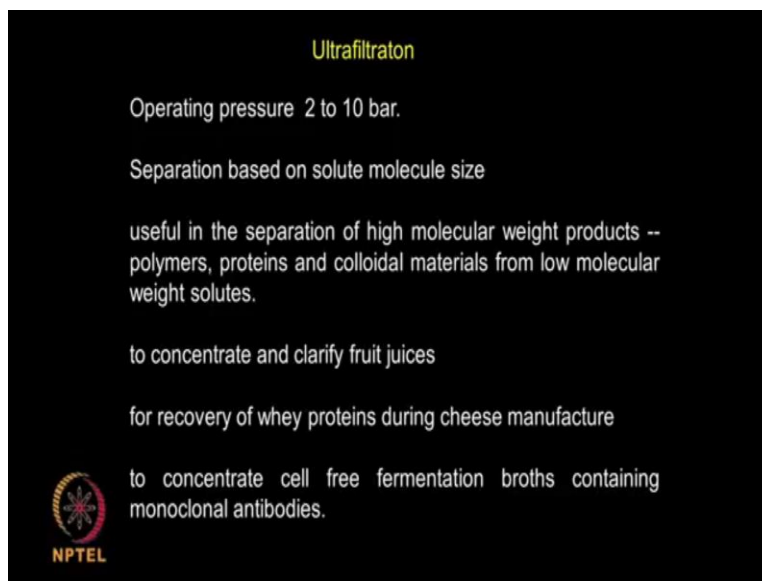


Principles of downstream techniques in Bioprocess – a short course
Prof. Mukesh Doble
Department of Biotechnology
Indian Institute of Technology, Madras
Lecture-12
Membranes (continued)

We are going to take one more class on membranes because membranes are very important processes and there are different types of membranes and they have different principles of operations. So I mentioned about quite a lot of membranes like reverse osmosis membranes, microfiltration and so on.

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Ultrafiltration

Operating pressure 2 to 10 bar.


Separation based on solute molecule size

useful in the separation of high molecular weight products -- polymers, proteins and colloidal materials from low molecular weight solutes.

to concentrate and clarify fruit juices

for recovery of whey proteins during cheese manufacture

to concentrate cell free fermentation broths containing monoclonal antibodies.



Now let us look at ultrafiltration, these are membranes pressure is generally of the order of 2 to 10 bar, you can use it for separating solutes based on the molecular sizes. So we can use it for separating high molecular weight products like pure polymers, proteins, colloid materials, low molecular weight solutes, we can use it for concentrating fruit juices for recovery of whey proteins from cheese, in concentrate cell-free fermentation broth containing monoclonal antibodies and so on actually.

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UF made from polysulphone or other polymers is finely microporous and may be asymmetric.

The pore size is smaller than that in MF and pore area per unit surface is also less and hence the flux is also much less.

Liquid flow through the membrane is by viscous flow through the pores due to moderate applied pressure.

The osmotic pressure is negligible because of the high molecular weights of the solutes.



So they are generally made up of polysulphone or other polymers and they have microporous, okay the pore size is smaller than the microfiltration, microfiltration will have largest pore then comes the ultrafiltration. So liquid flow through the membrane is by viscous, flow through the pores and you need apply some pressure these are the moderate pressure. So here they osmotic pressure is negligible because of the high molecular weight of their solutes actually.

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Microfiltration

resembles conventional filtration, the filter medium is porous filtering particulate matter or suspended solids not dissolved solute molecules.

pressure driven, =1 – 2 bar

disadvantage of microfiltration is --- frequent fouling of membrane due to deposition of solids

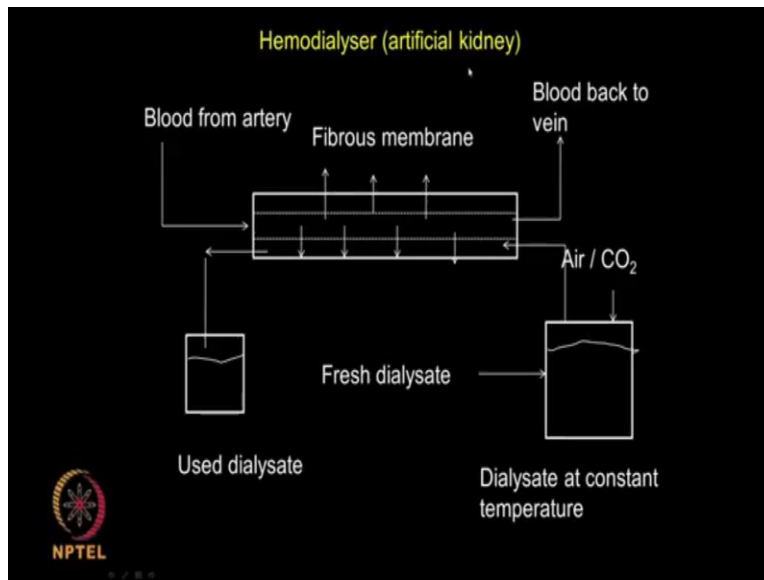
build up of solids on the membrane can be minimised by installing a depth filter upstream

Another disadvantage - concentrated slurry and not a dry cake is obtained.



Then you have the microfiltration, these are very large pore size, so they are almost like conventional filtration actually. So large pores so we can filter particulate matter the pressure of the order of 1 to 2 bar even normal filtration also pressure is say 2 to 10 bars actually. So disadvantage of microfiltration is fouling is big problem because of the deposition of the solids. So solids buildup happens at the upstream of it another disadvantage is concentrated slurry. So you will not get very dry cake okay when you do this microfiltration.

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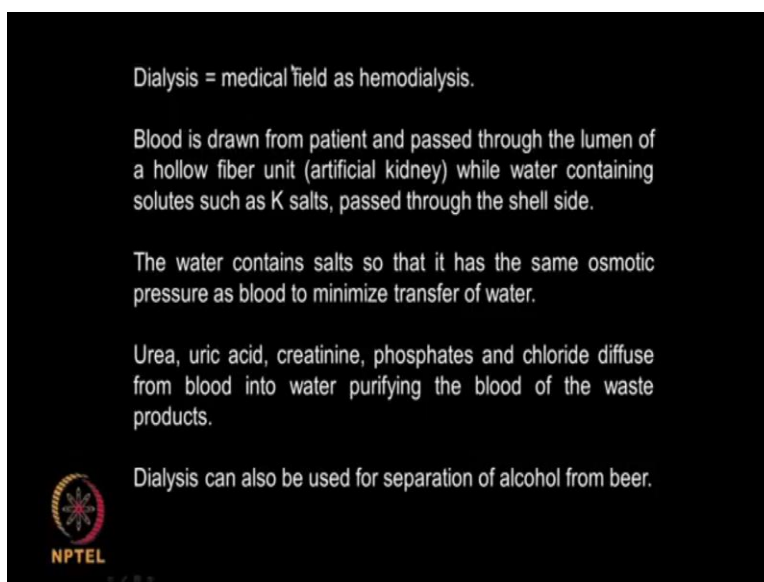
Now let us look at another important membrane process and this is called hemodialysis. It is an artificial kidney especially patients who have problem with kidney that kidney failure, the kidney is not able to do its job of separating the salt present in the blood into the aqueous urine, then such patients have to undergo this type of hemodialysis. Okay or it is called dialysis. Sometimes they may have to come to the hospital once every fortnight and get this done.

So what do you have here we have a fibrous membrane here, we have the blood from the artery goes and then it goes back to the vein actually. So blood is drawn from the artery through these fibrous membrane okay. On the other side, we have something called dialysate. Okay so that liquid flows on the other side and the used dialysate is collected, so the salts from the blood because the kidney is not able to remove the salt effectively. The salts from the blood because of

the concentration ingredient flows out goes into the dialysate which is collected and taken out actually.

So the blood is free of the so this principle is based on concentration gradient, okay so you have the dialysate that is flowing outside these fibrous long tubes and we have the blood flowing inside. Sometimes the dialysate may go into the blood stream as well that sort of possibilities are there actually so this is called a hemodialyser.

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Dialysis = medical field as hemodialysis.

Blood is drawn from patient and passed through the lumen of a hollow fiber unit (artificial kidney) while water containing solutes such as K salts, passed through the shell side.

The water contains salts so that it has the same osmotic pressure as blood to minimize transfer of water.

Urea, uric acid, creatinine, phosphates and chloride diffuse from blood into water purifying the blood of the waste products.

Dialysis can also be used for separation of alcohol from beer.

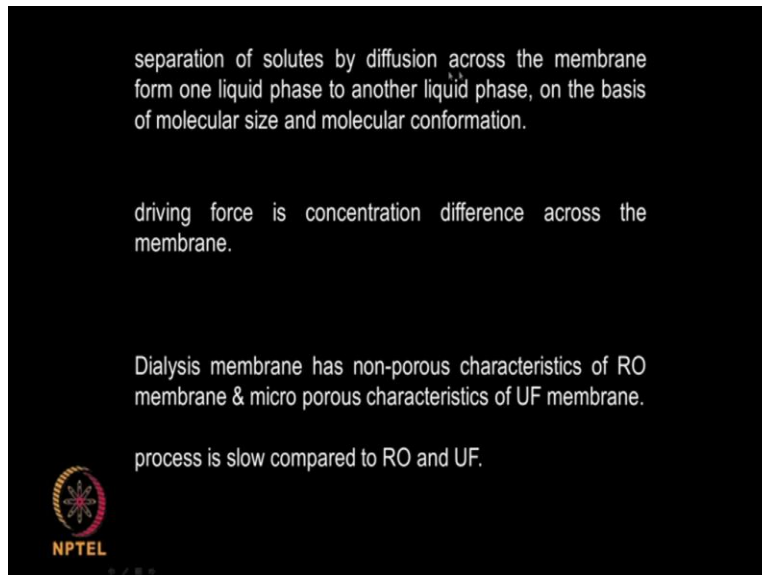


So it is generally used in medical field, as I said so the blood is drawn from the patient and passed through the hollow fiber unit, the lumen, it is called water containing solutes such as potassium salts are passed through the shell side that is called dialysate. Now you use salts because you want to osmotic make the osmotic pressure same as what is there in the blood as well as in the water side.

So urea, uric acid, creatinine, phosphates, chlorides, that are all present in the blood and which the kidney is not able to remove are removed in this and then the blood that goes back into the

vein is free of all these salts actually. So we can use dialysis also for separating alcohol from beer also.

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So separate of solutes this is through diffusion. So the driving force is concentration difference actually because as you know fixed law of diffusion we have the diffusion coefficient multiplied by the concentration gradient. So daily the dialysis membrane has non-porous characteristics of reverse osmosis membrane and micro porous characteristic of ultrafiltration, the process is slow when compared to reverse osmosis or uf, ultrafiltration actually okay.

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Solute flux $J = R \Delta C$

$R =$ membrane resistance + film resistances on both sides

The diagram illustrates a dialyzer setup. A central horizontal tube is divided into three sections: a left section for 'Blood from artery' (indicated by a rightward arrow), a middle section for the 'membrane' (a hatched rectangular area), and a right section for 'dialysate' (indicated by a leftward arrow). Vertical arrows point from the blood side through the membrane to the dialysate side, labeled 'solutes'. On both the left and right sides of the membrane, there are thin layers labeled 'film'. The NPTEL logo is visible in the bottom left corner of the slide.

The solute flux that is the $J = R$ that is the membrane resistance + film resistance on both the sides you will have both sides into ΔC ΔC is the concentration gradient. So if you have say a porous membrane in the middle okay, so you have the blood flowing like this and the dialysate flowing counter current the solutes okay diffuse out into the tube side of the dialysate okay. Now you can have films here on both side the film resistance inside on the blood side as well as the film resistance on the dialysis side both are possible. So they all contribute to the r that is the constant that is the membrane resistance + these film resistances on both sides.

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The dialyzer clearance (K_d , ml/min) determines the removal rate of a substance from blood

depends on = characteristics of the dialyzer & nature of treatment method.

Mass balance equation is

$$K_d C_i = Q_i C_i - Q_o C_o$$

Q_i and Q_o are the blood flow at the inlet and outlet of the dialyzer

C_i and C_o are the concentrations of solute in and out (mmoles/liter).

$C_o \ll C_i$



So ΔC is the driving force generally it takes hours especially if a patient is undergoing dialysis, so the dialysis clearance that is K_d it is called ml per minute determining the removal rate of the substance from the blood. So it depends on the characteristics of the dialyzer nature of treatment method and so on. So we can do a mass balance here K_d into C_i okay C_i is the concentration of solute in and the C_i not is the concentration out.

C_i is the concentration of solute coming in, C_i not is the concentration going out, Q_i and Q_0 are the blood flow of the inlet and outlet okay. The difference is what is getting transferred that is $K_d * C_i$ so C_i not is what is going out is much much smaller than C_i and generally Q_i and Q_0 are almost same actually. That is the total amount of blood flow; we assume that the blood does not diffuse out into the dialysate side of it okay.

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If Q_f is the ultrafiltration rate (ie some blood fluid also escapes through the membrane) then,

$$Q_i = Q_o + Q_f$$

$$K_d = Q_i - (Q_i - Q_f)C_o / C_i$$

In hemodialysis, $Q_i = Q_o = Q_B$ (ie. no blood fluids escapes) and $Q_f = 0$, then

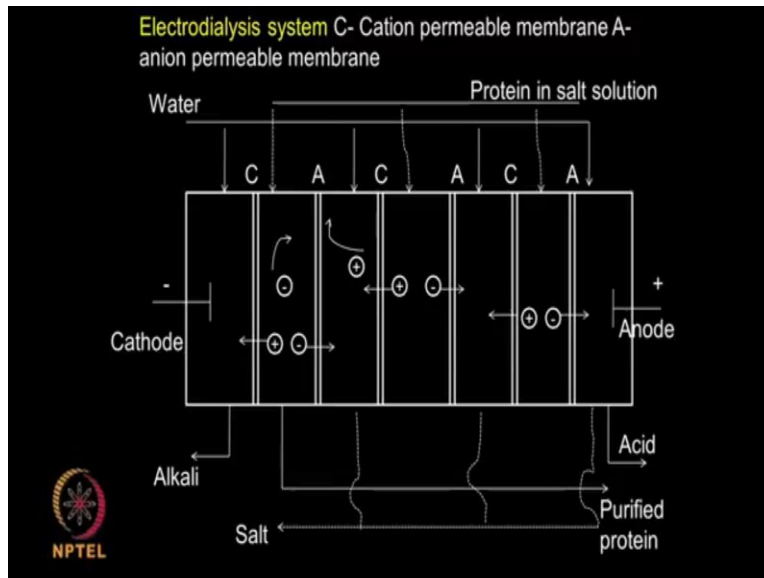
$$K_d = Q_B(1 - C_o / C_i)$$



So what we can do is, if Q_f is the ultrafiltration rate, that is some blood flow also escapes through the membrane then $Q_i = Q_o + Q_f$ but if no blood fluid escapes $Q_i = Q_o$ which = Q_B so we can have $K_d = Q_B * 1 - C_o / C_i$ okay. So if we assume there is some blood that is escaping okay then we will have slightly complicated equation okay but if you assume that there is no blood escaping into the dialysate whatever blood coming in whatever blood go out = blood same okay Q_B blood flow. Okay.

So $K_d = Q_B$ into $1 - C_o / C_i$ okay where K_d is this dialyzer clearance okay ml / minute okay C_o is the concentration of the solute going out of the dialysis unit, C_i is the concentration of the solute entering the dialysis unit and that is called the clearance.

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There is another system that is called electro dialysis, so the name implies we apply an electric field so that the salt that is ions cations and anions moved to the electrodes. Okay. So what happens here is we have compartments these are all called compartments and they are all separated by membranes. So you have an anion permissible membrane you have a cation permissible membrane anion permissible membrane cation and so on actually okay.

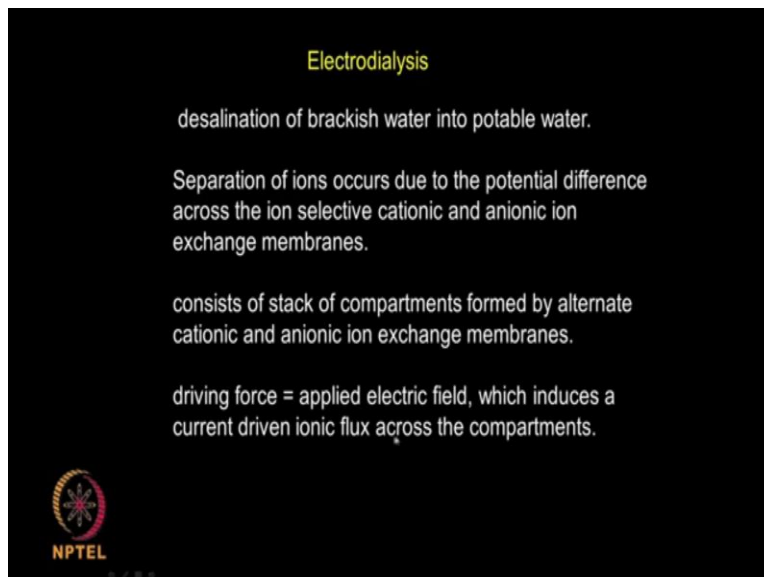
So you have say protein with salt that is entered and then you are applying a voltage here cathode - voltage here anode +. So what happens all the cations will try to move there okay all the cations will try to move there actually okay and the anions will go to the other side actually. So you will end up having pure salt collected in alternate compartments and okay and purified protein collected in the other alternate member of compartment.

So when we have a positive and negative, the cation and the anion for the salt. So pluses will try to go there minuses will go there, pluses cannot go there, because it does not allow it is an anion permissible membrane. So what will happen is there will be a concentration of the salts in the alternate membrane and there will be a concentration of proteins which are devoid of the salts in the alternate. So we can collect the purified protein and we can collect the salt solution in the alternate compartments

Or if you want to desalinate water while using this type of electro dialysis unit we can get pure water from alternate set of compartments and saltish or brackish water on the other set of compartment. So this can also be used for desalination of water especially if you have electrical power generating system there then this type of electro dialysis is very good instead of going for RO, RO if you are closer to a sea and you need to apply very high pressure

And if you are very closer inland and if you are closer to an electrical power generating unit then electro dialysis may be a better system actually. So both have advantages, disadvantages and you can select based on the conditions and what are the requirements actually. So electro dialysis can also be used for removing salt from protein solution for desalinating salt water and so on actually.

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Electrodialysis

desalination of brackish water into potable water.

Separation of ions occurs due to the potential difference across the ion selective cationic and anionic ion exchange membranes.

consists of stack of compartments formed by alternate cationic and anionic ion exchange membranes.

driving force = applied electric field, which induces a current driven ionic flux across the compartments.

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So the electro dialysis desalination of brackish water separation of ions due to the potential difference across the ion selective cationic and anionic exchange membranes, the driving force is the applied electric field which induces the current that is the ionic flux.

(Refer Slide Time: 11:06)

Mathematical relation in electro dialysis

$$I = \frac{FNQ\eta}{nE}$$

F = Faraday's Constant = 96487 coulombs/g-equivalent

I = current

N = solution normality

Q = flow rate, m³/s

η = removal efficiency

n = number of cells

E = current efficiency

Electrodialysis power is

$$P = I^2 R$$



So what is the mathematical relation I the current = F that is the Faraday's constant N is the solution normality Q is the flow rate eta is the removal efficiency / n, is the number of cells, e is the current efficiency. So the current can be calculated using the Faraday's constant, solution normality, the flow rate number of cells and current efficiency So the electro dialysis power is given by power = I square r okay. So the resistance is very high so power is power also will be very very high power requirement.

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Pervaporation

is a combination of membrane permeation and evaporation.

separation of two or more components is achieved with the help of a thin non porous polymer membrane which has different rates of diffusion for different components.

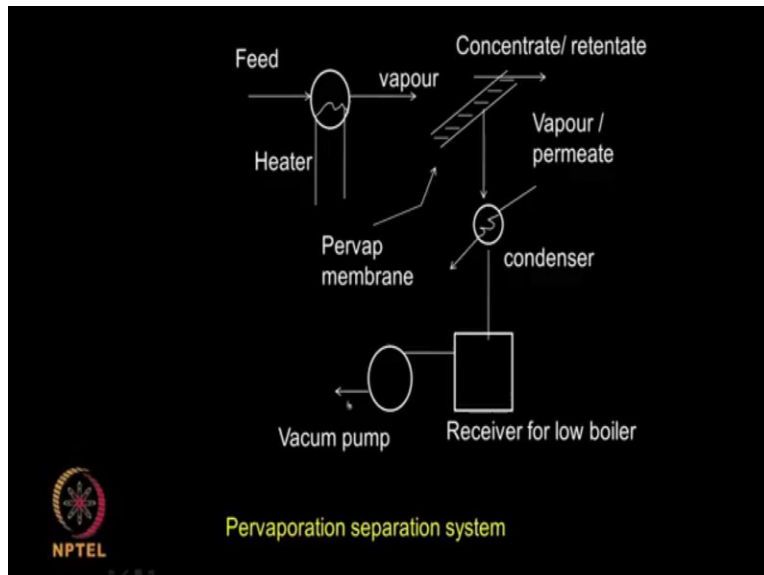
Evaporation is achieved by heating.



The next downstream membrane based technique is pervaporation. So this uses a membrane. It uses a pervaporation membrane, it is a combination of permeation and evaporation that is what it is called pervaporation. So the solution is initially evaporated by applying some heat as well as by applying high vacuum and then the solute molecules permeate or diffuse through the membrane material because there is an affinity for the solute to the membrane material.

So it diffuses and it goes to the other side where it is again becoming a liquid and that way it is collected actually. So separation of two or more components is achieved with the help of a thin non porous polymer. So you have to remember this in pervaporation the material is not porous unlike your microfiltration or ultrafiltration, where the material is porous. So depending upon the rates of diffusion of the solutes through the membrane material separation can be achieved. Okay so evaporation of the solution is achieved by little bit heating and applying vacuum.

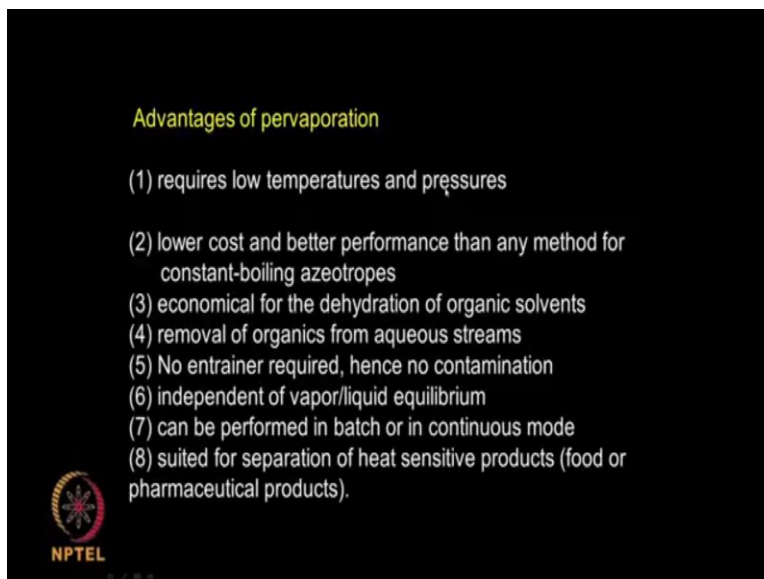
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This is a typical pervaporation setup, so what you have is feed, feed solution you are applying some heat here at the same time, you are applying vacuum on the other side. So the vapor comes here, it settles on the membrane material, pervaporation membrane material diffuses through on other side it is condensed using a condenser and a liquid is condensed and taken out actually.


So you apply vacuum on one side and heating on the other side. So there are no pores in the membrane material. So your solute travels through the membrane um because of diffusion and it is condensed here on the condenser side.

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Advantages of pervaporation

- (1) requires low temperatures and pressures
- (2) lower cost and better performance than any method for constant-boiling azeotropes
- (3) economical for the dehydration of organic solvents
- (4) removal of organics from aqueous streams
- (5) No entrainer required, hence no contamination
- (6) independent of vapor/liquid equilibrium
- (7) can be performed in batch or in continuous mode
- (8) suited for separation of heat sensitive products (food or pharmaceutical products).

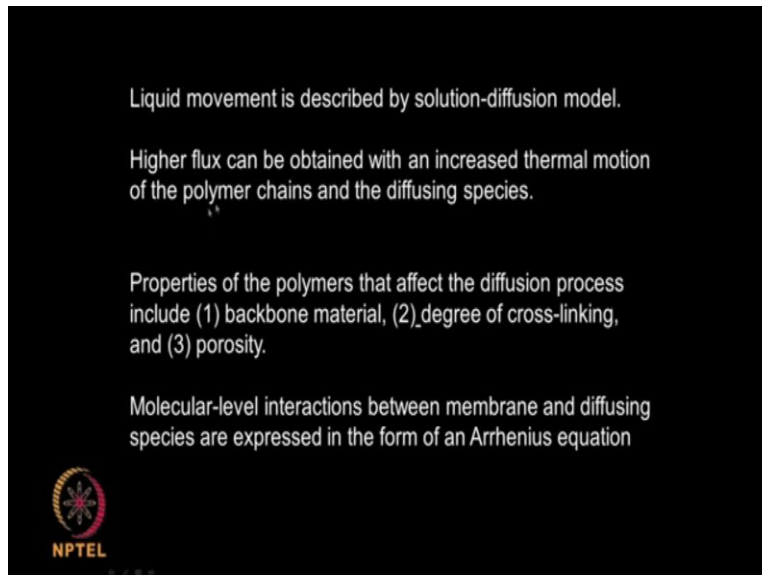
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So what are the advantages it requires low temperature and pressure. So if there is any thermally labile products like fruit juices or syrups sugar solutions are then it is easy to operate. It is lower cost and better performance than using say azeotropic distillation it is economical for dehydrating organic solvent, suppose I want to make 100 % butanol that means I want to remove all the water if want to make 100 % ethanol, then I may have to resort to azeotrope. I may have to add some third component to break the azeotrope so as pervaporation does not require there.

So we can remove organics from aqueous streams, there is no entrainment required, there is no contamination especially in azeotropic distillation. we have to add a third component which could be contamination. It is independent of vapor liquid equilibrium, So it does not depend on vapor liquid equilibrium like distillation, okay it just depends upon the um diffusion of the solutes through the membrane material. So it can be performed in batch or continuous it suited

for separating heat sensitive material food product food products pharmaceutical products and so on.

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Liquid movement is described by solution-diffusion model.

Higher flux can be obtained with an increased thermal motion of the polymer chains and the diffusing species.

Properties of the polymers that affect the diffusion process include (1) backbone material, (2) degree of cross-linking, and (3) porosity.

Molecular-level interactions between membrane and diffusing species are expressed in the form of an Arrhenius equation



So the liquid movement is explained based on solution diffusion. We can achieve higher flux increased thermal motion of the polymer chains of the diffusion. So the prop properties of the polymer affect the diffusion process backbone material degree of cross linking porosity all these will affect. Is there molecular level interaction because the solute molecule diffuses through the polymeric material actually that is what is happening. So it is generally mentioned expressed in term of Arrhenius equation.

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Pervaporation is accompanied by - change of phase of the species transported across the membrane, usually from liquid to vapour.

It is useful for azeotropic mixture.

Carrier gas may be used instead of vacuum which transport permeate away from the membrane.

Separation is due to differences in the solubility and diffusion of the species in the membrane.

heat of vapourization has to be supplied to sustain the process.



So pervaporation is accompanied by change of phase you need to remember because you are heating. So you are forming vapor then solute goes through on the other side solute is condensed it becomes liquid. So it is much more useful than azeotropic sometimes you can use carrier gas also So you can drive this. So the separation is not based on vapor liquid but it is based on solubility and diffusion of the species to the membrane. Okay so it is based on solubility and diffusion whereas distillation is based on vapor liquid equilibrium.

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P. Shao *, R.Y.M. Huang

Journal of Membrane Science 287 (2007) 162–179
Review - Polymeric membrane pervaporation



So this is the good book journal of membrane science, if you want to know if you want to know more about polymeric membrane related to pervaporation okay.


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When Pervaporation membrane is in contact with a liquid feed mixture, thermodynamic equilibrium reaches instantly at the membrane–feed interface

$$C_m / C_{feed} = K$$

C_m and C_{feed} = concentrations of a species in the membrane surface and the feed, respectively,

K = partition coefficient of a species between the membrane and feed phase



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Now pervaporation as I said you have a liquid in feed mixture, there is an thermodynamic equilibrium with the membrane mixture actually. So we have k the equilb partition coefficient will be = c_m by C_i feed c_m is the concentration of the species on the membrane surface c_{feed} is the concentration of the species in the feed solution. So that gives you the partition coefficient okay. So by selecting suitable membranes we can achieve very high partition coefficient.

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Membrane transport is a rate-controlling process,
governed by the Fick's first law

$$N = -D \frac{dC_m}{d\delta}$$

*N is the permeation flux of a species through the
membrane, D diffusion coefficient of the species in the
membrane*

$$N = DK \frac{\Delta C}{\delta} \\ = (DK/\delta) \Delta C$$



And then membrane transport that is transport of the solute through the membrane is by Fick's law of diffusion. So Fick's law is permeability flux = - D diffusion coefficient * dc / dx so or if you differentiate it we end up with N = D is the diffusion coefficient k is the permeability delta is the membrane thickness delta C is the driving force. That determines your flux on the left-hand side correct.

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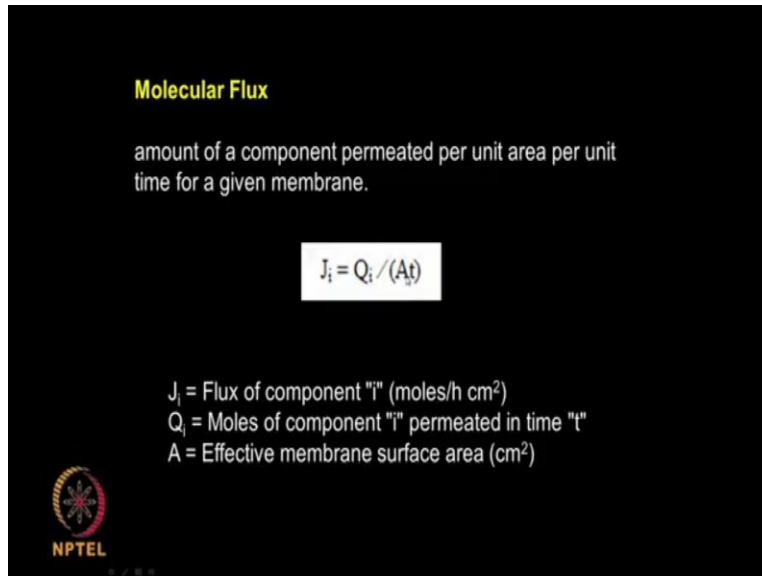
$$P = P_0 e^{-E_p/RT}$$

E_p = Activation energy
 P_0 = Permeability constant
 R = Gas constant
 T = Temperature



Then permeability is generally expressed like an Arrhenius type $P = P_0 e^{-E_p / RT}$, E_p is the activation energy okay, R is the gas constant, T is the temperature, this P gives you the permeability this is a permeability constant.

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Molecular Flux

amount of a component permeated per unit area per unit time for a given membrane.

$$J_i = Q_i / (A_i t)$$

J_i = Flux of component "i" (moles/h cm^2)
 Q_i = Moles of component "i" permeated in time "t"
 A = Effective membrane surface area (cm^2)

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So the molecular flux J is given by Q_i by $A_i t$, A is your area membrane surface area, t is your time obvious right, J is your flux that is component permeated per unit time. That is why it is called flux. So we have put I similarly we can have J we can have k different species. So for each of the species you can have different flux molecular flux here actually.

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Permselectivity

Describes performance of a membrane

$$\alpha = (V_i^p/V_j^p) / (V_i^f/V_j^f)$$

V = volume

"p" and "f" denote "permeate" and "feed" respectively

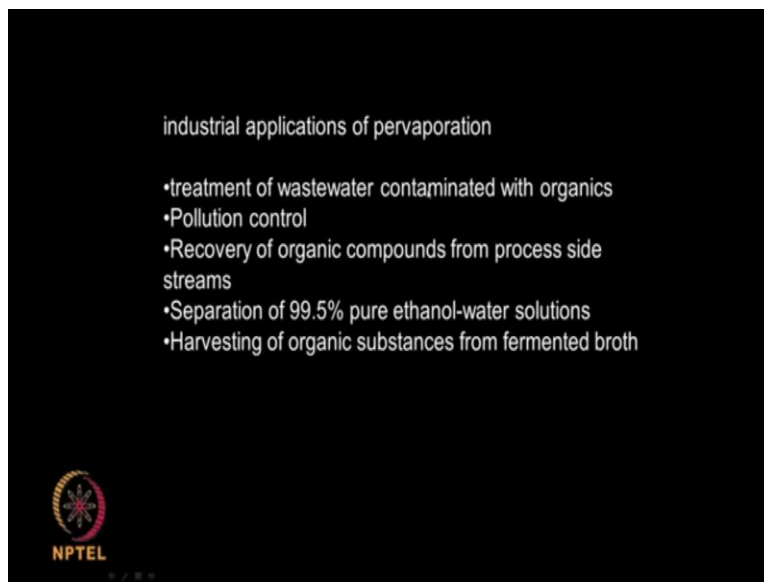
"i" and "j" represent individual components.



What is permselectivity? That means selectivity for one particular species if we have I, J, k, l, m, n and so on, the selectivity will be $= V_i^p / V_j^p$ okay for this species p and F denotes permeate and feed okay So we have I species I J species J then I species I J species C_i so this is p is permeate and F is your feed okay So this tells you what is the permselectivity that means what is the selectivity for species I with respect to species J that is what this particular equation tells you actually correct.

And p determines permeate F is your feed. So for given a feed, V_i the permeate is V_i^p for given a feed V_j permeate is V_j^p . So that ratio is what is called alpha permselectivity.

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So what are the industrial applications like we said we can do lot of things with pervaporation waste water contaminate with organics I want to remove only the organics pollution control recovery of organic compounds from the process side. We can make very very pure ethanol because ethanol in water form azeotrope after certain concentration. We may have to add a third component, if we want to completely remove one of the species.

Okay that is if I want to completely remove water whereas with pervaporation we can get even almost 100 % ethanol. So we do not need to add another component. Harvesting of organic substances from fermented broth, So pervaporation is very good.

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Types of Pervaporation

1. Batch pervaporation -

simple
high flexibility,
a buffer tank is required

2. Continuous pervaporation –

consumes very little energy,
best with low impurities in the feed,
best for large capacities.



Vapour phase permeation is preferred for feeds from distillation columns or for streams with dissolved solids

So two types of pervaporation, we can have batch we can have continuous. So batch is simple highly flexible. So you just needs the buffer tank. Continuous is consumes very little energy is very good for low impurities, large capacities it is very good vapor phase, permeation is preferred for feeds from distillation column or free from speech from feeds from dissolved solids.

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Hydrophilic membranes are used to remove water from organic solutions.

polymers with glass transition temperatures above room temperatures. Polyvinyl alcohol

Organophilic membranes are used to recover organics from solutions.

elastomer materials (polymers with glass transition temperatures below room temperature).

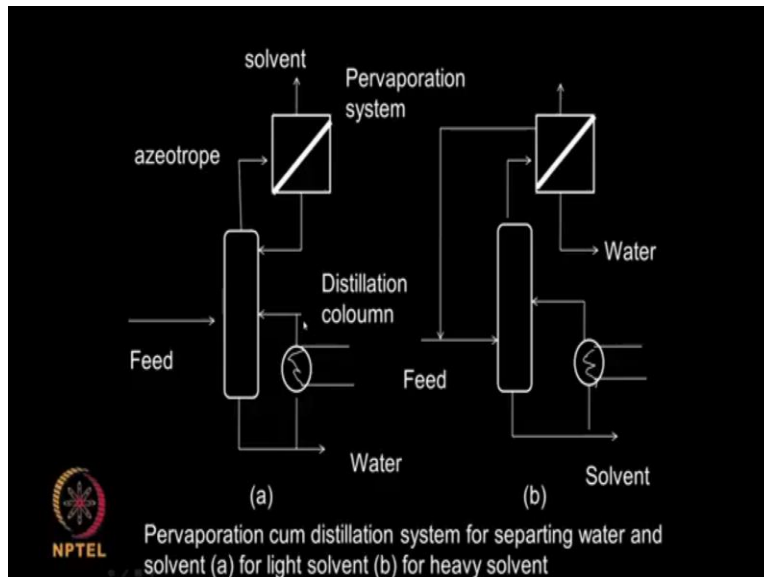
flexible nature make them ideal for allowing organic to pass through. (nitrile, butadiene rubber, and styrene butadiene rubber)



So hydrophilic membranes are used to remove water right. So because hydrophilic membranes will like water. So generally we use hydrophilic membranes polymers with glass transition temperature above the room temperature like polyvinyl alcohol. Organophilic membranes are used to recover organics obvious right if it is an organic. So you like organophilic membrane like elastomeric materials polymers with glass transition temperature below room temperature.

Nitrile rubber, butadiene rubber, styrene butadiene rubber, So if I have to remove water, I use hydrophilic membranes like polyvinyl alcohol if I want to recover organics from mixture, I use organophilic membranes like nitrile, butadiene rubber, styrene butadiene rubber and so on okay. So generally they have glass transition temperatures below room temperature whereas hydrophilic membranes will have glass transition temperature above room temperature. So that is how you select the membranes depending upon what you want to remove.

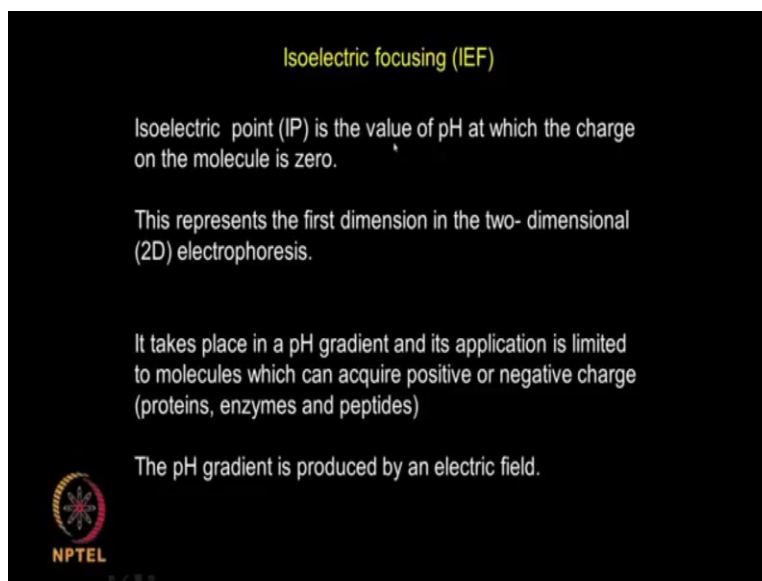
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So typically we can connect pervaporation and distillation like this so that we do not need to have azeotrope breaking at all suppose there are azeotropic mixtures which you want to break we can just add a pervaporation system to that. So if you have a lighter solvent, what we do is we do the feed and then here we collect the heavy like water now the solvent goes up. So we can use pervaporation system then collect all the solvent and then remaining is passed in.

If it is a heavier solvent okay, So here water goes down from the top and the solvent is collected here and the product goes out like this okay. So we can have different types of systems okay different types of systems for heavy as well as for lighter solvents and by combining here distillation column with the pervaporation system, we can easily break azeotropes whether the solvent is light or we can easily break azeotrope, if the solvent is heavy okay.

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Isoelectric focusing (IEF)

Isoelectric point (IP) is the value of pH at which the charge on the molecule is zero.

This represents the first dimension in the two-dimensional (2D) electrophoresis.

It takes place in a pH gradient and its application is limited to molecules which can acquire positive or negative charge (proteins, enzymes and peptides)

The pH gradient is produced by an electric field.

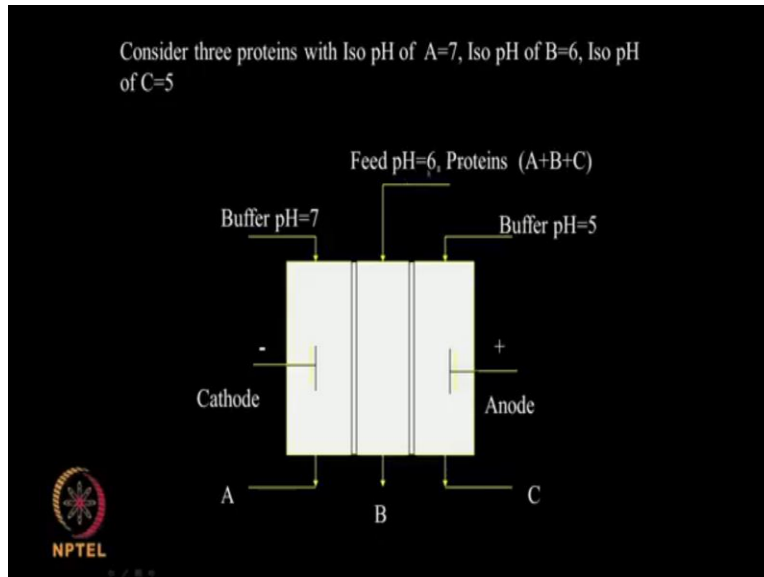


Then comes isoelectric focusing here also membranes are used for isoelectric focusing based concentration of proteins. What is isoelectric focusing? What is isoelectric point? This is the value of pH at which the charge on the molecule is zero. So if I have a protein, protein generally will have a charge because of presence of polar groups, non polar groups and so on. So that certain at the particular pH the charge will be zero that is called the isoelectric pH.

Okay generally isoelectric separation happens in a two dimensional electrophoresis the first part is isoelectric pH the second part could be molecular weight pH and so on actually. So if I proteins in a pH gradient okay, at a point where the charge becomes zero and the balance the

protein will stop moving okay and that is how you do separations in isoelectric focusing type of system.

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Suppose I have a feed passed at a pH of 6 I have three proteins a b Ci okay now protein a has isoelectric pH of 7 protein b has isoelectric pH of 6 protein Ci has isoelectric pH of 5. So what happens protein b will not have any charge because the pH and matches with the isoelectric pH of b. So this fed here you are applying a voltage okay you have an anode here a cathode here okay. When you are applying a voltage now this zone has a pH of 5 this zone has a pH of 7

And you are applying a positive charge and negative charge. So what will happen? Protein Ci will try to move to this compartment and once it moves the charge gets neutralized because isoelectric pH matches with the pH of 5. Same thing happens protein a will move here and once it moves here the isoelectric pH matches with the pH 7. So the protein a get separated in the compartment with pH 7 protein b will pass through, which is because this is pH 6 protein Ci will have compartment where pH is 5.


So this is how you separate this type of system is good in the isoelectric pH are quite distinct from each other, but still you can have little bit of mixing in the final compartments because you

have the anode and electrodes coming here. So the last compartment generally is not very very accurate or exact.

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Isoelectric pH values of some common proteins

	<u>Molecular weight</u>	<u>Isoelectric pH</u>
• Gelatin	10,000-100,000	4.8-4.85
Insulin	40,900	5.3-5.35
Cytochrome C	15,600	9.7
Myoglobin	17,200	7.0
Urease	480,000	5.0-5.1
Hemoglobin	66,700	6.79-6.83



So these are some of the disadvantages for example if you take gelatin of molecular weight this is the isoelectric pH 4.8 to 4.85, insulin 5.3 to 5.35 cytochrome C 9.7 myoglobin 7 urease 5.0 to 5.1 hemoglobin 6.79. So you see they are quite distinct in their isoelectric pH so separations are possible here.

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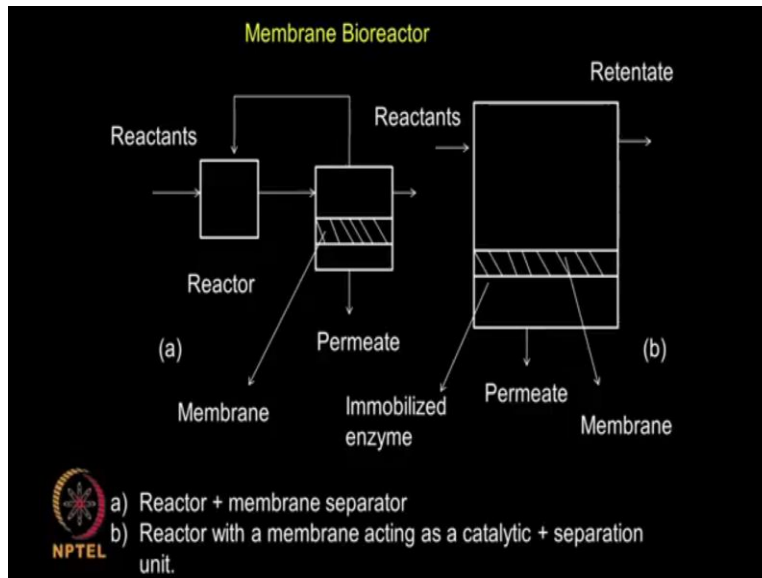
Problems in IEF

- (1) the continual remixing of purified materials with semi-purified or crude starting materials,
- (2) the joule heat that is generated during the process needs to be dissipated.



So what are the problems continual remixing of purified materials with semi-purified that can happen heat is generated during this process because when there is a mixing and then the pH changes lot of heat is generated so that mean o the setup needs to be cool. So these are the big problem. So purification simultaneously you are getting crude which is semi-purified that is the problem. Other one is the joule heat because of the heat because of the mixing heat is generated that is called joule heat which needs to be desiccated. So you need to have a cooling system to get rid of the heat that is generated okay.

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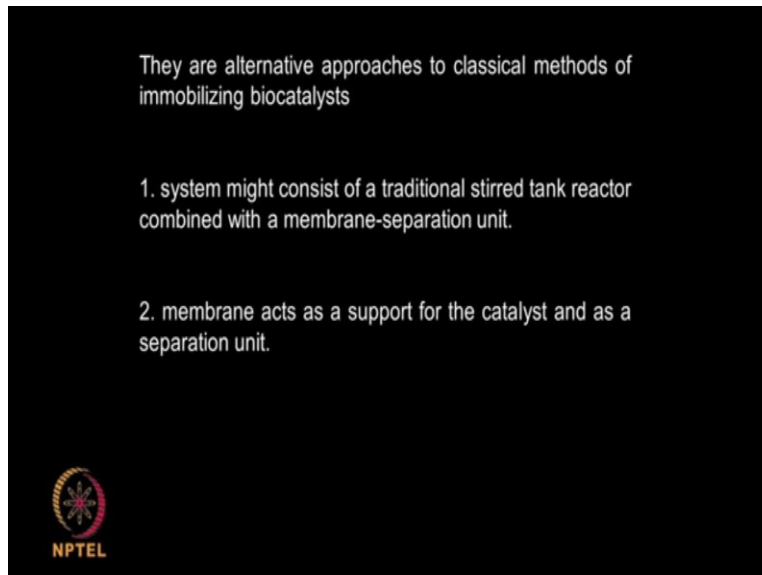
Then comes membrane bioreactor nowadays bioreactors are coupled with membranes so that we can achieve a combination of filtration and reaction together. So membrane bioreactors are becoming very fashionable. So we have two types where reactor and the membrane system are separate. So after the reaction the product comes out and there is separation taking place permeate comes down like your metabolite for example.

Membrane retains the biomass and other large molecules which are again put back into the reactor. So continuously for example I want to remove butanol as you know butanol butyric acid they can butanol can the organism can get it is deactivated because of presence of butyric acid. So if I have continuously removed the butyric acid here, the organism will be still alive so it can go back same thing with ethanol production many of the yeast are stable only up to 15 % ethanol.

If I continuously remove ethanol here and then put back my organism they will be active for a very long time so that is one type. Other system is internally you have the membrane, so continuously the product is formed the permeate gets removed and so the retentate will contain your biomass salts and other large molecules all the time getting fermented here. Okay so the retentate can be collected from the top so that is a membrane bioreactor where the membrane is located inside the reactor, these another membrane bioreactor where the system acts as a

filtration located outside the reactor and the products are recycled back that is the retentate or recycled back.

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So two different approaches which membranes can be used in combination with a bioreactor. So systems may consist of a traditional stirred tank reactor with the membrane un separation unit membrane acts as a support for the catalyst. Sometimes catalyst can be impregnated or supported on the membrane okay.


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The biocatalyst can be

- Flushed along a membrane module,
- segregated within a membrane module,
- immobilized in or on the membrane by entrapment, gelification, physical adsorption, ionic binding, covalent binding or cross-linking.

The advantages of immobilizing enzymes are

- increased reactor stability and productivity,
- improved product purity and quality,
- reduction in waste



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For example catalyst can be flushed along the membrane segregated within the membrane inside the membrane catalyst can be segregated. It can be immobilized in or on the membrane by entrapment gelification, physical adsorption; ionic binding covalent so the catalyst remains on the membrane products or the metabolites can be filtered out and collected on the other side that is the filtrate so the retentate can be on the upstream all the time.

So this is very advantageous system increases reactor stability, productivity, improved product purity, quality, production of waste, you do not even need a separate filtration unit. So your enzyme catalyst is kept very effective or very active for a very very long time.

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membrane bioreactors have been reported for

- synthesis of lovastatin with immobilized *Candida rugosa* lipase on a nylon support,
- production of diltiazem chiral intermediate with a multiphase/extractive enzyme membrane reactor,
- synthesis of isomalto oligosaccharides and oligodextrans in a recycle membrane bioreactor
- production of a derivative of kyotorphin (analgesic) in solvent media using α -chymotrypsin as catalyst and α -alumina mesoporous tubular support
- Biodegradation of high-strength phenol solutions by *Pseudomonas putida* using microporous hollow fibers .



So they have been used in large number of system synthesis of lovastatin with the candida rugosa production of diltiazem chiral intermediate using multiphase extractive enzyme synthesis of isomalto oligosaccharides using a recycle membrane bioreactor derivative of kyotorphin, analgesic okay using a alpha-alumina mesoporous tubular support and alpha-chymotrypsin. Biodegradation of high-strength phenol solutions using a pseudomonas putida trapped in microporous systems.

So large number of systems large number of examples are already coming into market where membrane is combined with the reaction to achieve separation or immobilization and so on actually.

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Membrane separation process - Summary

Processes for separating mixtures by using thin barriers (membranes) between two miscible fluids.

driving force across the membrane

- concentration
- pressure



So we have spent couple of mixtures on membrane systems so the process of separating mixtures by using thin barriers okay polymeric synthetic or non synthetic material between two immiscible fluids. So driving force also have set concentration pressure you can have voltage and so on actually.

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Important membrane separation processes

- (i) Microfiltration Ultrafiltration (nano filtration)
- (ii) Reverse osmosis
- (iii) Dialysis and Electrodialysis
- (iv) Pervaporation
- (v) isoelectric
- (vi) Membrane bioreactors



So large number of systems microfiltration ultrafiltration nanofiltration reverse osmosis we looked at dialysis which is very important in medical field electrodialysis pervaporation isoelectric focusing membrane bioreactor. So large number of applications for a membrane and it is growing day by day and a large number of polymeric systems hydrophilic polymers

hydrophobic polymers are being now coming into market. But the main problems are which I talked about in the last class things like formation of biofilms compaction of the membrane formation of scales closing of the pores and so on.

So these needs to be addressed in order to further increase the use of membrane in downstream applications as well as in the bioreactor applications. Thank You Very Much