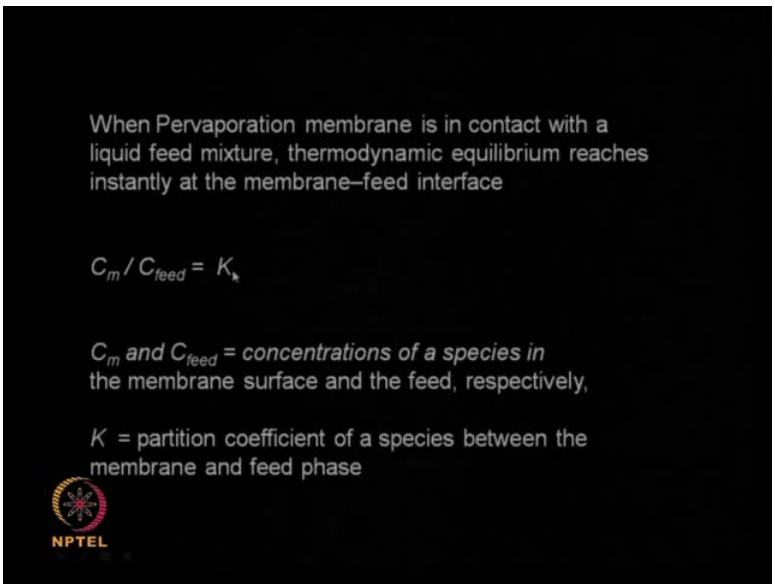

So, when you have pervaporation there is a thermo dynamic equilibrium between the membrane and the feed. So, we can put in here partition coefficient like your solvent

extraction. So, you will have a partition coefficient K, which is given by C m by C feed C m is the concentration of the species or the solute in the membrane surface, C feed is a concentration in the feed. And a K is of course, the partition coefficient between the membrane and the feed phases correct.

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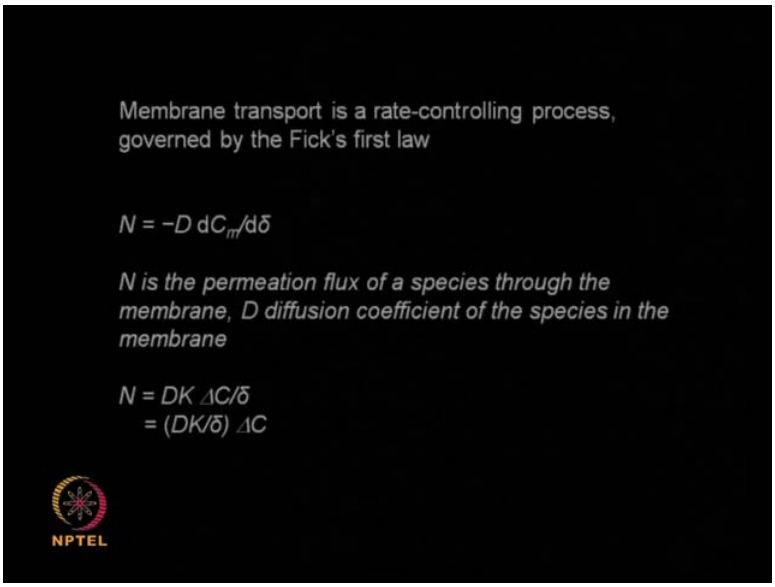

Now, membrane transport is a rate controlling process and it is given by Fick's law of diffusion we all know what is Fick's law of diffusion Fick's law of diffusion connects the flux with the driving force that is the concentration gradient and the diffusion coefficient correct. So, this is the Fick's law of diffusion, the permeation flux is equal to minus diffusion coefficient d C by d delta; that means, this is the driving force and this is the distance. Now, there is a minus term here because concentration will be going down you the driving force is a concentration gradient.

So, you are moving the solute from a higher concentration to lower concentration that is why you have a minus term. So, you can little bit simplify it and then we can put it as delta C here and this distance between this species can be called as delta, we can bringing the partition coefficient also inside. So, we will end up having an equation like the flux is equal to d K by delta into delta C, this is the driving force and this is the property of the membrane.

So, if you look into the property of the membrane, you will see terms like diffusion coefficient that is diffusion coefficient or the species through the membrane, which is a

function of the species as well as the membrane. Delta is like the thickness of the membrane and K is the partition coefficient; that means, ratio of the concentration that is just dissolved in the upstream vis-a-vis the concentration in the feed. So, these are the properties of the membrane and this is the driving force that is the flux.

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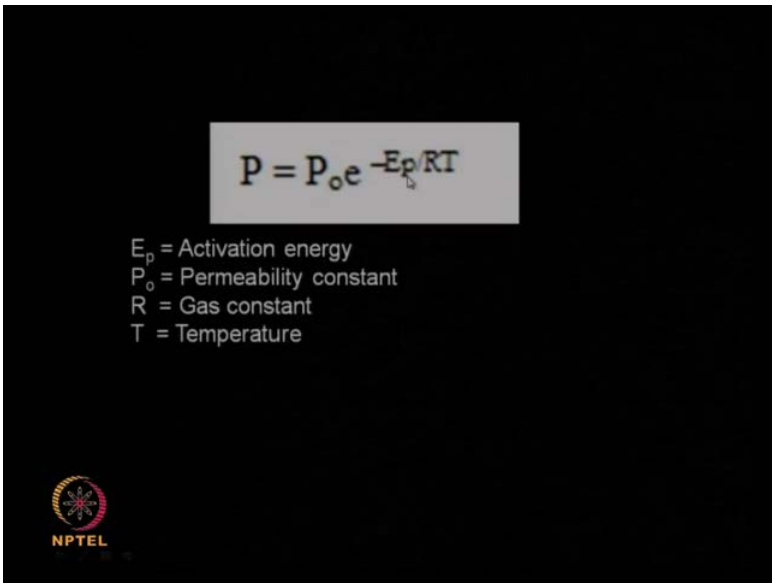

Now, we mention that it is a function of Arrhenius equation, so we have a the permeability and exponent rise to the power E p by R T, E p is the activation energy, R is gas constant and T is the temperature, so P 0 is the permeability constant.

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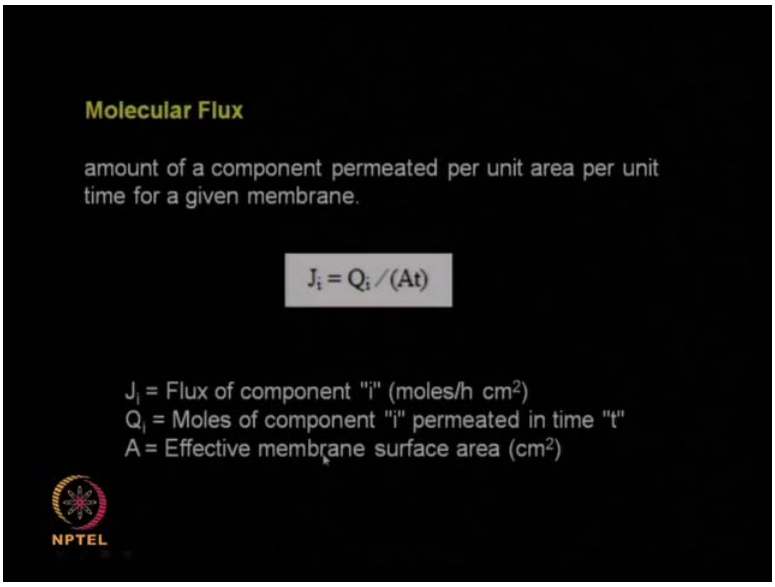

Molecular flux, so the solute is diffusing in and reaching the other side, so there is a flux cratered by each solute. So, the amount of component permeated per unit area per unit time is given by Q divided by A into T. A is the effective membrane surface area, T is your time we have put i here, because we are talking about ith species there could be a jth species, kth species and so on actually. So, each specie will have certain flux, so j i the flux depends upon the moles of component i divided by A T.

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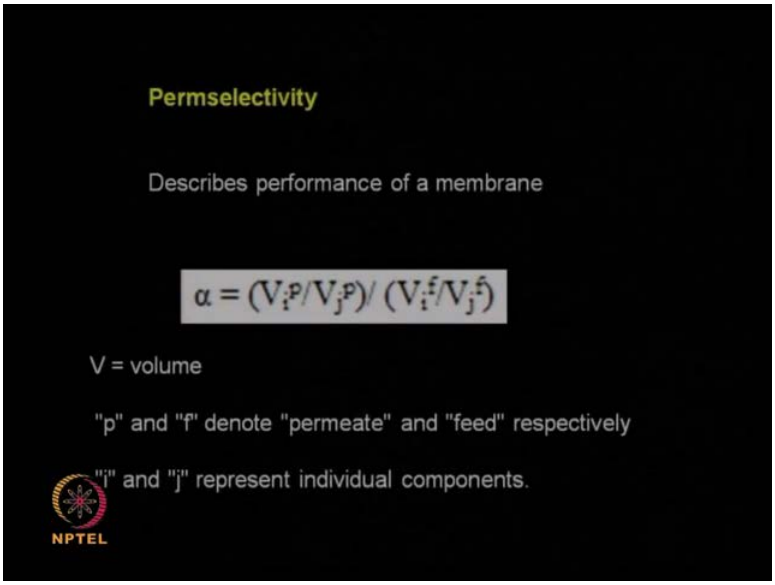

Now, there is some other term which is called permselectivity. So, suppose you have two species i and j what is the selectivity of the membrane for species i as against the species j that is what is called permselectivity. So, how do you define it we have V i P divided by V j P divided by V i f divided by V j f. So, the i and j represents individual species of component, p represents the permeate and f represents the feed. So, alpha that is the permselectivity is a function of the permeate to the feed of the volume actually.

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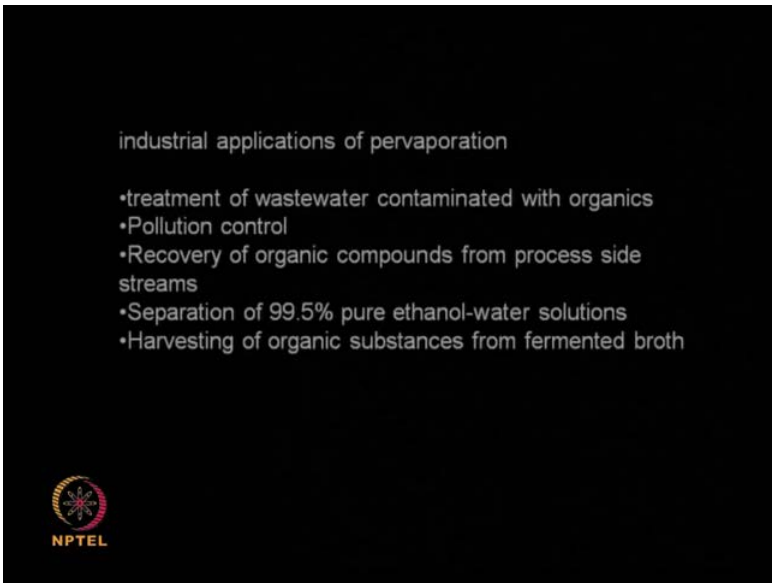

So, industrial applications of pervaporation are now becoming larger and larger, it is been realized that is got lot of advantages. So, there are large scale instillations of pervaporation. So, we can use it for treatment of waste water contaminated with organic, I am just interested in removing some amount of organic present not large amount of organic only very small amount organic contamination is there and Iwant to remove it.

So, pollution control recovery of organic compounds from process side streams sometimes, I am doing a reaction there could in organic contamination. So, I just want to remove that, so that I can recycle the process stream separation purification of 99.5 percent pure ethanol from ethanol water systems harvesting of organic substances from fermented broth. So, quite lot of applications of pervaporations are coming into the market.

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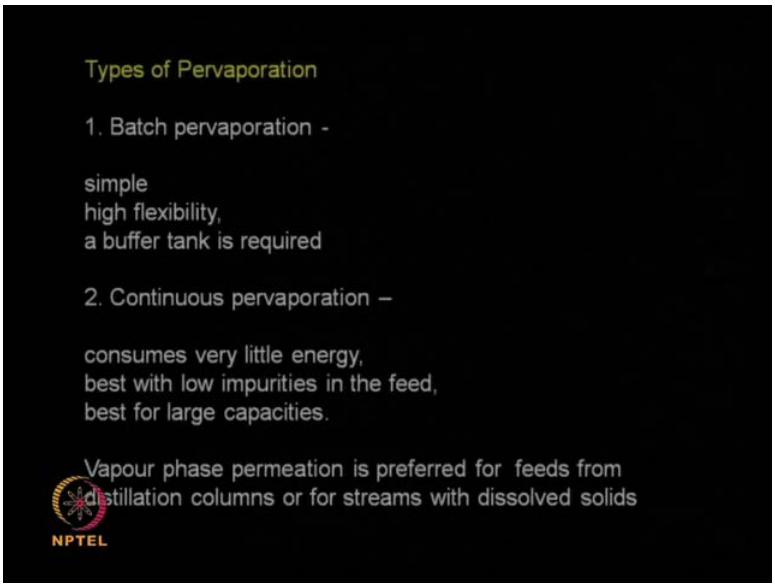

Now, as I mentioned we can do it in batch mode or in the continuous mode so; obviously, the batch of pervaporation is very, very simple high flexibility. So, I can use the same setup for different types of components and so on, but you will require a buffer tank. So, you will require you will have a feed tank into which your feed may come in then you will have the pervaporation system and the product has to be collected in another tank, so you need a buffer tank.

In a continuous process you will be using less energy why in a batch process I will be heating I will complete the pervaporation, I will stop the entire pervaporation, I will charge another lot of material, so you are heating and cooling, heating and cooling. So, the energy consumption is much higher whereas, in a continuous process you are continuously passing in the hot stream. So, you do not have to heat cool heat cool and so on actually so; obviously, it will consume less energy. It is very good for low impurities in the feed.

So, I want to remove only small amount of impurity and I have large quantity of this stream, so in that case it is very, very good, so it is best for large capacity. So, large quantity of a stream needs to be processed and it is got very little amount of impurity which needs to be removed using this concept. So, now a days his type of pervaporation is being prepared even for in distillation column, especially if we have distillation columns systems where you are talking about dissolved solids and so on. So, we will talk

about how pervaporation can be used in distillation column later in this particular course itself.

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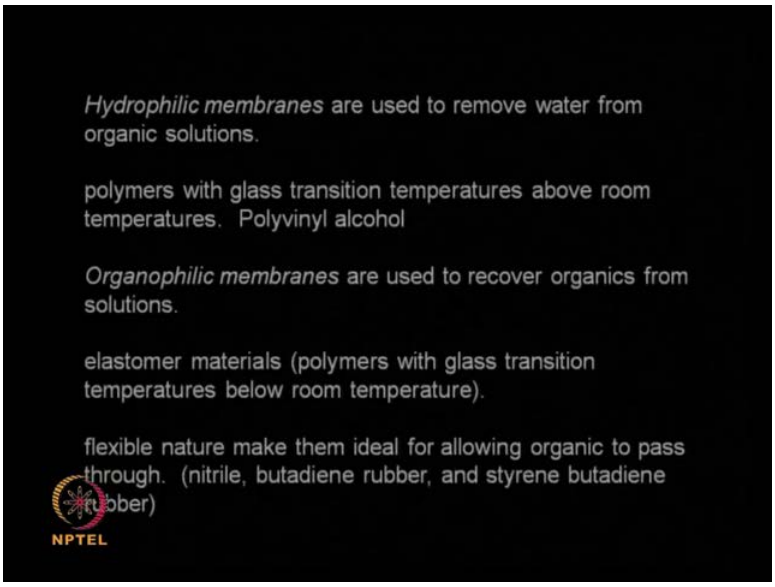

Now, membranes let us look at membranes, so as I said you have two types of membranes hydrophilic membranes organophilic or lipophilic membrane or a hydrophobic membranes. Hydrophilic membranes are very good for removing water from organic solutions; that means, the amount of water present in a mixture of organic solvent is very little. So, I am interested in only removing that water, so obviously you have to have membranes which are water loving or hydrophilic.

So, polyvinyl alcohol type of membrane polyvinyl acetate and so on. So, these membranes should have glass transition temperatures above room temperature. So, the membranes will have glass transition temperatures above room temperatures organophilic membranes on the contrary they love hydrophobic material, so obviously, this is very good for recovering organics from aqueous solution, so I have a very long aqueous stream and there is some organic contaminant.

So, I want to remove only that, in that situation I need to use organophilic membranes. So, these are very good elastomer type of material, polymers with the glass transition temperatures below room temperature. And of course, you should have membrane bit flexible also, because then organics can pass through at nirtile, butadiene rubber, styrene butadiene rubber and so on actually; so the organic material can pass through.

So, two types of membranes depending upon what you want to remove, do I want to remove little bit of water present in a large amount of organic solvent or do I want to remove little bit of organic solvent in present in a large amount of aqueous stream.

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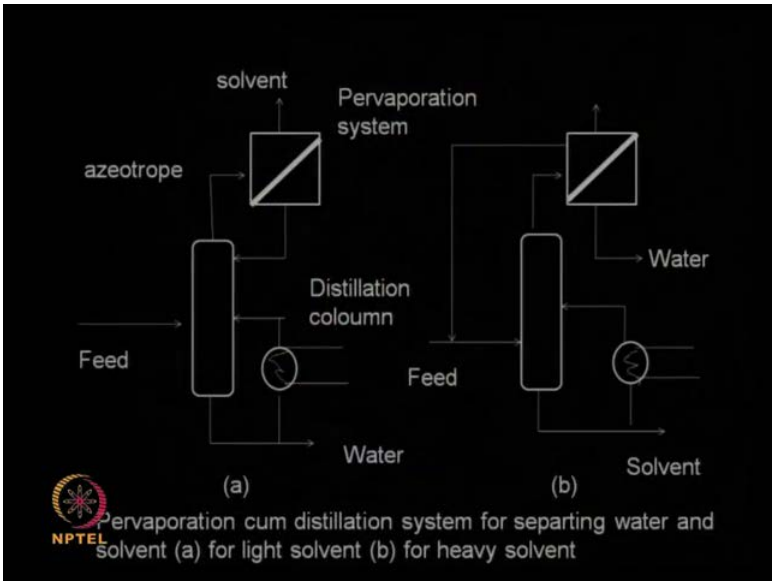

Now, pervaporation can also be used in distillation as I mentioned before, we can use it for separating water from a solvent the solvent could be heavy solvent like chloroform or it could be a light solvent. So, both types of situations we can handle pervaporation, otherwise you may have to resort to say azeotropic distillation. So, let us look at aqueous light solvent system like this you know. So, you have the distillation column, you are introducing the feed here and then this is the boiler, the boiler material is being heated up and it is fed up.

Now, if it a azeotrope; obviously, we will have a constant boiling system then you will be in trouble and as I mentioned before you may have to add entrainer, so I instead of that if you pass it through a pervaporation system. So, the light solvent can be removed in the pervaporation membrane and water can come down and again come down through the column. So, the light solvent all the time rises and then in the membrane you will have something like a hydrophobic membrane and it will separate out the solvent, so the water will come back.

Otherwise if you are resorting to a normal conventional of breaking azeotrope we may have had an entrainer, then again distill, then the entrianer has to be removed, so again

distill. So, you will resort two or three distillation columns, which a heavy solvent the solvent will be in the down and the water will be in the up right. So, if it is in heavy solvent, then what do you do the solvent will be collected pure, in the top you are going to have solvent and water again you will have a pervaporation membrane, water alone can be recover.

That means, you I use a hydrophilic membrane here and then the solvent which is coming out can be either mixed with the feed or you can dispose it of. So, this type of system is very good for heavy solvents, so solvent will be collected at the bottoms, this type of system is very good for light solvents where the solvent is collected at the top and water is collected at the bottom actually.

So, imagine in a normal solvent azeotropic distillation, you may require two or three distillation columns, whereas here we are talking about one column and a one pervaporation membrane system. So, you are talking about using less equipmence talking about using less energy that is why it is becoming quite useful to have.

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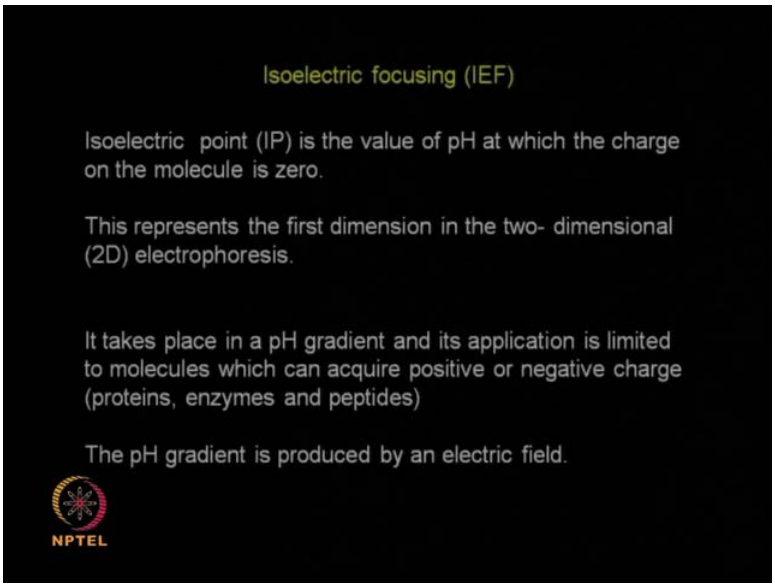

There is another principle, which we need to now introduce that is called isoelectric focusing. Now, you might have right that proteins have charge, why proteins have charge, because proteins contain acid group they contain amino group, so you are going to have charge. Now, the isoelectric point is the value of the p H at which the charge on

the molecule is 0. So, we sometimes use this particular principle in a many in 2D electrophoresis also, so we separate based on isoelectric p H.

So, we have a p H gradient and each protein will move and it will stop when it reaches the isoelectric p H. Now, all proteins enzymes peptides they will all have amino acids the amino acids will have both types of positive and negative. So, you can have positive and negative type of a proteins actually. So, in isoelectric focusing what do we do, we have the change in p H and at one particular p H, when the protein charge is 0, it will not further migrate or travel.

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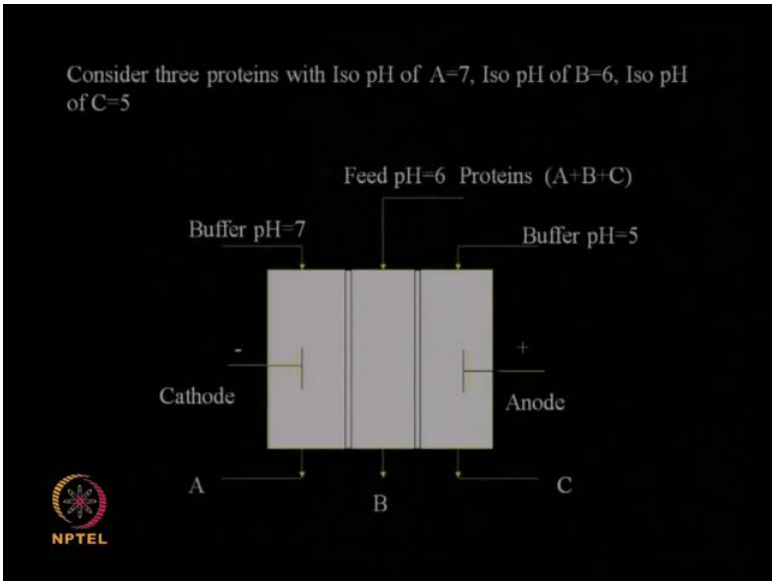

So, this principle can be used also for separating out proteins of various isoelectric point. Now, consider very simple system I have three proteins and a protein A has an isoelectric p H as 7, protein B has an isoelectric p H as 6 and protein C has an isoelectric p H as 5, so this is 5 and B has 6 and 7. And imagine I have a mixtures of all these three proteins and I am feeding at a p H of 6. So, this protein B will not have any charge; that means, it'll be neutral in this particular p H; whereas, the other two proteins of course, will have charge, because they are not in the isoelectric point.

So, if I apply a large voltage protein A and C will be moving agreed. Whereas, protein B will not be moving, so imagine I have here three chamber and I am feeding the mixture of protein at a p H of 6, B will not move, B will just travel down. So, I will get extreme very concentrated in B, but on the contrary, suppose I have another chamber where I am

passing a buffer of p H equal to 5 and another chamber in which I am passing a buffer of p H is equal to 7, the protein a will move to it is isoelectric p H and protein C will move to it is isoelectric p H.

So, this chamber will be predominantly A, this chamber will be predominantly C and this chamber will be predominantly B. So, this type of a separations based on isoelectric p H can also be achieved. So, the separating chambers are made up of membranes, so these membranes will allow these proteins to migrate towards it is isoelectric p H. So, this is another way of separating out proteins having different isoelectric p H actually, but this is not very a popular type of large scale separation process you know.

But, it can be used in a small scale in laboratory setting, but the main principle here is based on a isoelectric p H proteins with the charge becomes neutral at it is isoelectric p H. So, when they have charges by when I apply a voltage they will be migrating until it reaches its isoelectric p H. So, proteins will be located in their respective isoelectric p H and that principle is used in this type of separations.

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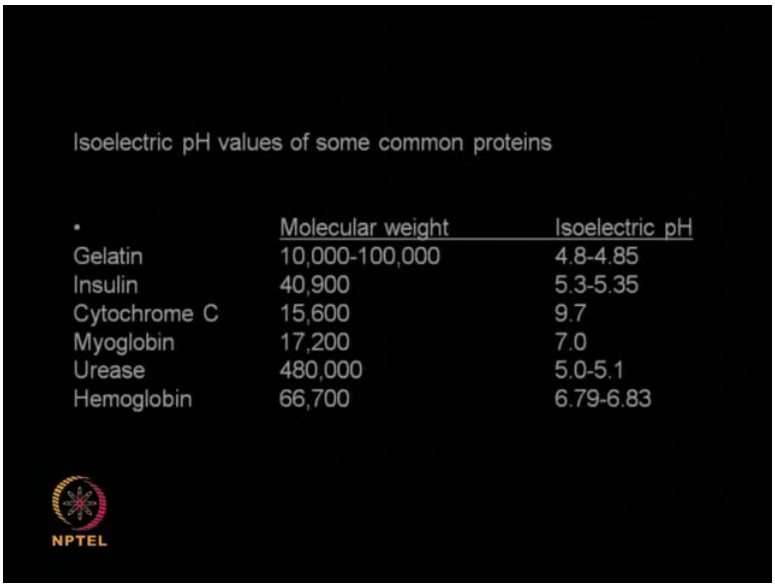

So, each protein has different isoelectric p H. In fact, this table tells you that look at gelatin now it is got a high molecular weight material it is p H is 4.8 to 4.85, insulin 5.3 to 5.35, cytochrome C 9.7, myoglobin 7, urease 5 to 5.1, hemoglobin 6.79 to 6.83. So, you see a differences in their isoelectric p H. So, I should be able to make use of these

differences in separating out of course, you need to keep in mind if the differences are very small you might not be able to really achieve it is fantastic separation.

So, the differences in isoelectric p H are large then I may be able to achieve a separations very efficiently or effectively, so we need to keep that particular point in mind actually. Look at the difference in molecular weights of these material you know gelatin very large molecular weight myoglobin 17,000, cytochrome C 15,000 dalton; so the molecular weight differences are pretty high.

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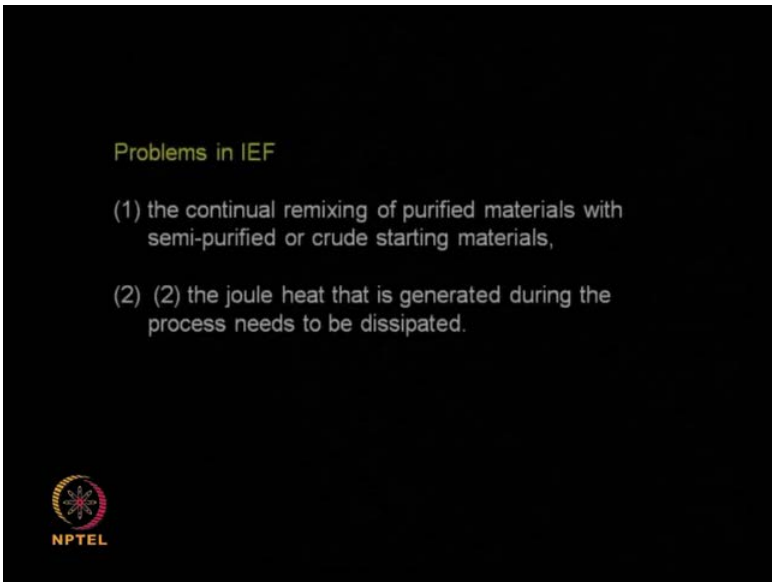

Now, the problems are there in isoelectric focusing, there is always going to be remixing of purified materials with semi purified materials or crude starting materials. So, there is always going to be that, there is going to heat generator quite large, because you are applying a large voltage, so heat is getting generated. So, you need to cool it otherwise the heat generator may denature your protein that is a point we need to keep in mind.

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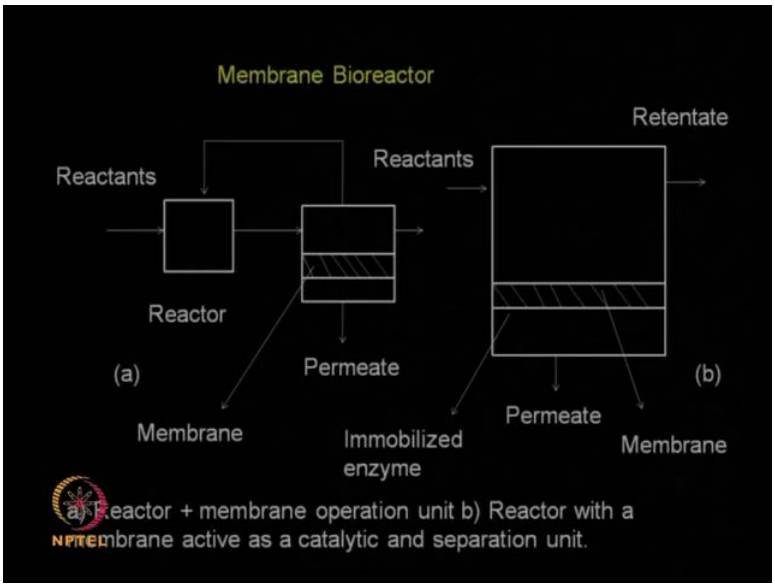

Membrane bioreactors; that means, a combination a bioreactor with the membrane. So, what are the advantages, I can use the membrane for separation the bioreactor for the bioreaction and I can combine membrane and bioreactor together. So, it is like telescoping, I just have one system which will do the reaction come separation, so I will not require a reactor, I will not require a separator separately.

So, let us look at a membrane bioreactor. So, I have a reactor, I do the reaction and then I go through a membrane setup. So, there is permeation taking place and the remaining material, which is not permeating through this fed back into the reactor, where do I use this, I can use this for suppose I am doing a biotransformation and I may having whole cells or enzymes in the reactor. I want to retain the enzyme or the bio biological molecule like bacteria or fungi, but I want to remove only the metabolized products.

So, what I can do, I can do the reaction continuously I can pass it through the membrane system. So, the small molecule or metabolite will permeate through, then I can recycle the enzyme back, so I can do this operation continuously. Where do I use this for example, I have a fermentation where I am producing alcohols like ethanol or butanol. Now, they are not the microorganisms are not very tolerant beyond a particular concentration.

So, in a normal conventional fermentation we just stop the reaction, but if I have a membrane I can continuously remove part of the alcohol that is produced and the

remaining active biomass can be sent back. So, the advantage is the concentration of the alcohol will be much lower all the time in your reactor. So, that is the main advantage of this type of setup actually. So, continuously I remove the alcohol that this produced to the concentration of alcohol in the reaction media is very small.

So, I can be rest assured that the microorganism or enzyme is not going to get denatured, because of the buildup of the alcohol. So, I am not allowing give alcohol to buildup that is one design. Another design I can have the membrane itself as a active catalyst; that means, I can immobilize my enzyme in the membrane. Suppose I am doing a biotransformation using enzyme instead of immobilizing it on a glass bead or encapsulating it on alginator or so on.

I can immobilize it on membrane itself, so the feed when it comes in contact with the membrane which contains my catalyst it will get reacted and the product will permeate through and go out. So, the enzyme itself is immobilized on the membrane material. So, the advantages I do not have to have a separate filtration unit for filtering my enzyme and again putting it back into my bioreactor and so on. So, I can avoid the second operation of filtration that is the advantage of a the combination of a membrane bioreactor here.

So, the first design you saw where we are continuously removing a metabolite or a product, so that you do not allow it to a buildup if you allow it to buildup you may be denaturing your bacteria or fungus or enzyme. The second design is you are immobilizing your enzyme itself, so that the membrane becomes a active catalyst and the product is removed continuously as a permeate here. So, these are the two different designs by which I can achieve tremendous flexibility with the help of a membrane into the bioreactor technology.

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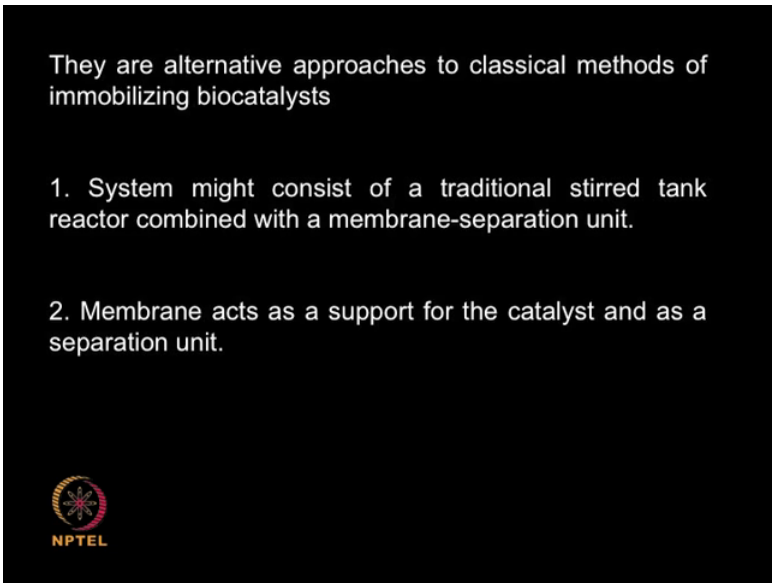

So, both are alternate, so I can have as the first one I can have a traditional stirred tank reactor and then I can have a membrane separation unit. In the second one the membrane acts a support for the catalyst, catalyst is your enzyme or active cell and then separation also automatically happens because it is immobilized on a membrane. So, your metabolite may be just diffusing through or permeating through. So, by choosing your membrane, we can achieve this type of permeation or diffusion or filtration type of process.

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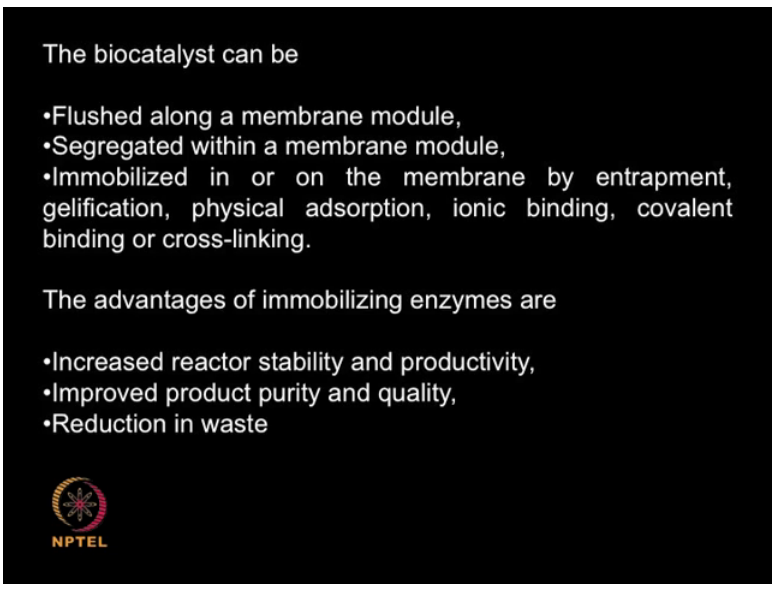

So, the biocatalyst can be flushed along a membrane module it can be segregated with a membrane module can be immobilized in or on the membrane by entrapment, gelification or physical adsorption or ionic binding, covalent binding or cross linking. So, all these can be achieved and you will have the membrane acting as a support or immobilizing support.

So, what are the advantages, we can increase reactor stability, we can increase productivity we can have improved product purity and quality, we can have reduction in waste the product can be continuously removed. So, if the product is toxic to the biological molecule or it is an inhibitor to the biological molecule by continuously removing it we are we are preventing it is accumulation.

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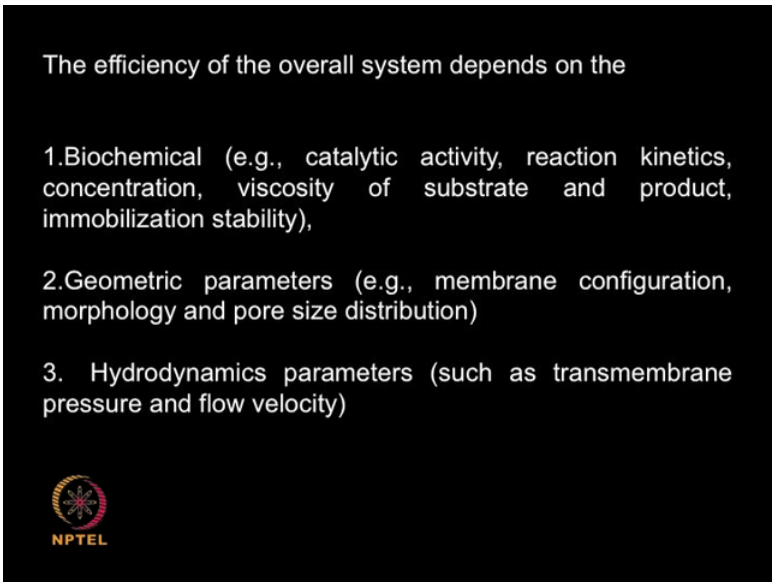

So, the efficiency of the overall system will depend upon the biochemical that is the catalyst activity, reaction kinetics, concentration viscosity of the substances, product, immobilization stability. How stable is this enzyme when it is immobilized on your membrane that is a very important point to consider, because enzyme may lose it is activity when you are trying immobilize it on the support.

The geometric parameters the membrane configuration is it a flat plate, it is a tubular and so on the morphology and also the pore size distribution. Then of course, the hydrodynamic parameters such as the pressure, the flow, the velocity, so all these

parameters come into picture. So, the overall efficiency of this type of a immobilized systems will be biochemical related, geometric related and hydrodynamic related.

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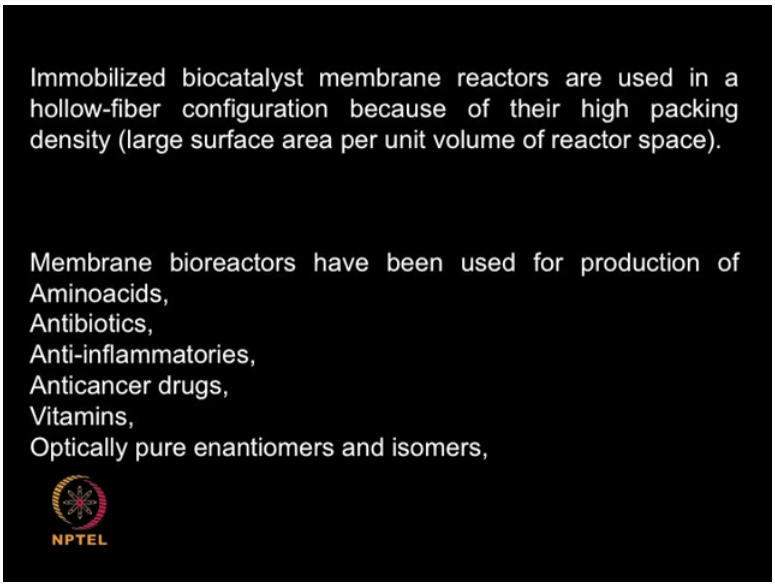

So, they are used in a hollow fiber configuration you can have a hollow fiber and your enzyme could be immobilized inside of the tubes. So, we can have a very high packing density; that means, large surface area per unit volume they have being, already being used in production of bio amino acids, antibiotics, anti-niflammatory compounds, anticancer drugs vitamins optically pure enantiomers and so on actually. So, lot of applications are slowly coming up in the market and I think it is because of it is advantages, they will be replacing quite lot of the conventional reactor followed by separators actually.

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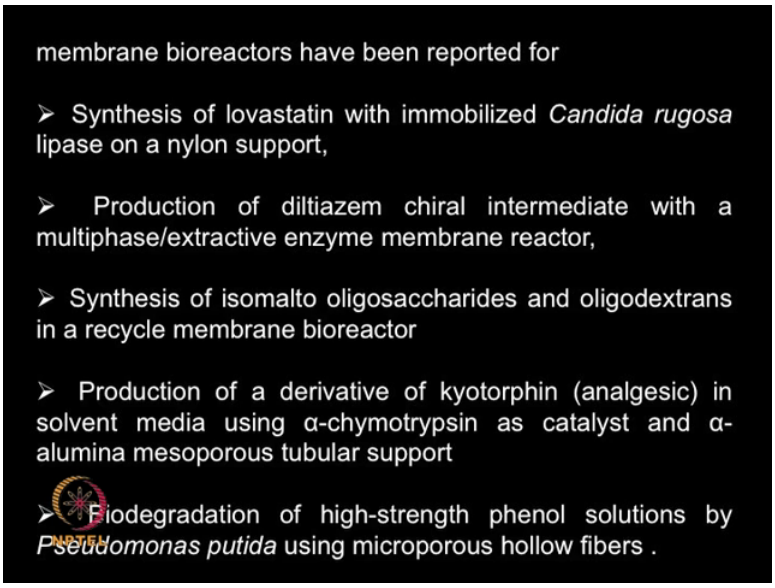

So, there are examples of synthesis of lovastatin with immobilized candida rugosa lipase on a nylon support production of diltiazem, chiral intermediate using a multiphase enzyme by a reactors, synthesis of oligosaccharides and oligodextrans in a recycle membrane bioreactor. Production of derivative of analgesic, kyotorpin using a alpha chymotrypsin a catalyst and alpha alumina mesoporous tubular support as membrane. Biodegradation of high-strength phenol solutions using pseudomonas putida using a microporous hollows fiber membrane, so lot of applications are already being investigated.

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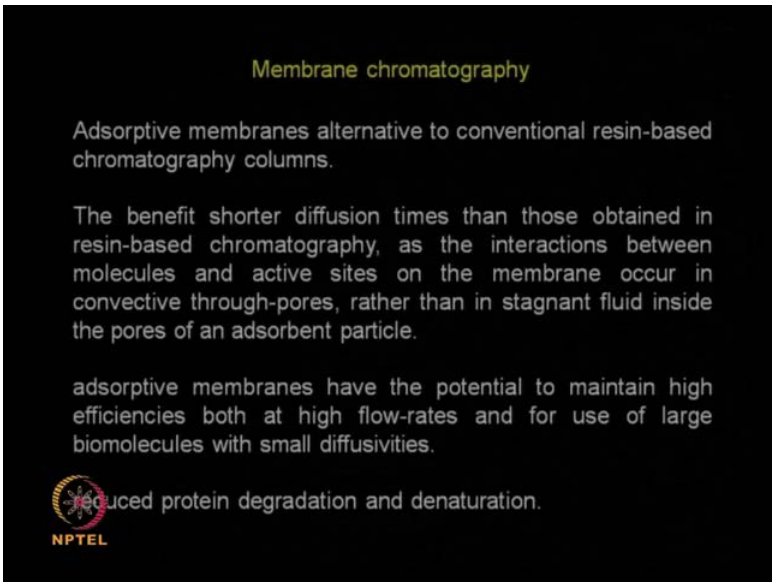

Another area where membranes are come into being it I would call it much more recent is the membrane chromatography unlike the normal solution based chromatography. So, membrane chromatography it is an alternate to conventional resin based chromatography you know. So, what are the benefits shorter diffusion time, when compare to resin based chromatography, because the interaction between molecules and active sites on the membrane is through convection; that means, flow.

Whereas, in a normal chromatography there is stagnant fluid inside the pores of a adsorbent, material or particle, so the diffusion coefficients are much slower, so diffusion times are much larger. So, adsorptive membranes they have the potential to maintain high efficiencies, because you can use high flow-rates you can use it for large biomolecules with small diffusion coefficient. So, by doing this short diffusion times, we are preventing the protein degradation or even denaturation of the protein, so it is ideal for biological molecules.

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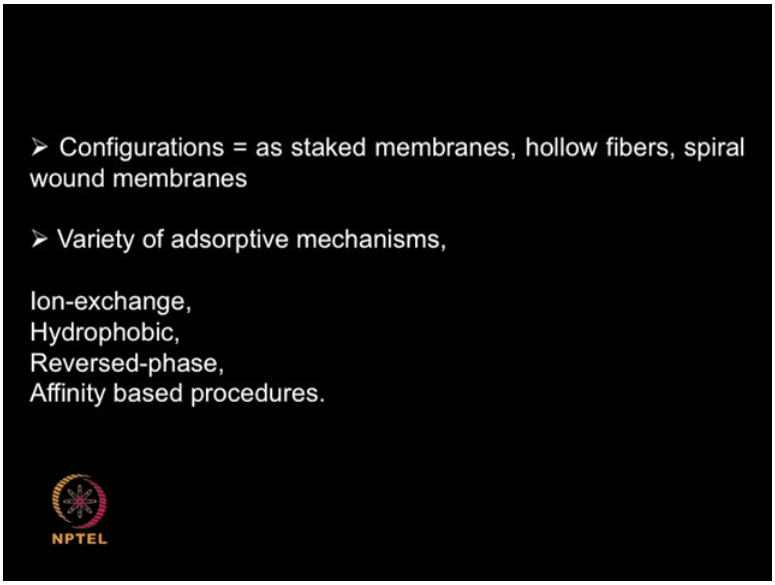

So, you have staked membranes, we have hollow fiber membranes you can have spiral wound membranes for membrane chromatography. In a normal adsorptive mechanism you may ion exchange, hydrophobic, reversed phase, affinity based procedures. So, you can use all these procedures for adsorption of the active ingredient on top of the membrane material. So, you have the active ingredient sort of immobilized on the

membrane material and this type of immobilization can be achieved through different mechanisms, ion exchange, hydrophobic, reversed phase, affinity based procedures.

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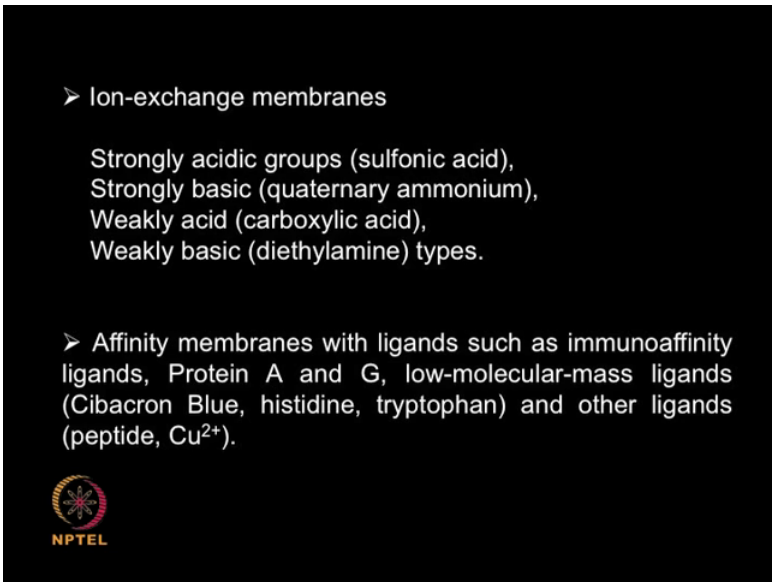

So, ion exchange membranes they will be strongly acidic groups like sulfonic acid or it can be strongly basic groups like quaternary, ammonium could be weakly acidic like carboxylic acid or weakly basic like diethylamine types actually. You can also have affinity membrane, so you will have lignads such as immunoaffinity ligands protein A and G low molecular mass ligands like cibacron blue, histidine, tryptophan and other ligands like copper to plasants so on.So, we can also have affinity ligands, immobilized on membrane, so we will get affinity membrane type of systems.

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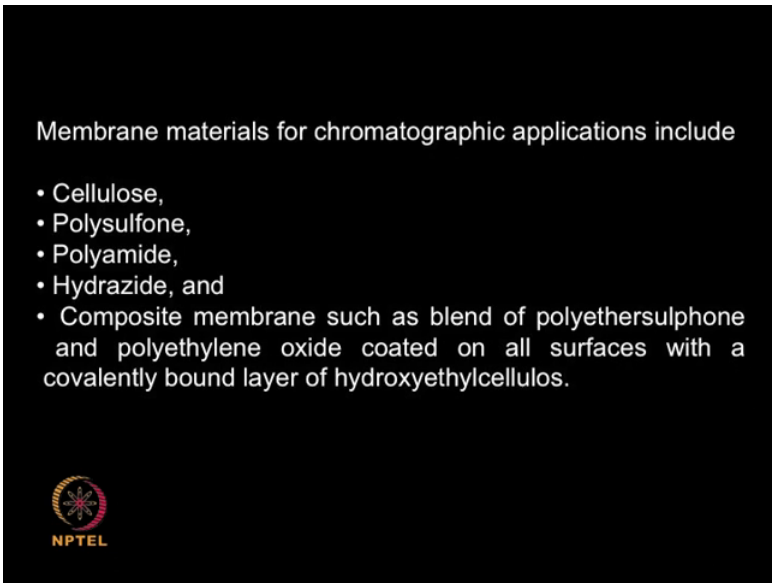

So, what type of membranes we can use cellulose based material, polysulfone based material, polyamide based material, hydrazide. We can also have composite membranes you know such as blends of polyethersulphone polyethylene oxide coated on all surfaces with covalently bound layer of hydroxyethyl cellulos. So, we can have different types of membrane surfaces, polymeric natural materials, hydrophilic as well as the hydrophobic.

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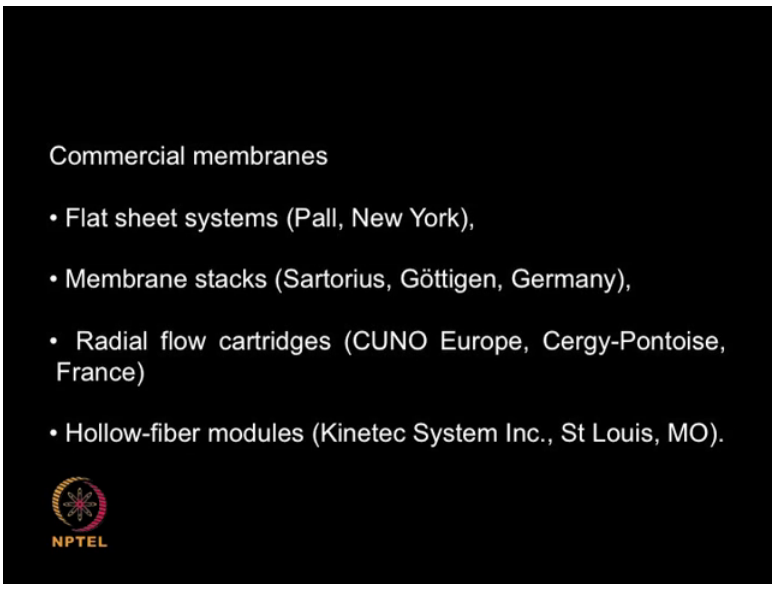

So, commercial membranes flat sheet systems this is the company, which is manufacturing there we can have stacks membranes several company in Europe and US.

Radial flow, cartridges hollow fiber modules, so different morphologies or different systems and different companies, which manufacture these commercial membranes.

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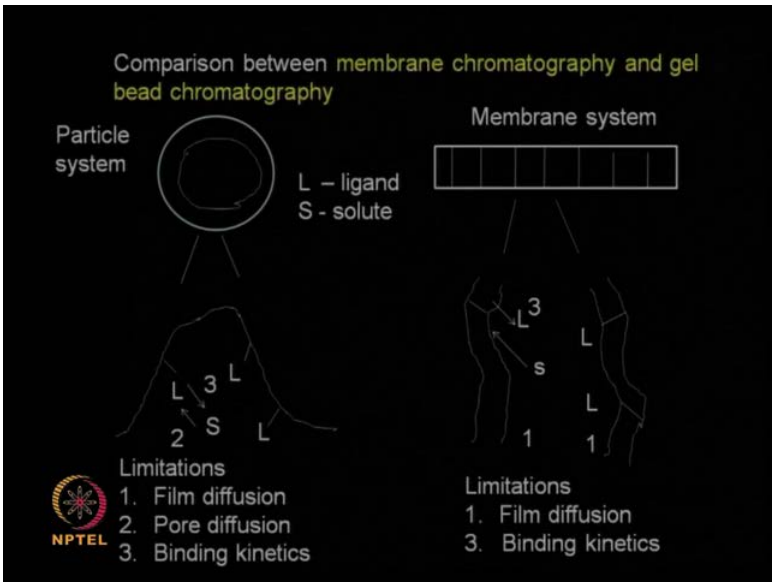

So, how does a membrane chromatography and gel based chromatography look like they are all familiar with the gel based or the liquid chromatography. So, you have you have a particle, particle is nothing but here support then we will have the ligand molecules here and then we have the solute which will get in contact with the ligand. So, you are going to have film diffusions, you are going to have pore diffusion and then you have the binding kinetics.

Whereas, in a membrane system if you see you will have the membrane and then you have the ligands attaches to the membrane. So, here we do not have pore diffusion coming into picture, so we will have film diffusion as well as the binding kinetics. So, you are getting rate of the pore diffusion, so that is one of the main advantages of this, so you diffusion times will be much smaller or shorter.

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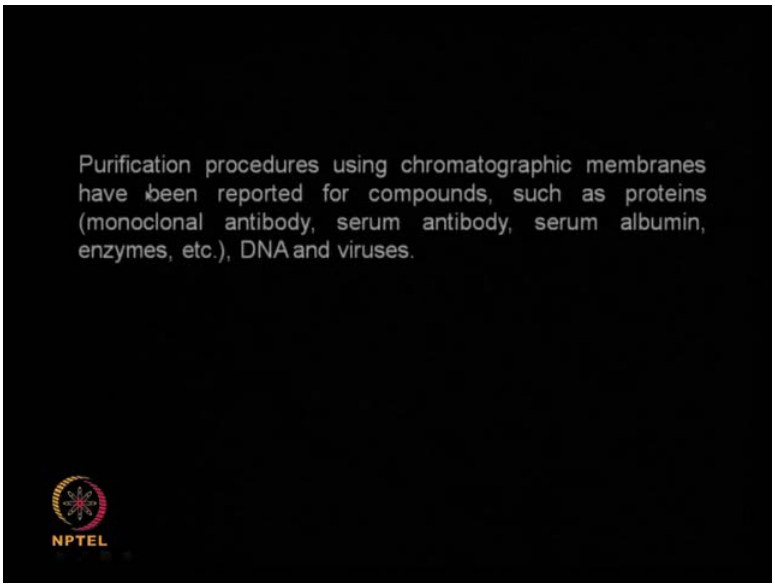

So, lot of examples have been coated, where membrane chromatography has been used vis-a-vis the conventional liquid phase chromatography. So, membrane chromatography have been reported for compounds such as proteins like monoclonal antibody, serum antibody, serum albumin, enzymes or DNA's and viruses and so on actually.

Of course, they are still not come into large scale commercial operation but they are still in the lab, but they seem to have quite a good advantages. Where convert to the conventional chromatography, where we are talking about standard stagnant liquid film. So, you are going to have a different types of diffusions coming into picture, which will slowdown your process.

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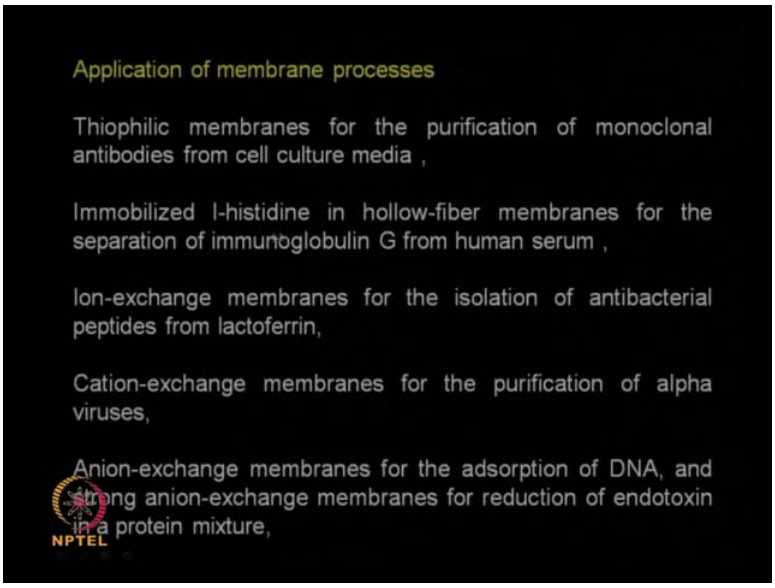

Application of membrane processes thiophilic membranes for the purification of monoclonal antibodies from cell culture, immobilized l-histidine in hollow-fiber membranes for the separation of immunoglobulin G from human serum.

Ion exchange membranes for the isolation of antibacterial peptides from lactoferrin, cation exchange membranes for the purification of alpha viruses, anion-exchange membranes for the adsorption of DNA and strong anion-exchange membranes for reduction of endotoxin in a protein mixture. So, lot of applications have been reported using membranes for separations. So, different principles like anion exchange principle, ligand based principle all have been exploited.

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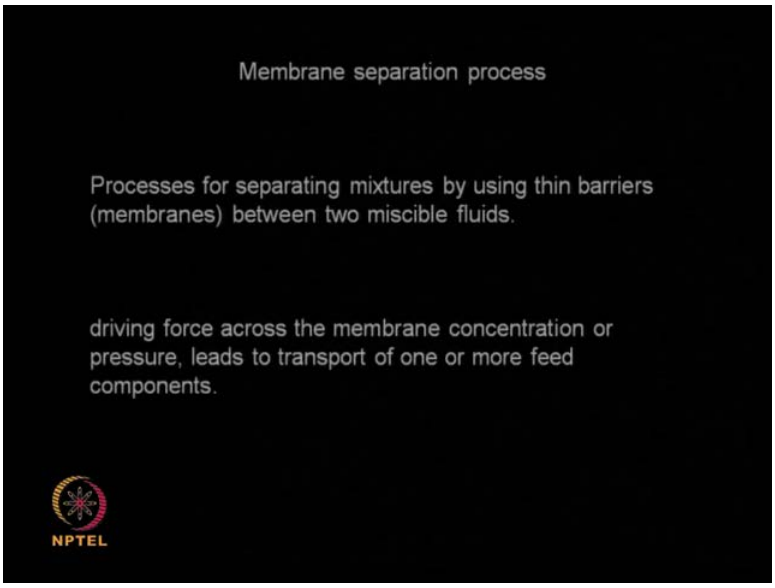

So, membrane separation processes are used for separating mixtures by using thin barriers, it is a synthetic material or it is natural material. So, we are separating two miscible fluids, the driving force in a membrane process is concentration gradient pressure gradient, so there is going to be a transport of one or more feed components.

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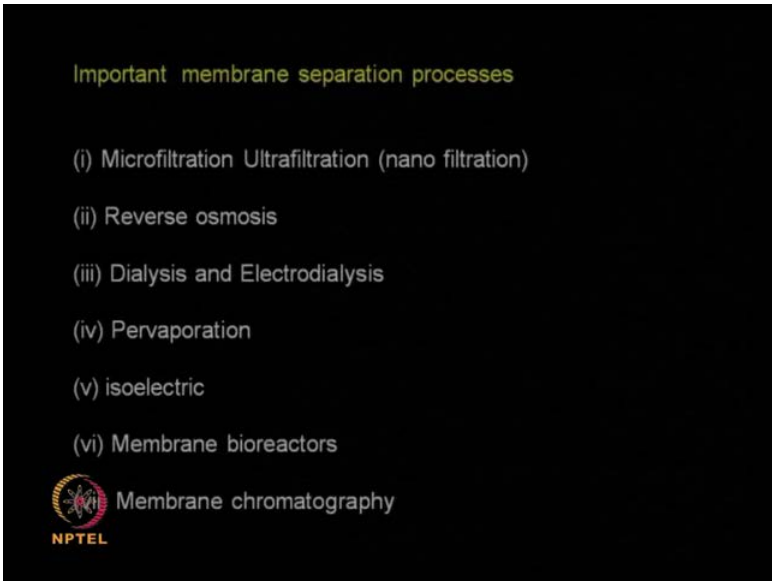

So, we looked at large number of membrane separation processes for the past few classes, some of them have fine pores some of them do not have pores. So, the process is like a diffusion, the processes which are based on pores is like a filtration. So, we have

microfiltration, which is almost exactly like your filtration then you go to altra filtration and nano filtration. Then we looked at reverse osmosis, which is trying to overcome the osmotic pressure, so you are applying a large pressure. So, that the solvent flows out pure.

Then we looked at dialysis; that means movement of ionic material, ionic proteins or ionic salts. Electro dialysis where you are applying an electric field, so the cations and anions moved to the respective electrodes, again dialysis is used to quite a lot in artificial kidney for removing salts from blood and purifying blood and electro dialysis is used again for separating out salts from protein mixtures.

Then we looked at pervaporation, very ideal system for removing small quantities of water from your solvent or small quantities of solvent from an aqueous stream, it just uses nominal temperature and vacuum. So, the energy consumption is very, very low when compare to the normal distillation type of approach and pervaporation is very good if we are talking about temperature sensitive material. Then we looked at isoelectric, so all proteins have isoelectric p H at which the protein the charge on the protein is 0.

So, you make use of it and you separate proteins of different isoelectric p H, using a p H gradient. Then we looked at membrane bioreactors, so where you are combining extraction or removal or filtration of the metabolized in a fermentation broth, but simultaneously carryon your fermentation. So, you are combining two things, the fermentation or biotransformation with separation, then you can also immobilize your enzyme on your membrane.

So, you can again get the advantages of the enzyme as well as you can get the advantages of the separation of the metabolite. This is very, very good if you want to continuously remove your metabolite, which could be toxic which could be inhibiting your biocatalyst or biomass or enzyme or; so, membrane bioreactors are extremely useful in that area. Then we looked at a membrane chromatography as against the conventional liquid phase chromatography, where you have the ligands cover by liquid. So, you are going to have the diffusion slowing down the entire process.

So, diffusion times are much larger when compared here in a membrane chromatography the ligand is immobilized on the membrane surface, so the diffusion is are much faster. So, I can have ion exchange different types of cation membranes anion membranes and

so on or ligand based membranes, where I am immobilizing a active ligand on a membrane surface. So, we achieve very fast diffusions, we achieve very high separation rates, but membrane chromatography is of course, is still in the early stages.

Whereas if you look at the filtrations like micro ultra fitration well established, reverse osmosis is also well established, dialysis electro dialysis is also well establish, pervaporation is also well well establish. Isoelectic focusing is more in the lab scale, membrane bioreactors are already in the market in much commercial scale.

So, you see membranes have a tremendous a application and use in downstream, where you are handling a small molecules where you are handling organic solvents, organic chemicals, where you are handling biological molecules like proteins or enzymes.