Biological Inorganic Chemistry
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Lecture 21
Transport Across Membranes

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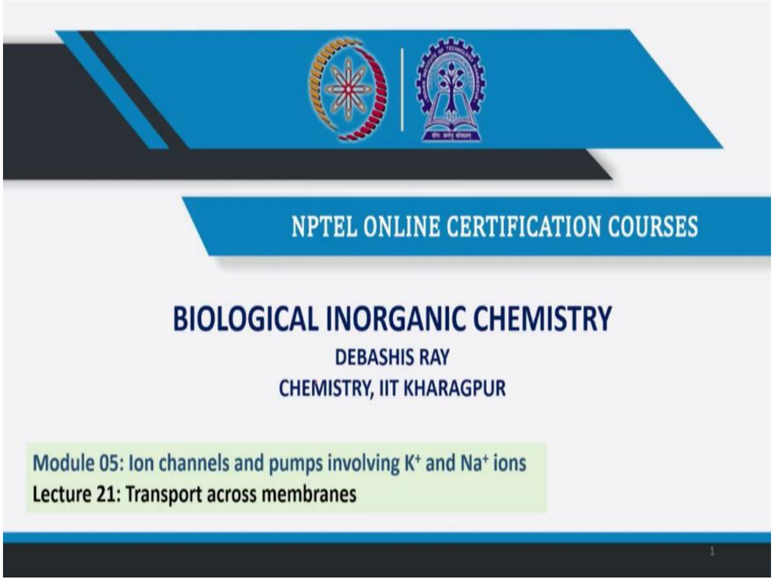

Hello, good morning everybody. So, where we finished last time, we will definitely will continue. So, we reached Model 05. So, the 5th week we are starting. And in this Module 05, that means also the week five we will be talking about the very basic thing the ion channels and pumps, involving only two metal ions, the potassium and the sodium ions.

And this lecture number 21 will be devoted to the transport across the different membranes, particularly, the biological membranes, but we should have some very basic idea, what are the artificial membranes and how we use those artificial membranes such as that we know we use some membrane for dialysis.

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So, the concepts what we basically try to cover are these two ions and their roles, and how they are transported. So, it is not that typically only the diffusion, which can trigger or which can carry these ions from one side to the other. Then the basic definition, starting from basic definition basically, ion channels then membrane potentials, how the membrane potentials can be developed, because these potentials have very important role to play for the movement of these two types of ions.

And finally, a little bit about the transporter proteins. So, not only this class, but also the following class also we will have the total picture, we will give you the total picture about these ion channels and the ion pumps.

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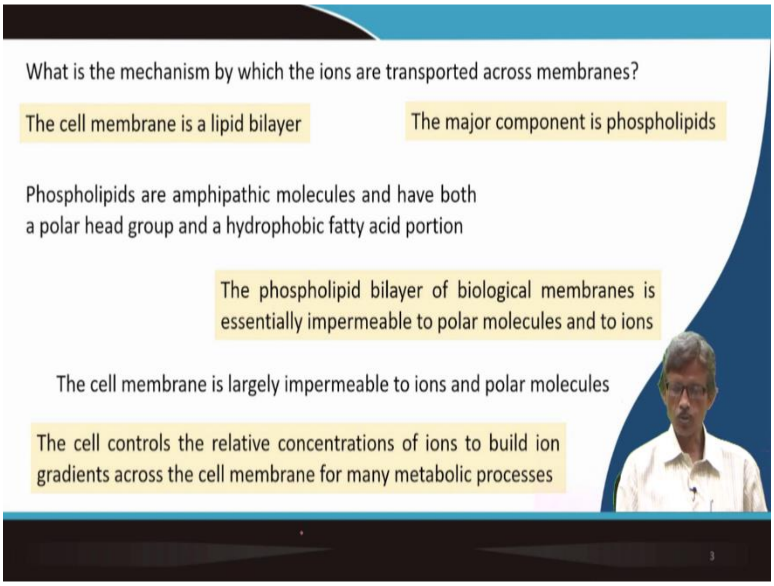

So, if we just think now, about the mechanismby which the ions are transported across the membranes. It can be typically artificial membranes or the laboratory PPR membranes or it can be the very basic one that means the biological membranes. Because the physical chemistry or rather the corresponding electrochemistry and all other things are always important, and we all know that we had the separated chamber, separated compartments for your electrochemical studies also.

So, similar type of thing, if we can have two compartments, and if we consider that one is inside the cell, and another is outside the cell, we can think of that particular role of that particular membrane, such that, it can enclose everything within the cell and you can have some other material and ions outside that particular cell.

So, here, we will be talking about the cell membrane. And we all know is the lipid bilayer. So made of lipid and is the bilayer, so face to face bilayer thing is there. And in all cases, it is the phosphor lipid. So, not only lipids, but one phosphoryl group is attached because in biological world we have seen, and we also try to know also that the phosphorylation reactions are very ubiquitous and everywhere, they take some important role to play where the phosphorylation can take place, even if you have some OH function available like that of your ATP and ADP is all these phosphate groups are there.

So, the phospholipids that is why come into the picture and all these phospholipids are basically of one particular type. They are amphipathic molecule and have both, sorry, amphiphilic molecules then both have both polar head groups and hydrophobic fatty acid portion. So, if you have a polar head group and hydrophobic fatty acid part, so long chain fatty acids we all know, and that particular fatty acid if you consider that apart from your functional group as a carboxylic function, it basically the other part is definitely hydrophobic in nature.

So, when they are present in biological membranes, what they impart? They impart something that in terms of the ions, because everywhere we talk most of the time that metal, metal, metal is not that metal is all are ions, ions, ions. So, everywhere we have the metal ions, and particularly these two metal ions what we are considering today, we do not know much about these two ions in terms of its coordinates in chemistry and the solution chemistry.

So, in this particular case, that the biological membrane, which is definitely impermeable to polar molecules or to ions. So, that is the very basic statement what we can make here that we are talking about something where the membrane will not allow to pass the individual molecules, which can be polar or nonpolar, but particularly the metal ion, because we are focusing our attention on those metal ions only.

So, if you have sodium ion and the potassium ion, and definitely, all we know that bare metal ions will not remain even in your test tube as well as in the cells, they all are hydrated. So, water molecules will come and bind to those metal ions, but since the water molecules are neutral in nature, it cannot neutralize the corresponding positive charge attached to that particular metal ions. So, overall, the same mono-positive charge, which was originally present in case of sodium ion, as well as in the potassium ions will still remain when they are also hydrated.

So, these impermeable membranes, therefore, can take some care about these ions and the polar molecules. So, these polar molecules and ions whether we are able to pass, therefore, the entire cell basically what do you consider the cell controls the relative concentration of ions. Because inside the cell and outside the cell, we know basically from our school days also and the early college days also that we need the corresponding sodium chloride, we take as your salt, the table salt what we take with our food, we take extra sodium chloride when we take some solution when we take some sharbat and all these, but we never take potassium chloride. Why is it so?

So, the mechanism, which is inbuilt mechanism what we can have, that inbuilt mechanism is such that you can have a different concentration of sodium ion which is higher outside the cell and a different concentration of potassium ion, which is higher within the cell. So, we must have then ion gradient across the cell membrane, and that is why it can control many metabolic processes also.

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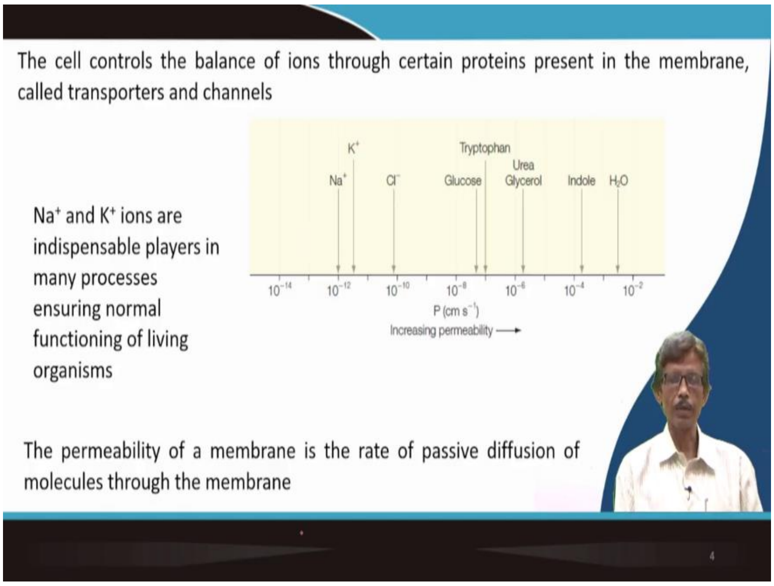

Since, this is there, and whether we can control or take up that particular concentration gradient. So, when they control these, so they balance the ions through certain protein present in the membrane. So, membranes are there, the phospholipids are there, but further to that, there are certain points where you can have other proteins.

So, these proteins are basically will be called the channels, if they are selectively passing some ions from one side to the other or the other side to the inside. Then they also can function as transporters, that means, they can transport the ions. So, these two ions are basically indispensable players in many processes, which they ensures basically the normal functioning of our human process, the bacterial processes, the fungal processes and even in the plants.

So, in all living organisms, what we can have, if we can see. Basically, if we consider in terms of the permeability, because there is another important parameter, the physical parameter what we should consider when we talk in terms of the membrane. So, how much the membrane is permeable to these ions. So, their basic characteristics is such that, if we go from left to right, you find that you can have the increasing permeability and for the sodium, as well as the potassium, which is 10 to the power minus 12. Whereas, you have for water it is 10 to the power minus 2 only.

So, these sodium and potassium are 10 times, the 10 to the power 10 times permeable compared to your water molecules. So, not only the ions because here in this particular class we will be talking in terms of only the metal ions, every time I write as the MIs. So, the transportation of these metal ions, and which is also very much available for the alkali and alkaline earth metals. So, these two classes are devoted for sodium and potassium ions, afterwards we will see also about the calcium and the magnesium ions.

So, along with these ions basically, if we bring the other molecules, other important molecules such as your tryptophan, glucose we always need along with our oxygen for the synthesis of many ATP molecules. So, their permeability is definitely important, and it basically controls the rate of passive diffusion of molecules through the membrane. So, we are not doing anything only the passive diffusion. Then we should know about their order, how good they are in terms of that permeability.

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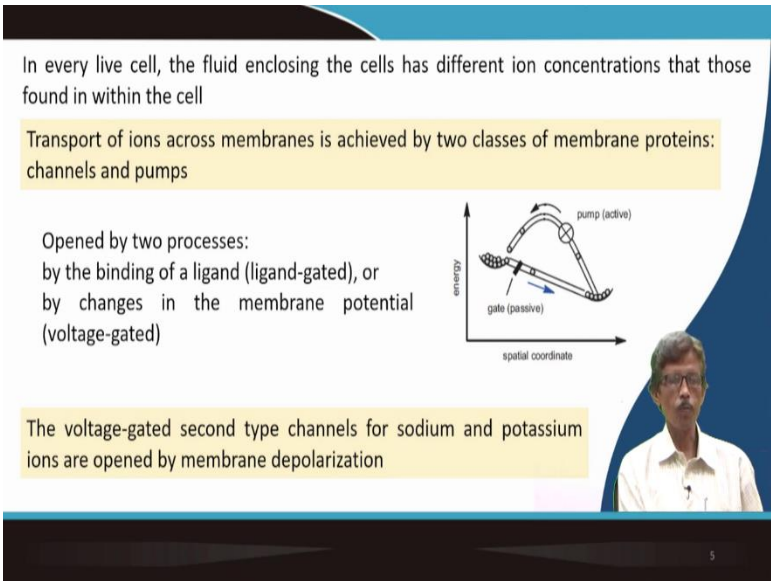

In every live cell what do you find that the different concentrations can be achieved within the cell. Just now, I told you that, you can have a different concentration of sodium and potassium ions inside the cell and outside of the cell environment. Therefore, we need a transport mechanism, so, such that, we can have the ability to transport the ions across the membrane, and that is basically achieved by two classes of these proteins. One are known as ion channels and others we will be knowing as the ion pumps.

So, ion channels and ion pumps are, therefore, very important class of these molecules, which can basically control the movement of these ions. So, basically, it is opened up by two processes, by binding a ligand. So, if we can have some gate or the channel, we try to open it up or then at one point you can close it. So, if we consider only the opening up such that something is there, and we can open it up such that you can allow the flow of those ions.

So we can have the two processes. One, we can consider as by binding of a ligand, we all know the ligand, the typical definition to a coordination chemist always have that we know the particular thing, which can bind the metal ion.

The same knowledge basically, what we all know that a particular ligand, like your water, water molecule is also a ligand we consider is a monodentate ligand. Whether a different type of ligand, special category of these organic molecule can function something where you can open up this particular channel or sometime by changing the membrane potential, which is known as the voltage gated. So, we can have two different processes. One, is the ligand gated and another is the voltage gated.

So, if you have the voltage difference for this particular movement, so, you can go for the electrical pulse to give it and that pulse basically allow to open up that particular channel to see that particular opening.

So, if we consider that something is happening like your reaction coordinate, you can have the spatial coordinate and you put some, give some energy. So, from uphill to the downhill transfer the gate is there, the black point is here, you see this gate. So, in this figure, you have the black point, so that black point is your gate, and that gate only allows the passive moment. What just I told you that you can allow the passive moment.

So, something the spheres are moving from this side, from uphill to the downhill, so many speres are moving at the downhill. So, once you move this particular one, then if you want to get it back to that particular cell encloser, you have to do something. That is why we know, that the water is flowing from the uphill to the downhill, so is automatically through gravity, it can pass from the up to the downstairs.

And if we want to push or if we want to move that amount of water from a bottom side to the upside, you need some pump. So, that is why the mechanism is also a pump, and which is active one. So, you will have some crossed within a circle is your pump. So that you require then a pump.

So, the pumping mechanism like your electrical water delivery pump and all like these here also the biological ion pump is required, and that will basically carry those items or those ions from a down place to an upper place position. So, the second category, the voltage-gated one, for sodium and potassium are opened by membrane depolarization, that means, it is charged and then the depolarization. So, depolarization is basically helping for that particular type of moment.

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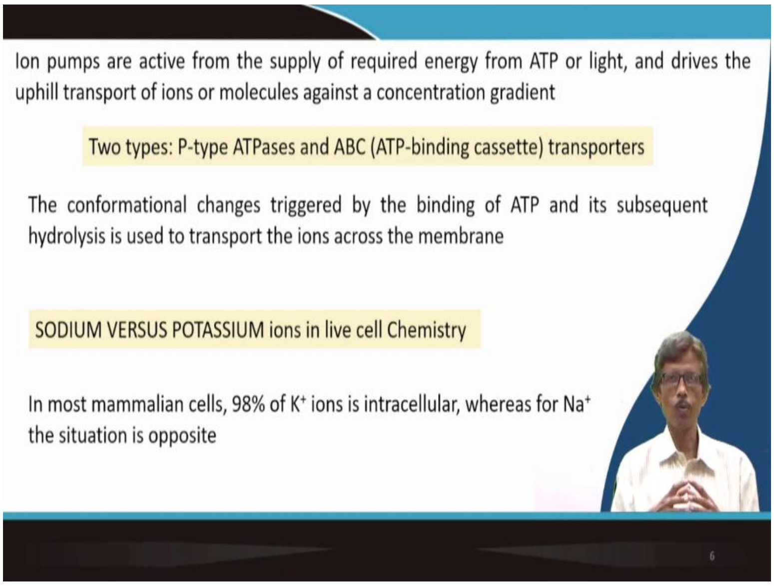

So, all these ion pumps are therefore active from the supply of required energy from ATP. So, we need energy. So, we have burned the glucose material through the presence of oxygen dioxygen molecule. You have produced huge amount of ATP, which we all know or energy currency for our all the activities. When I am talking in this particular class, I also need the regular supply of these ATP molecules, because I am consuming energy.

How you consume the energy? We consume the energy by burning the food material, but that food material is giving you the corresponding energy currency of ATP molecules. So, if these ion pumps can be dependent on ATP, so the transfer of these ATP and the ATPases will be there we will find afterwards, that ATPases,that means, the hydrolysis, the phosphate ester hydrolysis, so ATP after phosphate ester hydrolysis giving you ATP molecules.

And during that process definitely the protons will also come, and this proton pump will call even the movement of the proton, not only the sodium and the potassium ion, the movement of the proton pumps are also dependent of similar type of thing or similar type of mechanism. And other type also you can have the light.

So, light can also go for the corresponding function of these ion pumps, such that you can have the uphill transport. Just now, I have showed you there is uphill transport of ions and molecules against the concentration gradient.

So, one particular concentration gradient is basically following a spontaneous process for movement of the ions from highly concentrated part to the lower concentrated region. But when you require the pump, you can move into the reverse direction. So, that is why the ATP hydrolysis is there. So, they are of two types only.

We will again come back at some point, but right now, you know definition wise that you go for the hydrolysis of ATP molecules and those are ATPases. And then another con is also ABC, which is ATP-binding cassette.And they are basically nothing but the transporters only.

So, when you go for this, we find that the binding of ATP is important. So, you have to bind it otherwise, you know that is a, if we go for some catalytic thing that means the organic molecule is bound at some point, and you cut the corresponding cleavage or the CC bond, CN bond or CO bond, the bond hydrolysis can take place here also we are going for the bond hydrolysis type of thing. But, the best way of doing so, is that, you have to trap or you have to bind the ATP molecule.

Following you have the hydrolysis, and that particular entire process is being utilized, will be utilized definitely for the transport of ions across the membrane, but it is not over there. I am just staying from that and trying to explain in that way that, ATP and its hydrolysis in presence of ATPases will be there, but you have to supply for the required number of sodium and the potassium ion. So, they are sodium potassium ion dependent ATPases.

So, if we now consider the character or the nature of these two groups of ions or the one type of ions, but they are of different character because the sodium is smaller one, potassium is bigger one in live cell chemistry. Because in the human body and the most mammalians basically 98% of potassium ions are intracellular that is why I am telling you that a huge concentration only within the cell. And whatever sodium ions you require, we get everything from your food material. But you have the surrounding sodium ion, which is highly concentrated outside the cell.

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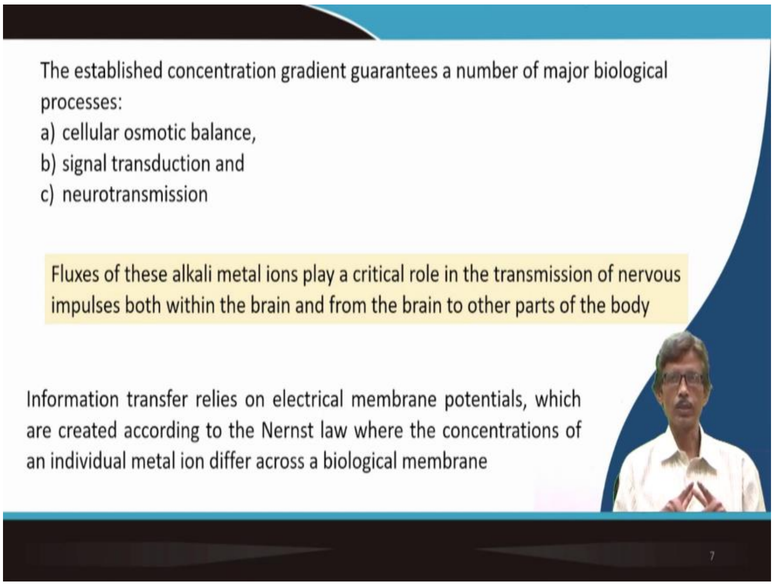

So, these concentration differences and other things can be established, basically. And when we established that concentration gradient, and if you establish that particular gradient, you are fortunate enough to see some of the very important biological functions. One is that a cellular osmotic balance. So, you must have some good osmotic balance, because that osmotic pressure is also there within the cell. If the pressure is huge the cell can bust, but that is not happening.

Then signal transduction. So, during that particular transfer, it can give you some signal and that signal can be transferred to some other functions or some other activities. And then neurotransmitters, that means, for our neurological processes and everywhere the nerve impulses, the neurotransmission is required for your supply and movement of your neuro chemicals.

So, we will have the fluxes that is why it can be electrical fluxes or other type of fluxes of these alkali metal ions, and they are important for the transmission of nervous or the nerve impulses. That is why you have the neurotransmission, both within the brain, and from the brain to the other parts of the body. So, even the impulses because our brain is controlling everything.

When I am taking this class, our brain is controlling that you should say this, you should not say this, all these things. So, you have the electrical impulses from that particular moment. Therefore, one particular thing is that, that your cells are different from your whole body cells, as well as your brain cells. So, you just ask yourself. We will come to that particular question once again, if time permits at the end of this when we talk about the neurological things and the dependence of those neurological processes on the metal ions, that whether you should have the sodium and the potassium ions in the brains also.

So, this information transfer basically can be guided by the corresponding E0 value type of thing, the electrical membrane potential. Because the membrane and the different concentration gradient is responsible for your potential development, and again, we can apply the Nernst law we know the Nernst equation, and now you have the two different concentrations.

We know that the concentrations, electrochemical cells are there, but in this particular case, the biological membrane is giving us that particular opportunity to study where you can have you can follow the Nernst questions, and that particular thing can be developed only due to the variation in the concentrations.

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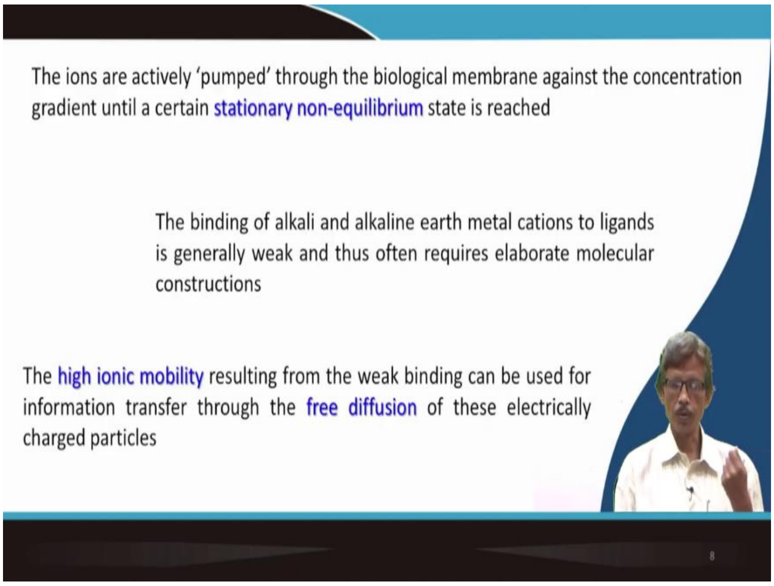

So, one highly concentrated one, another is low concentrated one, so you have the membrane, and you can get the corresponding membrane potential. So, the ions, which are there at the topor at the bottom can be pumped through the biological membrane against the concentration gradient just now, we are seen, until a certain stationary non-equilibrium state is reached. So, how long the pump will work to delivered the ions what is there at the bottom side, at the lower side to the upside or the upper side.

So, we will have a stationary non-equilibrium situation, but that suit also has some limit. You cannot cross that particular limit, such that, you can enrich that particular level. So, you will have a particular level, the maximum concentration of say 150 millimolar concentration or at the lower you can have the 5 millimolar concentration with respect to these two ions that means the sodium ions as well as the potassium ions.

So, now we will consider about the binding. So, these two alkali metal ions, even the alkaline earth metal cations like your magnesium ion or the calcium ion, because these four metal ions are very important for our health also, our body also, our diseases also to the different ligands, and they are definitely weak compared to your binding of copper, compared to your binding of iron and compared to your binding with nickel.

And that is why you require a very elaborate molecular structure or the molecular construction what you can say, and the high ionic mobility of these ions resulting from these weak binding can be used for the information transfer through the free diffusion of these electrically charged particles. So, at one point they are weakly bound the sodium ion is weakly bound to some ligand part or some protein part or some enzyme part, but at the other point, with small expense of energy these ions can be released.

So, when you have these free ions, if the ligands are not grabbing this. Again, another group of ligands are not coming and grabbing those ions, you can allow the corresponding movement of those liberated ions from that particular organic molecule. They are free ions now, so you can have the corresponding free ions of these charged, so positively charged. Those are again also like electron, they are also electrically charged particles. So, movement of those electrically charged particles are important.

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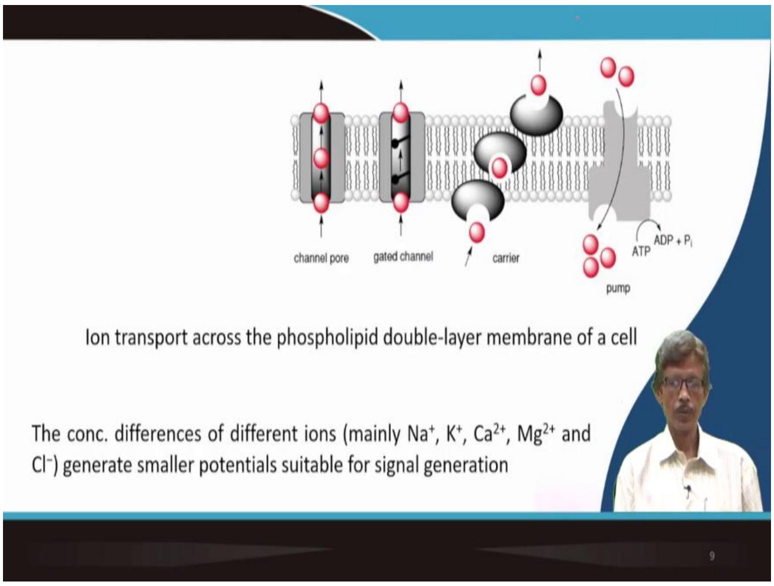

So, you can have pictorially, what we can see, the ion transport across the phospholipid double-layer membrane of a cell. So, this is the schematic or the cartoon diagram, what you can see, you can have a channel pore, and channel pore you can have the direct movement of the ions. So, these red spheres are your ions and arrows are showing that you have no other thing, no disturbance. It can move straight way from the bottom to the top or from left to the right or right to the left.

But is the gated channels you have some gate, which has to be opened up. So, this black, the rod and sphere at the head, so, it will be opened up. So, it will be opened up in this side or it can be opened up this side. So, there should be some mechanism for that like your valve in your tube well, what do we know, that that the tube well you have the valve, so which can allow the passage of water only in one direction.

So, this is particularly a particular type of direction, then you can have some carrier molecules. And everything you see the membrane, the lipid bilayer, the everything, the background you see they are the lipid bilayer. So, this bilayer thing is there, and within that bilayer thing you can have that. So, something the ligand part will come, so is the carrier. So, the carrier is your metal ion, so that is there, and if it is moving in the other direction.

So, it is like this, and if it is opened up in the other direction, and it can move the iron to the other direction, and lastly you can have the pump. So, these basically shows us that, if there is a concentration difference for these ions, we are considering all four together, as well as the chloride, which is also a very important and the fundamental, anionic thing in our body. So, if time permits, again, at some point we will, little bit we can talk about the corresponding ions which are not of metal ion origin.

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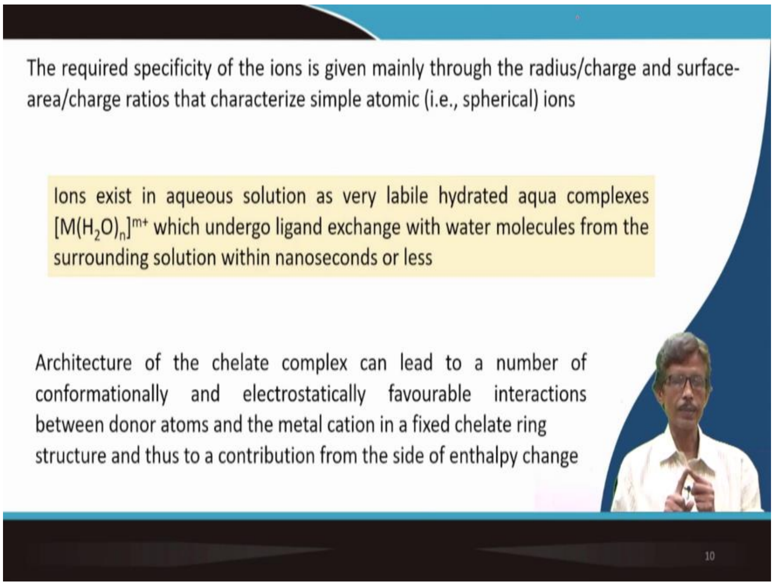

So, for giving you the potential difference and the signal generation all these are there with us. So, then if you consider there is a specificity of these ion, is mainly, through due to the radius and the charge. So, radius and charge are charge by radius ratio is important always we know how good it is, as a metal ion to bind the ligand by the sodium ion or by the potassium ion.

Then the surface area and the charge also. How much a surface is? Not only the radius or the surface area also sometime is important, and for a spherical ion, we can consider these as because we will be considering that the hydrated M.

So, MH2O whole n m plus, n is the number of water molecules which are attached which is unknown to us. So, number of water molecules attached to the metal ions centers and m plus is your overall charge. For sodium and potassium it is 1 m is equal to 1, but for magnesium and calcium m is equal to 2.

So, the ligand exchange reaction will also be very fast because water will also be competing. Because in all these cases, we will see that oxygen atoms of these ligands are there and oxygen atoms are binding, and exchange reaction is very fast within few nanoseconds only or sometime it is less.

So, this architecture of this chelate basically, complex can lead to a number of conformationally and electrostatically favorable interactions. So, if you have the movement or the confirmation, such that your oxygen centers that are available and your metal ion is here, so, it can come and bind to that particular center.

Sometimes, also, you have the charge thing, that means, if you can have some negatively charged species there as the ligand head or the ligand and surface. So, due to the charge compensation, it can drag the positively charged metal ions also. So, the metal cation can have the fixed chelate ring structure and thus a contribution to from the side of enthalpy chain.

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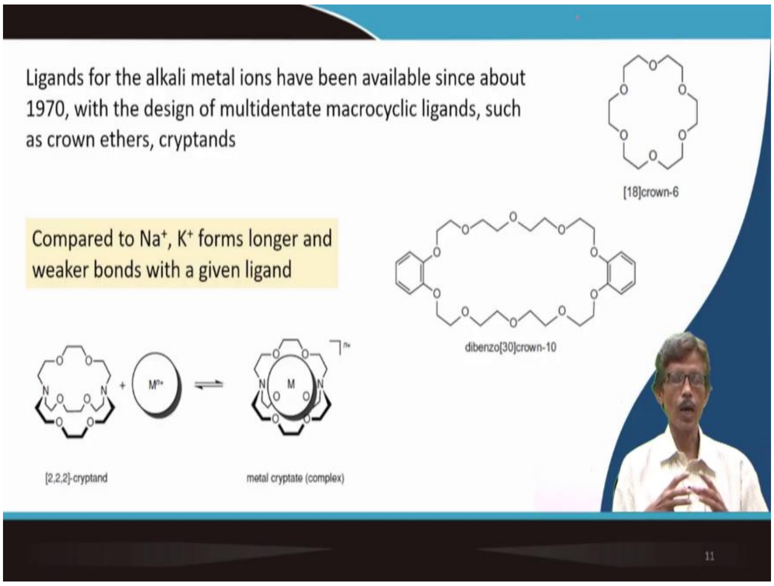

So, the enthalpy change that means, when it is binding to a particular ligand anion or the ligand and you can have the removal of many number of these water molecules. So, the number of species are changing, so you have the contribution from the entropic point of view. So, some of these, one such macrocyclic ligand we will take the example is your crown-6, 18 crowns-6 because the 6 oxygen donors are there, so is the crown ether type of molecule then another one is dibenzo 30, crowns-10.

So, 10 oxygen centers are available, and your whole macrocyclic size is 30 members, so 30 atoms are there to give you the macrocyclic structure. So, if you consider that this particular ligand is available for coordination to your sodium, as well as the potassium ion, what should be the structure? For the first case, since we have chosen a 6, number is 6 is good, that it can give you octahedral complex. So, you get some crown ethers for the good ligands as well as the cryptands.

So, the crown ethers will drag the metal ion within the cavity, but the cryptand is the bicyclic one, two rings are there. So, it is not a single ring, but you can have two rings, so it is 2, 2, 2, cryptand. So, is a one arm 2 another arm 2, another arm is also, but you can have the variation. So, basically, when the metal ion cryptid, not metal, the metal ion cryptid is formed, the metal ion complex is formed, you get the right structure of this octahedral one.

So, compared to NA plus K plus forms a longer and weaker bonds with the given ligand because the size of the K plus is different. So, the cavity size of all these ligands are important and that basically gives us a very good importance for the knowledge, where we can understand the different natural afford also.

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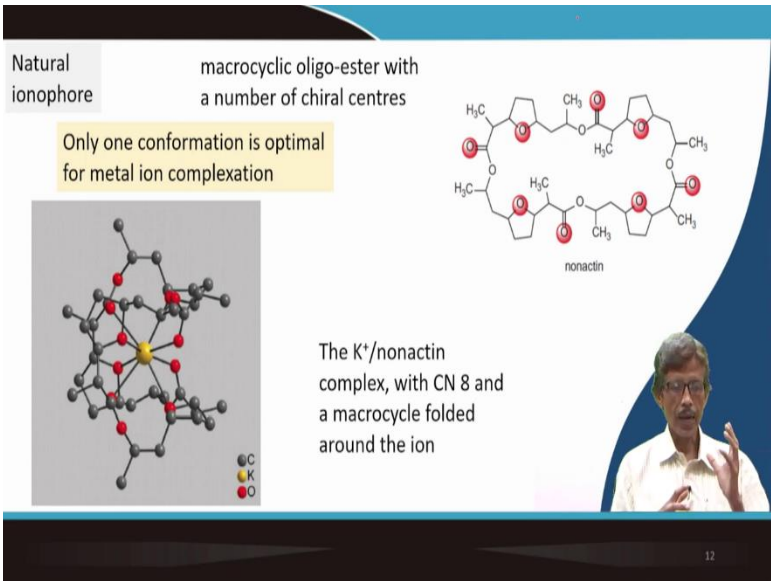

So, one is nonactin. So, just think of the crown ethers, what I showed you just now. Compared to that is a naturally occurring thing that is why it is natural ionophore, and that naturally occurring ionophore is available, how it can bind.

So, if the structure is given, you should think nicely, that how you bring the different number of donor centers, because you see here 3 plus 2, 5, 5 plus 3 on the right, so is altogether 8 oxygen centers, and which are marked as red. So, you can have 8 donor centers available for coordination of any metal ions say sodium, as well as potassium ion.

So, how it will basically bind that particular metal ions. So, is the oligo-ester thing. You see the function is COO, OCO so it is not amide function, but is the ester function is there, and you can have many chiral centers available. And this particular thing is available for binding only in one conformation.

So, you see the structure, so the structure tells us that, when the potassium ion is allowed to react with nonactin complex with a coordination number of 8 and a macrocycle is folded around this ion. So, this folding is important. So, you should be able to find out what sort of folding is taking place from that particular molecule. And from this particular metal and structure also you should be able to know, what sort of natural ionophore we are talking about, and how it is binding to that particular metal ion.

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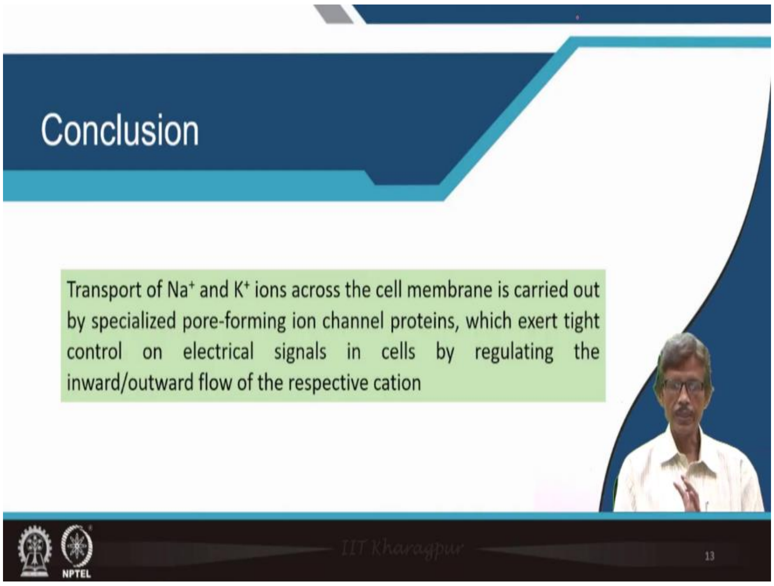

So, to conclude, at this point, what we can see that, for all these ionophobic things, is required for grabbing or trapping the metal ion, and then you can pass the metal ion from one side to the other. That is why we are talking about the transport of sodium ion, as well as the potassium ion across the cell membrane and the pore forming ion channel proteins are there. That is why you have certain ports, and within those ports, the metal ions are moving, and that can have a tight control on electrical signals in cells by regulating the inward and outward flow of respective cation.

So, the movement of those cations are therefore, is responsible for getting those electrical signals, and those electrical signals are responsible for giving you a control, such that, you can have very weakly bound sodium or you can have a weakly bound potassium ion to those ionophores, which are maybe there as integral part of your all these channels over the protein.

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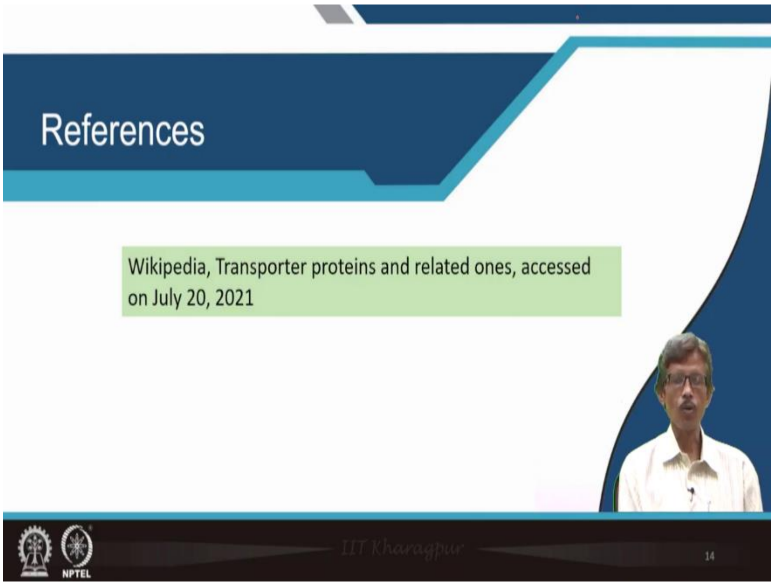

So, these are all oxygen-based ligands in your hand. So, you can think or you can start from the transporter proteins, and related ones basically from the Wikipedia page and the book of R Crichton. Thank you very much for your kind attention.