Neuroscience of Human Movement
Department of Multidisciplinary
Indian Institute of Technology, Madras

Lecture - 02
Membrane Physiology – Part 1

Good morning. Welcome to this class on Neuroscience of Human Movement. This is Part 1 of our discussion on Membrane Physiology. We start our discussion about the physiology of the biological membrane. So, this forms the foundation of this course neuroscience of human movement ok.

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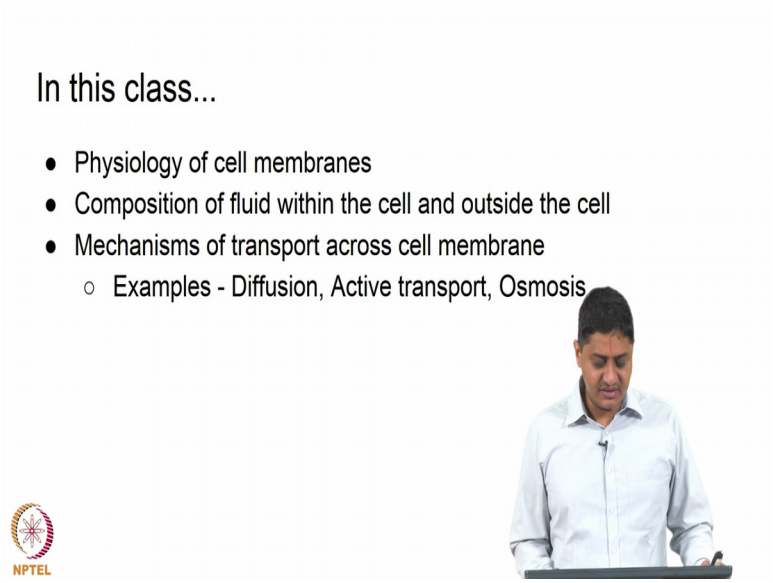

So, in today's class, we will be talking about physiology of cell membrane. And what is the composition of fluid within the cell membrane and outside the cell membrane? So, this is expected not to be the same. So, that means, that there is different gradients. So, there may be concentration gradient there may be other gradients. I will discuss this, and also transport across cell membranes. And there is going to be diffusion, active transport and osmosis some of the examples of transport. Also there are other forms of transport such a such as facilitated diffusion, such as co transport counter transport etcetera.

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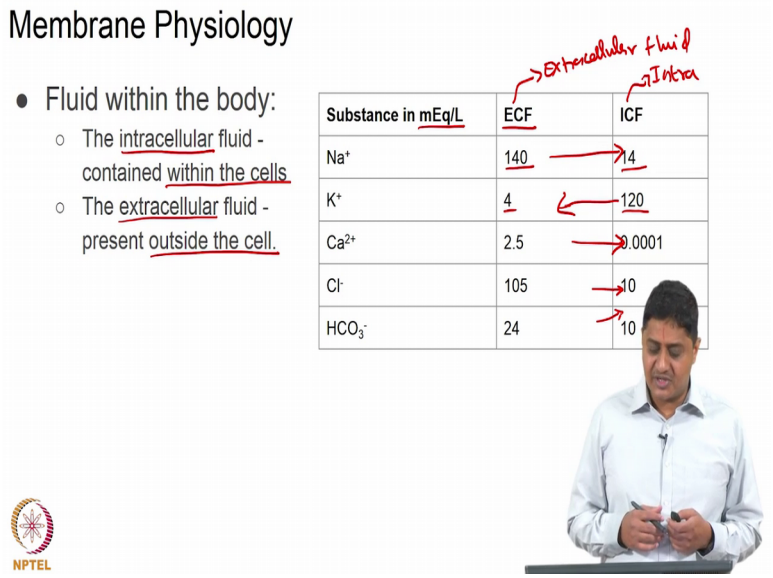

So, excitable cells are subclass of cells and they maintain a steady potential difference across their cell membrane. Typical concentrations are for different substances in excitable cells. For example, are given in this table. So, there is extracellular fluid ECF means extracellular fluid. And ICF means intracellular fluid right. So, there is fluid everywhere in the body. The body is composed of about 50 to 70 percent water. It changes between individuals between groups of individuals. So, people who have a higher fat content; for example, have lower amount of water and vice versa.

How? Where is this fluid present? Of this, about 2 thirds of the fluid is present in the intracellular matrix or within the cell and about one third of the fluid is present in the extracellular matrix right. So, the fluid that is contained within the cell is called intracellular fluid, and the fluid that is present outside the cell is called extracellular fluid. And typical concentrations in milli equivalent per liter of different substances are given here for some substances it is been given here. So, for sodium 140 million per liter is present outside the cell and 14 is present inside the cell. So, that means, there is a gradient, and what is the direction of this gradient?

So, suppose there was an opening that allows transport of sodium across the membrane, it is going to be transported in that direction. Please note where the arrow mark is. So, potassium is present in very small quantities outside the cell and relatively large quantity inside the cell. So, once again there is a gradient, and suppose there is a channel that

allows transport of potassium, it is going to be transported in that direction, unless there is going to be expense of energy. So, note the arrow mark in this case.

Likewise, for calcium the gradient is in that direction, for chloride the gradient is in that direction, gradient is in that direction, and for this the gradient is that direction not. So, different substances may be transported in different directions depending on the concentration gradient of for those substances.

How is this transport happening will form the discussion for the first few [vocalized-Noise] lectures right.

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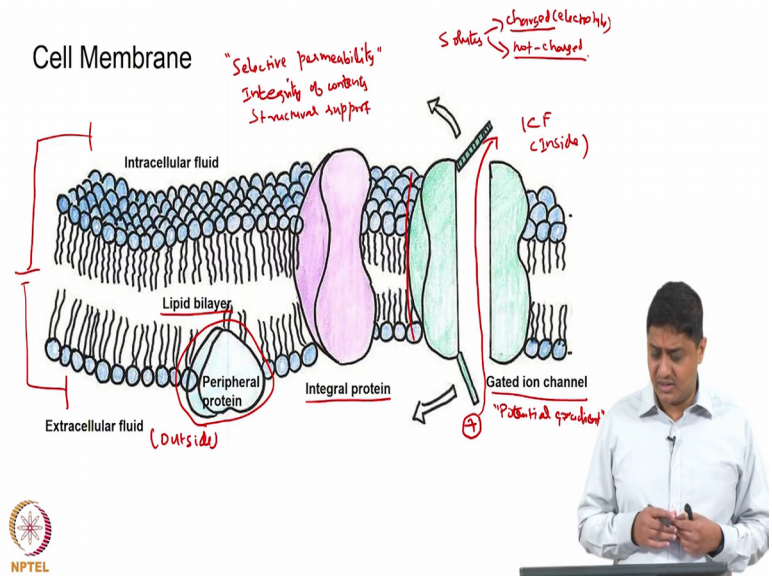

So, there is the cell membrane. The cell membrane is composed of both hydrophilic and hydrophobic substances. This is basically a lipid bilayer, a lipid bilayer that is composed of both hydrophilic and hydrophobic substances. And it also has what are called as membrane proteins that are generally classified into multiple types. Integral proteins are transmembrane proteins are those that span the entire membrane. And then there are peripheral proteins that are attached to one side of the membrane right.

Turns out that the plasma membrane of the cell membrane is a crucial innovation of a evolution. Suppose there was no plasma membrane. What would happen is that there would be no such entity called as a cell. There would be no difference between the inside of the cell and the outside of the cell.

I compare this usually using the example of a room that has no doors. Suppose there was only walls and the roof, and floor. And there was no window or no door, that room would have practically no application or no utility right. Or suppose if there was it if it was a completely open space. Other than playing sports that space has very little utility for example.

So, in other words, the crucial aspect that is desirable for the plasma membrane is that, we want the transport to happen at specific points in space and our specific points along the membrane and at specific points in time; are what we desire is some form of selective permeability. And this is the most crucial feature of the plasma membrane. Selective permeability, if there was no selective permeability if all ions can be transported in all directions then there would exist no gradient. So, there would be no difference between the inside of the cell and outside of the cell. So, function of the cell itself would be would be affected in a great manner right.

So, function or healthy function is primarily due to selective permeability of the plasma membrane [vocalized- noise]. So, important functions of the plasma membrane are basically integrity of the contents of the cell. Other than structural integrity, also the contents of the cell contents of the cell. Also structural support pause these are important functions of the cell membrane. More importantly it also enables or facilitates transport of specific substances in specific directions, right.

So, in general a concentration gradient is present substances are present in different concentrations inside the cell and outside the cell. So, in many cases it is desirable to maintain this concentration gradient. And these substances may be; what are these substances? This maybe these are solutes; these solutes may be charged or they may be electrolyte. Or they may not be charged, may be not a non-electrolyte.

Suppose the substance is charged then it has important consequences, because if a positive charge says for example, this is the intracellular fluid. So, that on top is the inside of the cell. In the bottom is the outside of the cell, right. Suppose that is a positive ion outside the cell and it is moving inside. Suppose it is getting transported inside; that means, one positive charge has moved from outside to inside effectively making the inside of the cell has bit more positive with respect to the outside slightly more positive with respect to the outside. In other words, it has created a slight amount of charge

separation. If this happens in relatively large amount you would expect what is called as potential gradient to develop.

So, also note that transport of the charged and non-charged particles differ in one other fundamental manner. The non-charged particles are not affected by any potential gradient that maybe previously present between the inside and outside the cells.

Suppose there is a potential gradient between the inside and outside. Suppose there is some gradient or somebody is, you know, stimulating something of that certain electrode, there then electro suppose something of that sort is existent. In that case the non-charged particles are the non-electrolytes will not be affected by the potential gradient, but the charged particles will be affected. Or in other words if the inside of the cell is having a higher potential when compared with the outside, then it is difficult for a cation for a positive chance to move inside from outside, because the inside is already at a higher potential. For example, this is true, this is just an example.

So, depending on the presence or absence of a potential gradient, transport of electrodes or charged substances will vary, will be affected and also that the chance substances movement itself will create a potential gradient. So, there are two important consequences for the transport of charged or electrolytes, charged particles are electrolytes. This is not true with an uncharged particle, but mostly in this course we will be talking about transport of sodium, potassium ions or electrolytes (Refer Time: 11:17)

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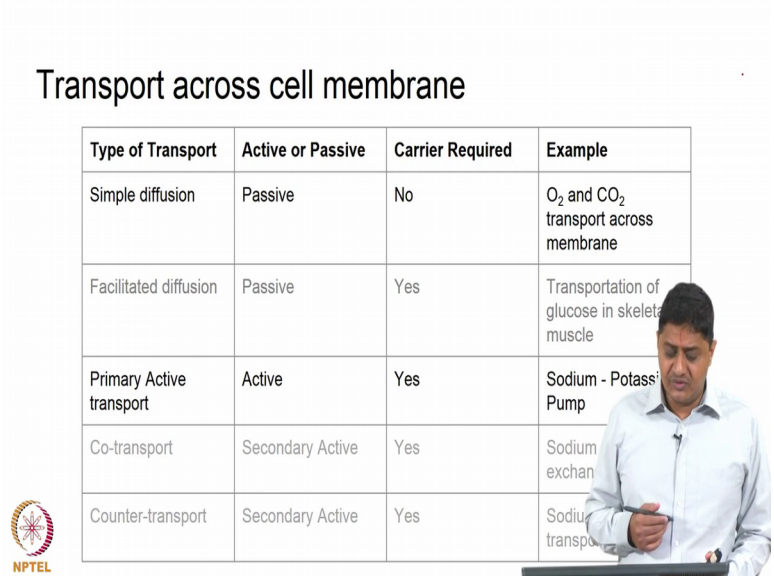

So, and there are different forms of transport suppose there is a concentration gradient, then if there is a channel available for transport, then usually there is going to be diffusion of this substance from the region of higher concentration to a region of lower concentration.

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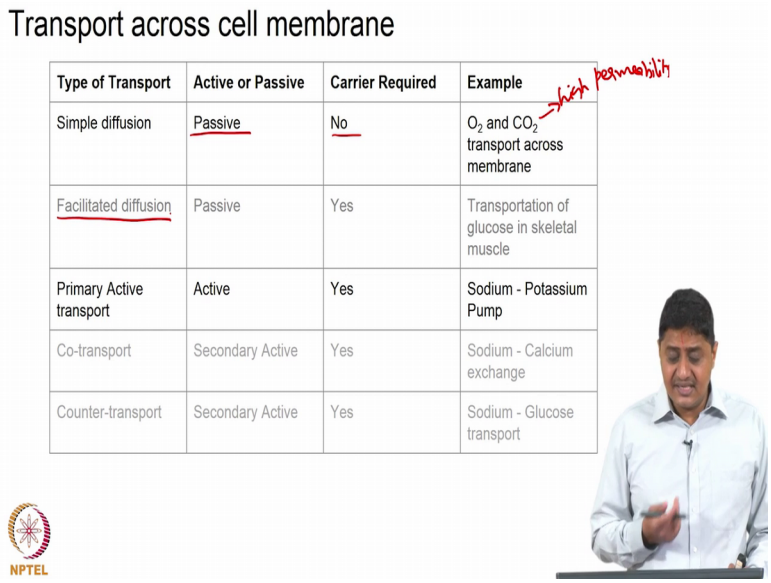

This is usually a passive process no carrier is required. Usually, oxygen carbon dioxide and other such substances can easily be transported across the membrane that is a relatively high permeability of the membrane for these substances. No specific carrier is required for this transport. Then there are cases called carrier mediated transport or facilitated diffusion. In such cases, there is a need for a carrier or a membrane protein. The example is the case of glucose transport in skeletal muscle right.

So, this is also a passive process. Then there are processes in which there is a need for substances to be taken against the concentration gradient. In general, this requires expense of energy right. So, suppose you are climbing to the first floor or suppose you are climbing to the second floor. As you are climbing up the stairs you are expending energy right; however, it is easier for us to drop a ball from the second floor balcony to the floor, because there is a gradient, that is an existing gradient no energy expense is required for that process right.

So, in general transportation against the gradient requires expense of energy right. There classic example is the example of sodium potassium pump which we will see in greater

detail later. And then there are other forms of transport, such as co transport, counter transport that are called as secondary transport mechanisms right. So, in this course we are interested mainly in these two topics. Those that are in bold and we are less interested in the other topics that are in grey ok.

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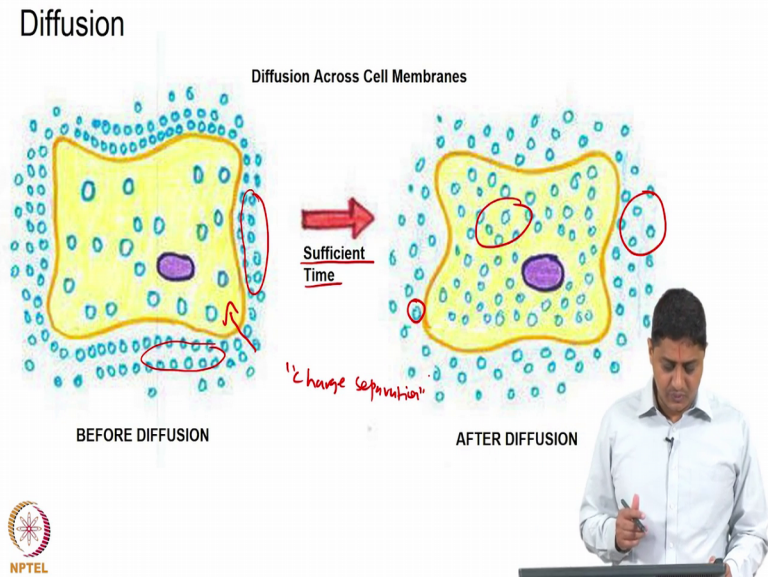

So, if you take the case of diffusion for example, right suppose a substance is present in large concentration outside the cell membrane like this. So, you can see that the concentration of this solute is much higher outside the cell membrane. And assuming that this cell membrane is permeable to the solute right. So, it is selectively permeable to this solute let us assume that. Then with sufficient time you could expect that the concentration inside the cell and outside the cell is approximately the same with sufficient amount of time.

So, as time passes after some time there is going to be an equal concentration of this substance inside the cell and outside the cell. And the net movement of particles from inside and outside is going to be approximately 0 right.

Once again importantly it is crucial whether this solute is an electrolyte or whether it is non-charged particle, because if it is an electrolyte then movement of this substance from outside to the inside will create a charge separation or a potential gradient. And that could affect movement of other ions in future. So, that is something that we would like to discuss in future classes right.

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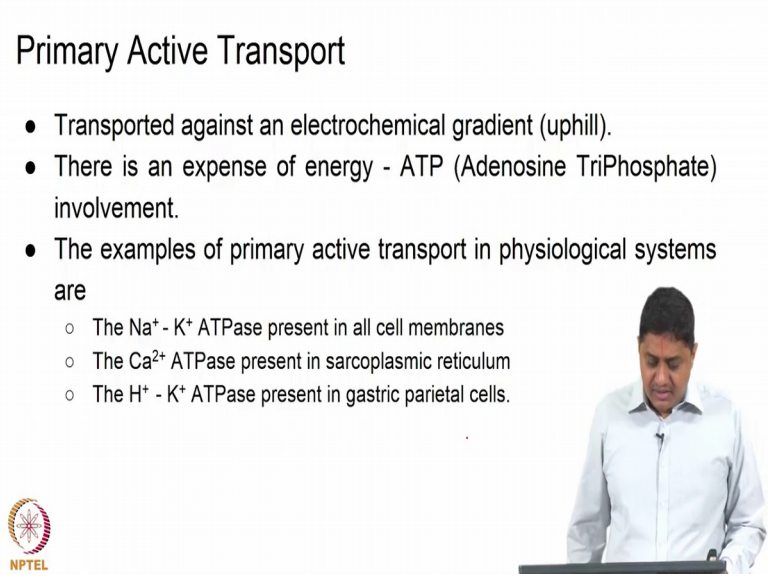

So, an example of primary active transport is the case of sodium potassium ATPase that is present in cell membranes in general this involves, active transport in general involves an expense of energy as we discussed some time ago. And the transport is usually uphill so involves transport against a gradient. So, you have to go uphill so; that means, you had to spend energy. The classic example is the sodium-potassium ATP is that we will see in the future slides right.

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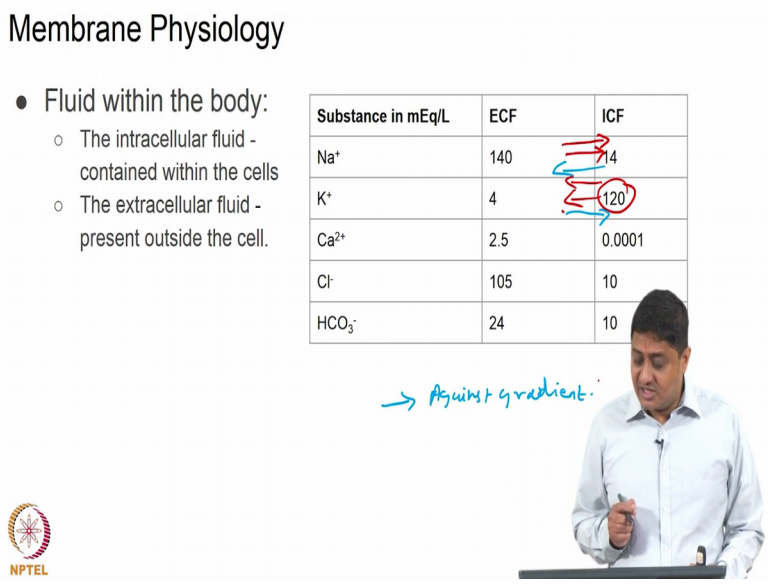

So, let us remember before we move on, let us remember the composition of or the concentration of substances within and outside the cell. Sodium is present in great quantity outside the cells. So, the gradient is in that direction, and potassium is present in great quantity inside the cell. And the gradient is in the opposite direction right.

So, if the channel is available for transport and if it is open then what you would expect is the natural movement of sodium would be from outside the cell to inside this, in that direction and the natural moment of potassium would be from inside the cell to outside the cell. This is what you would expect, but in some cases there is a need for transport to happen in the opposite direction. I am using a different color just to show that the transport direction is against the gradient. This color means, against the gradient, is it not? So, there are cases then this is of interest and for this; obviously, energy must be expended. How is this achieved that is the question, that is what we will see in the next few slides right.

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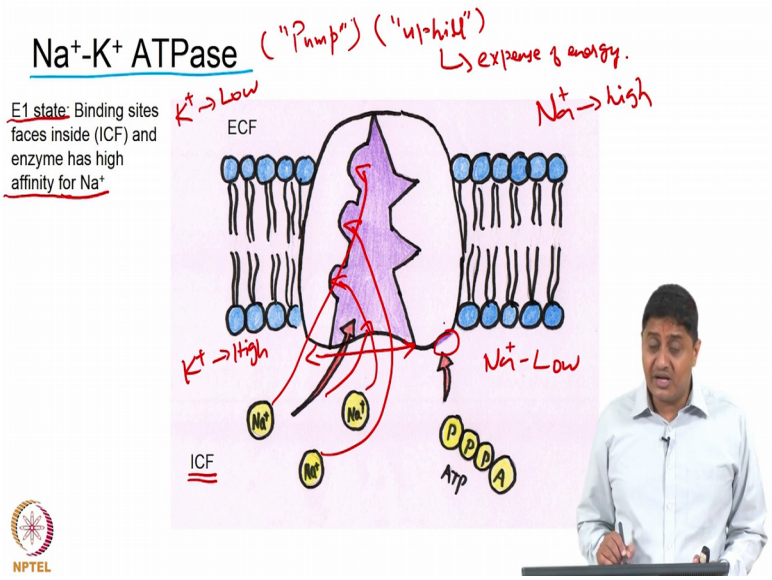

This is achieved by a membrane protein or a transmembrane protein called as sodium potassium pump or the sodium potassium ATPase right, sodium potassium pump. So, we use the word pump because so, the classic case of the water pump for example, transports water from a sump which is at a lower gradient which is at a lower height to a overhead tank, that is of interest for us.

So, we want to keep the water stored in the overhead tank so that when we open the tap water will flow right. But for this energy is expended we have a motorized pump, that takes the water from the sump or from some source maybe from a bore well and pumps it up to the overhead tank. Suppose this water is we are not able to pump, then there will be no water in the tap right. So, that is obvious so, pump means pushing the water upward or transporting the substance against a gradient or involving uphill transport and generally involving expense of energy right.

So, in the case of sodium potassium ATPase, this is a transmembrane protein that takes up energy and undergoes conformational change. So, this substance this membrane protein has 2 conformational states. And E 1 state in which the binding sides are open on the inside of the cell like this. So, this is the opening. So, the pump at the binding site is open on the inside of the cell, and has very high affinity for sodium in this state.

So, then what happens and let us remember, sodium is high outside so, and sodium is low inside. And potassium is low outside and potassium is high inside right. But this pump has high affinity for sodium in this E 1 conformational state. So, sodium from inside where already the concentration of sodium is low goes and attaches.

So, there are 3 sodium ions that attach to the 3 binding sides of this membrane protein. And ATP molecule attaches to it is binding site. When ATP molecule attaches to it is binding site the high energy high energy third phosphate bond is broken, and it is converted into a d p plus phosphate.

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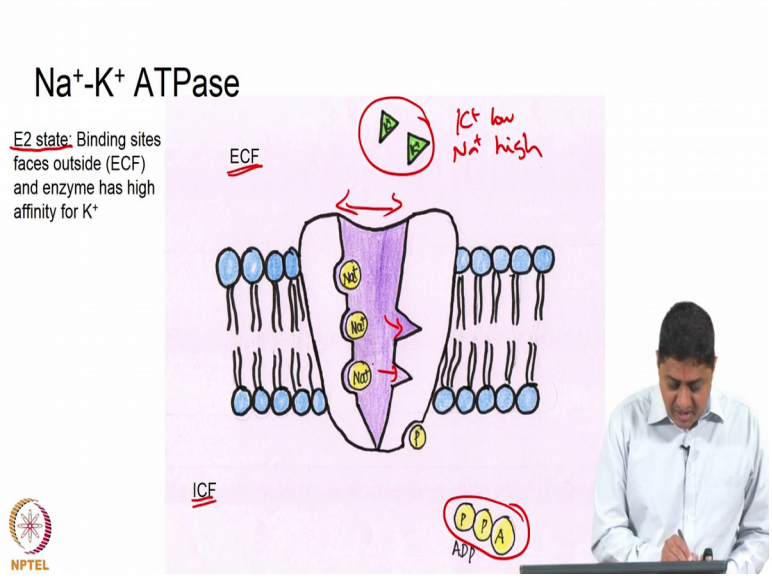

So, a d p leaves the leaves the system and this energy released due to the breakage of this bond, makes this pump makes this ATPase to undergo a conformational change. So, earlier note it was open, earlier this was open on the inside. So, that is the opening, but once ATP attaches and the phosphate bond is broken and energy is released, it is open on the outside, once again this is the outside of the cell and this is the inside.

So, here you see that the pump is open on the outside, right. And in this state this is called as the E 2 state. In this state, this enzyme has high affinity for potassium. So, what happens is that when it is open in this state it has a relatively low affinity for sodium.

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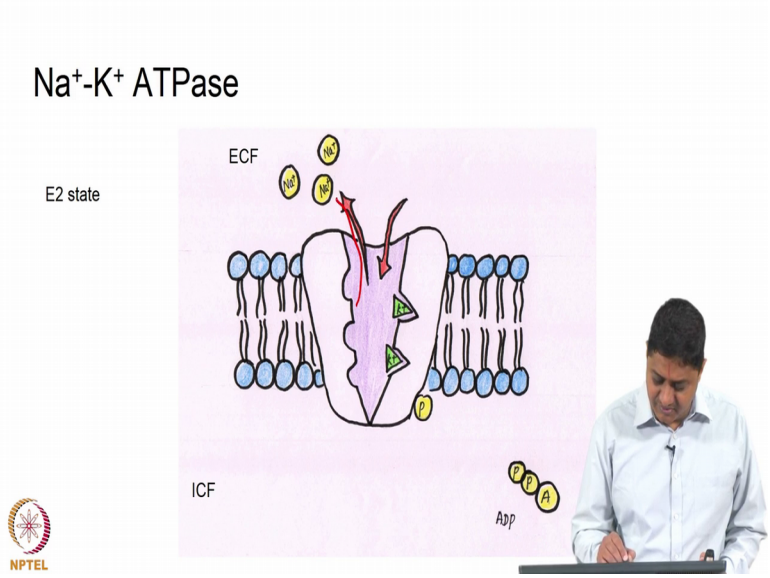

So, what happens is that sodium escapes the system from here and potassium that was present that was earlier present in relatively low quantity. Let us remember K plus is low outside and Na plus is high outside right. Potassium that is already present in less quantity outside, gets attached to these points, why? Because of the high affinity of this pump in the E 2 state. So, potassium gets attached to these 2 binding sides, and the pump undergoes one more conformational change.

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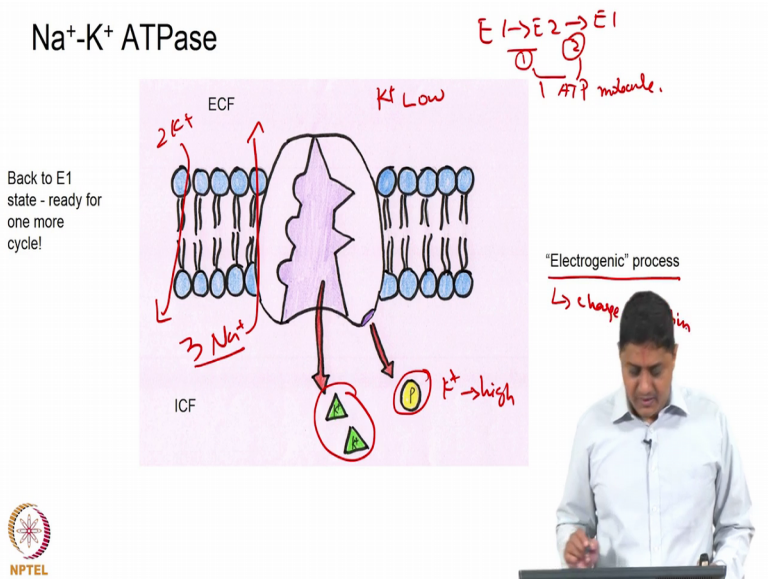

And opens up on the inside releasing potassium here. Once again you know so; that means, from a region of lower potassium concentration to a region of relatively high potassium concentration transport has happened.

So, and [vocalized- noise] and the phosphate also leaves the system. So, with the expense of one ATP molecule, the number of conformational changes; that is undergone by this enzyme or 2. So, that is basically between E 1 to E 2 and once again, from E 2 to E 1. The cost for both this conformational changes; so, that is the first change and this is second change, the cost is for both included the cost is one ATP molecule. At the expense of one ATP molecule, this enzyme undergoes 2 conformational changes; thus transporting substances transporting sodium and potassium against their concentration gradient right.

So, also note early on there was 3 sodium that gets transported from this side to that side and it is there is 3. And it is actually 2 potassium's that are transported in that direction. Effectively each cycle of this pump creates one less sodium or makes the inside of the cell a little less positive, or a little more negative. So, this is an electrogenic process of one more time. So, since there are 3 sodium ions that are transported from inside outside. And 2 potassium ions that are transported from outside to inside effectively one positive charge has left the cell. Because of this reason the cell becomes a little less positive or a little more negative with each cycle of this ATPase function right. So, this is an electrogenic process or it creates charge separation right.

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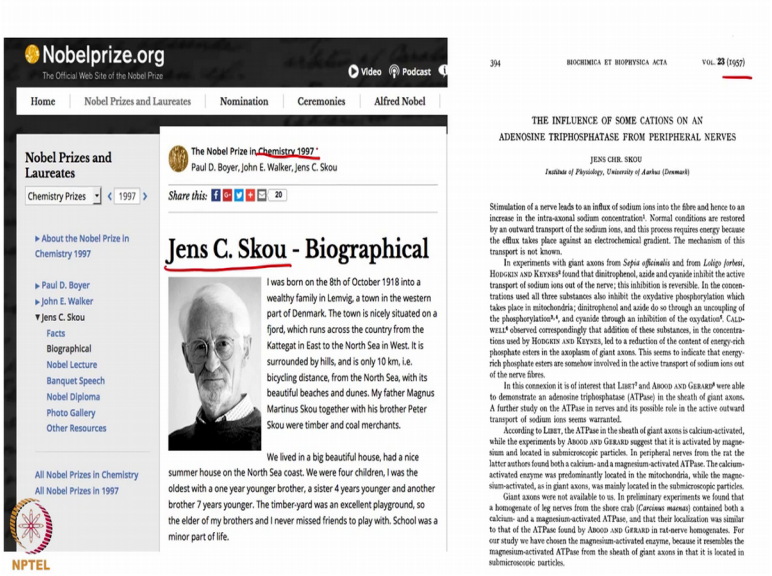

So, for his discovery of this important function; so, this paper was published in 1975 Doctor Jens Christian Skou was awarded nobel prize in chemistry 1997. So, an important discovery, very impactful; so, Dr. Jens Christian Skou wash Danish physician who contributed to this field of research in a great manner. So, he received the Nobel Prize in chemistry in 1997 right.

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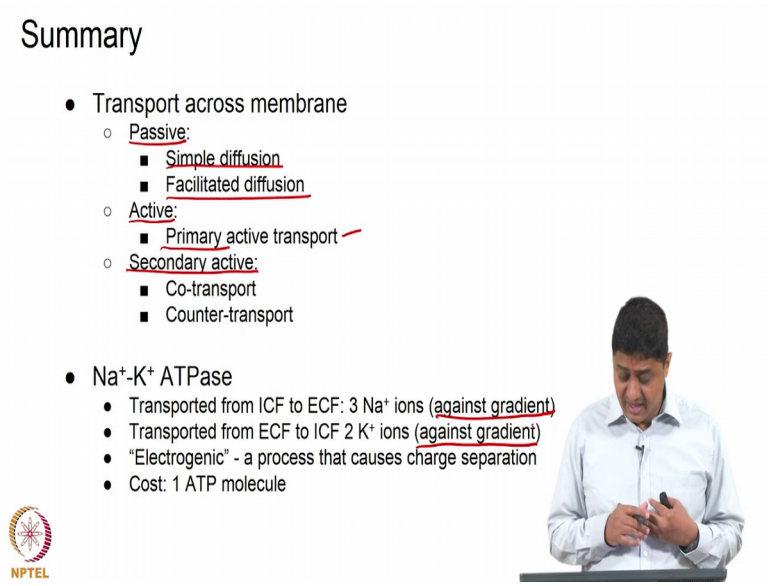

So, in summary what we have seen in today's classes that transport involves simple diffusion and facilitated diffusion or in general, these two can be called together as passive processes. And then it can be active processes of which there are 2 types. There is primary active transport and there is secondary active transport and then there are 2 types of this second active transport. And we have seen that one example of primary active transport is sodium potassium pump or sodium potassium ATPase.

What is happening is that 3 sodium ions go from inside of the cell to outside of the cell against the gradient. And 2 potassium ions go from outside the cell to inside the cell one. Once again against the gradient and these causes a charge separation effectively it makes the cell a little less positive, and the cost of this is one ATP molecule. So, with this we come to the end of this lecture. We will continue this conversation in the next class.

Thank you very much.