Neural Science for Engineers

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Lecture - 04
Action Potential -I

Greetings once again, we start another session in our journey on understanding Neural Sciences, the brain and its functioning. So far I have covered various aspects or the groundwork for understanding the nervous system function. We start to revise a bit, we started with something called as the Gibbs Donnan equilibrium which basically indicates the kind of equilibrium which exists in biological systems.

So, you have molecular concentration and ionic concentrations determining the distribution of charge and molecules across a semi permeable membrane, that forms the basis of most functions of the living cell. We will come to a later greater detail sometime subsequently; it is necessary to know that also.

Now, in the same study I also discussed about the presence of pumps; ionic pumps which are powered by biological energy sources, basically glucose and oxygen which produce a negative resting membrane potential. So, all living cells have negative resting membrane potential with the negative charge towards the inside and the basis of all transactions which happen within the cell is based upon this crucial resting membrane potential.

Now, when I say all cells, we are looking at very typical cells in different parts of the body say cardiac cell, gastrointestinal cells within the retina, eye, ear, everywhere. So, resting membrane potential is a fundamental property of all cells. Now nervous system as I was discussing earlier is a specialized form of tissue which is evolved from basic cells.

Now, how does it differ? It differs in that the nervous system is essentially composed of some set of cells called as excitable cells. So, from that I think we start the discussion on action potential. The action potential is the fundamental method of communication within the nervous system, the basis, the methods of generation and what are its implications will be discussed in this class.

We will be discussing a lot more on action potential and its implications later on also in different parts of parts of the course. Because it is as fundamental as the Gibbs Donnan equilibrium, and one would need to know a great amount of detail for the action potential.

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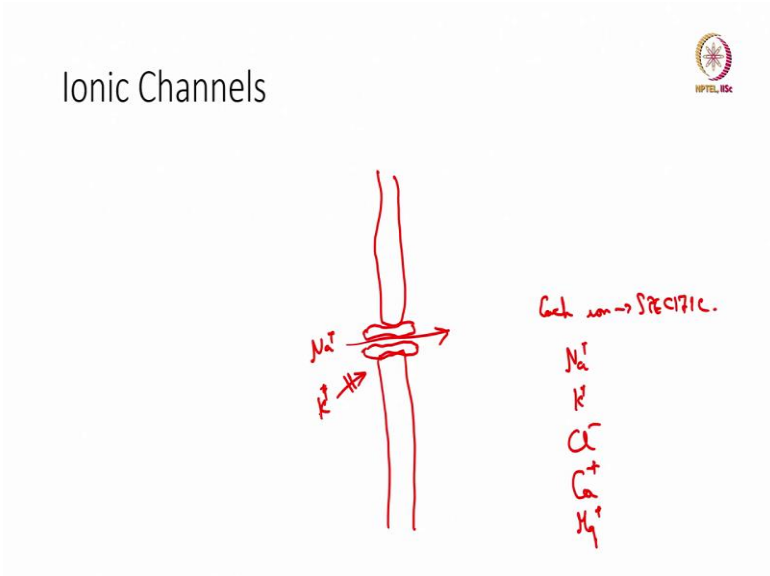

So, with that we start with discussions on the related matter. So, we discussed the presence of the semi permeable membrane. So, a semi permeable membrane is basically lipid bilayer and then the lipid bilayer has got some gaps within it through which ions and material go through.

But these gaps are not simply gaps they are actually protein complexes, and these protein complexes are not just any protein complexes they are very specific they have evolved very early in evolution. So, these have not only evolved very early in evolution, but have remained consistent in their protein structure across several billions of years in several groups of organisms, hierarchies of organisms have very similar kinds of channels.

And channel related diseases are very devastating and cause significant damage, they basically become untreatable because they are such fundamental structures within the life process. So, I did hint in my earlier class that whether channels are specific. So, each ion has a specific channel. So that means, that you have separate channels for sodium, you have separate channels for potassium, you have separate channel for chloride and there you have separate channels for calcium.

So, what that means is that a particular ion can go only through that particular channel. So, if you have a sodium channel, it means that you cannot have potassium going through it and or incidentally there is also magnesium channel. So, you they are very specific to each other.

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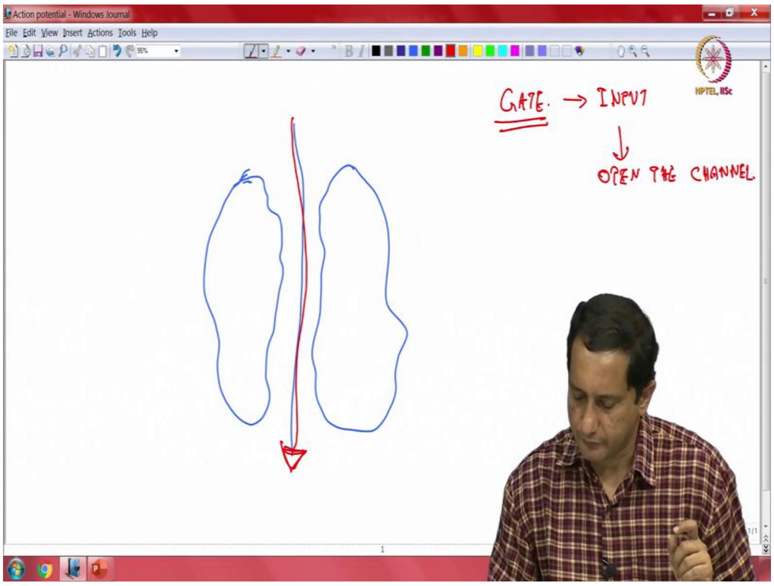

How do channels function? So, channels basically are large protein molecules, and they have very conserved structures as I told you between different kinds of organisms. Now, how does channel become you know restrictive to particular ionic movements?

Now, ions just cannot pass through the channel just like that, but there are some channels which can be you know, the ion can actually go through the channel without any kind of obstruction. So, these are actually not the significant channels.

The significant channels are channels which have a gate effect. So, what gate effect means is you need to have an input to open the channel. So, what do I mean by that?

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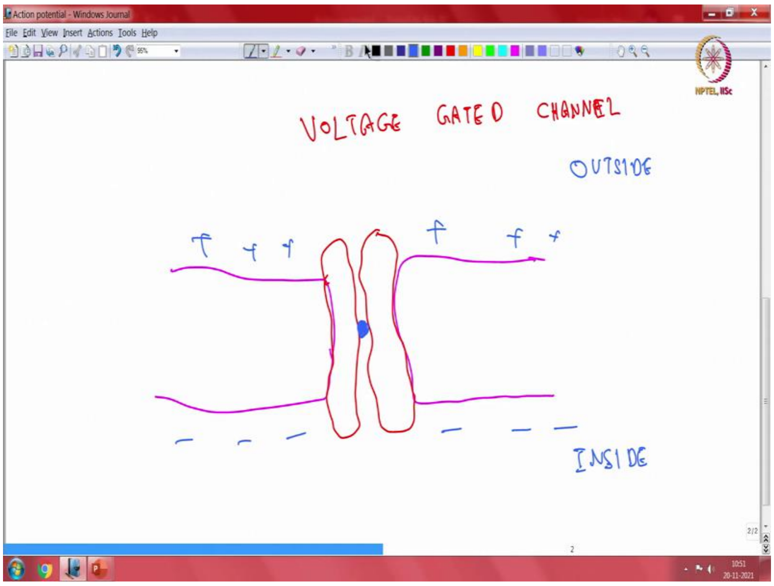

So, suppose that we have something called as a voltage gated channel which is the point of our discussion today. So, voltage gated channel means that when there is a particular voltage across the protein molecule between, they say outside and the inside of the cell. Once the trigger voltage is reached the channel opens up. So, what I mean is you have membrane and then you have the channel and then it is blocked in its native state.

So, native state means there is negative charge here, positive charge here, this is of course, the outside and this is the inside ok. So, you this is the native state.

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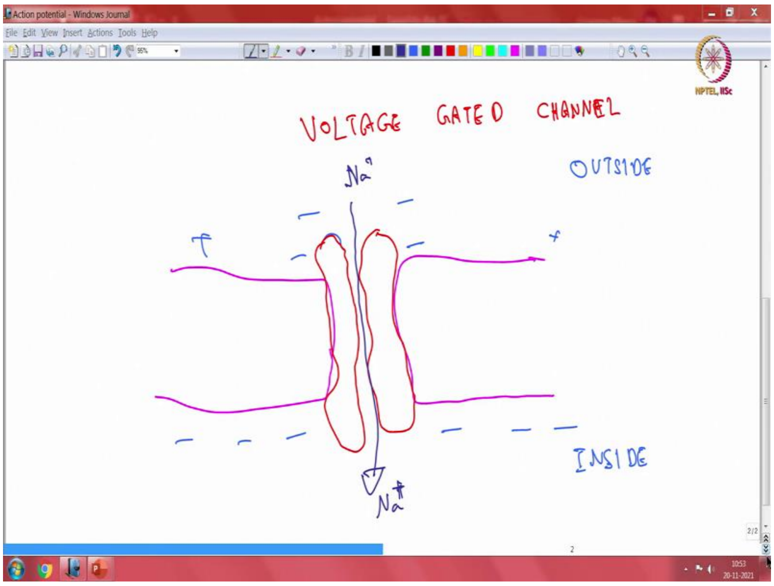

Now, suppose you change this organization and ensure that surrounding the channel you apply negative charge. See outside was positive, but in the local area of the channel you have negative charge. Then this particular channel undergoes a conformational change and that actually triggers something to open the channel.

And by which means you would ensure that there are ions going across their gradients. Now, the gradients if you remember were basically ionic gradients and concentration gradients.

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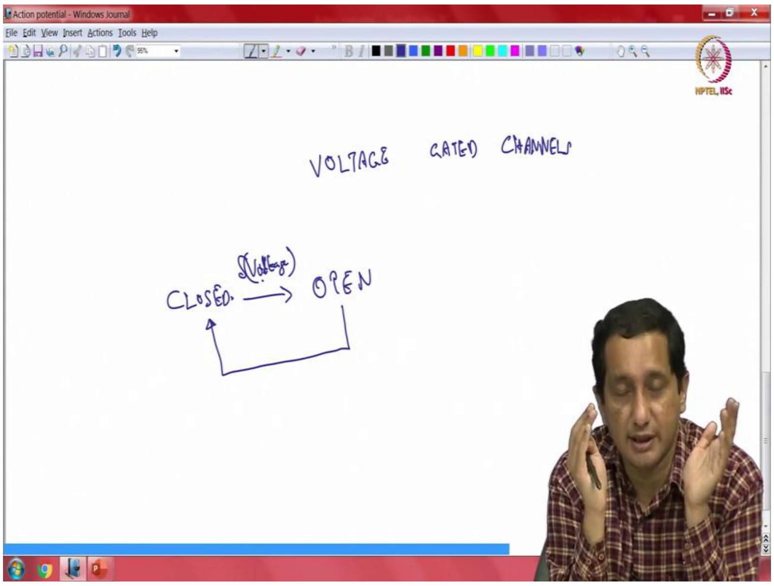

So, what happens is you have now two configurations of the channel. So, voltage gated channels, open and closed. So, voltage change, that change in voltage causes the channel to open up, but it is not that simple. These channels after a particular amount of time they actually go back to the closed stage, and you do not need anything to be expended.

So, it is a change in shape which is reversible and what is open goes back to the closed stage. Not only that once it goes back to the closed stage you reapply a voltage you can again have the open configuration. So, it forms a gate and gate as we know from electronics and things like that is a fundamental necessity of for logic operations.

Gate ensures that there is some kind of calculation which can be done by passage of ions and biologically this is the fundamental unit of calculation, the ability to restrict ionic movements across a cell membrane by whatever means, by ionic means or concentration means or by means of a pump.

So, you would ensure that gate ensures that there is some logic transaction which is happening from before and after a particular event which in this case is change in voltage. So, that needs to be understood clearly. So, it is curious, why or how something like a protein which is a very chemical molecule can undergo change in configurations.

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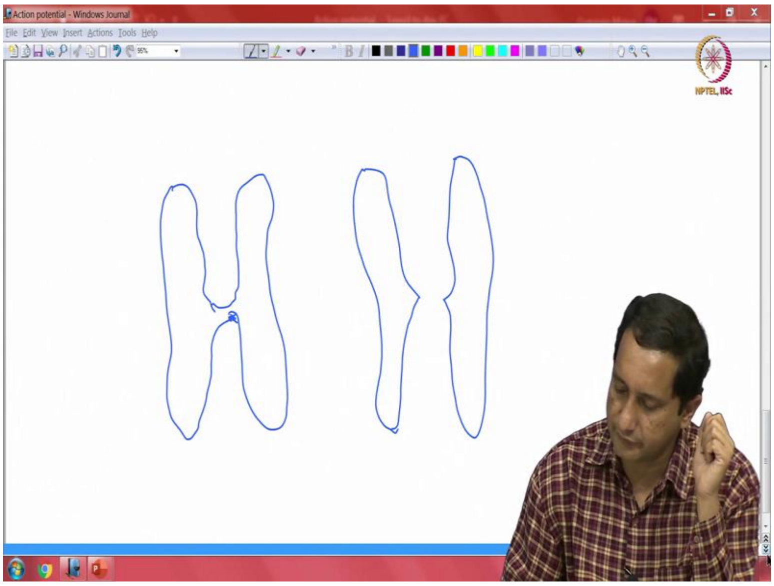

So, generally there are apparently three kinds of protein molecular configurations which can change. So, you have molecules which can change like this to like this which basically indicates the opening and closed stage. You can also have of course, there is a gap within this, which once the protein changes its conformation. Conformation is basically change in the three-dimensional structure of the protein.

So, when there is a change in the conformation of the protein you have an open conformation and the closed conformation. Closed is default and open in voltage gated channels is dependent upon voltage. You apply a voltage, it opens up. Now, you can also have different configuration in which the whole molecule itself can change.

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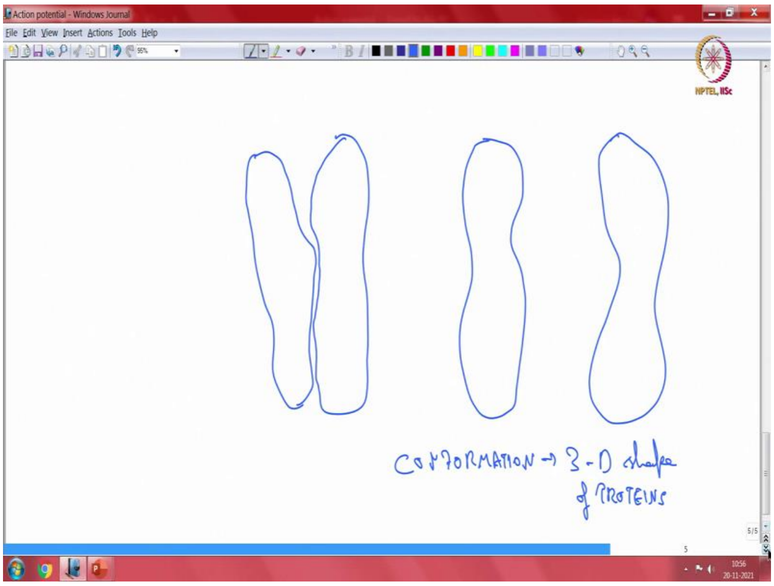

So, you have closed in which the entire molecule is very tightly packed so as to say and in the open configuration, the entire molecule changes its shape. These do have some biophysics implication, but for the purpose of understanding it is necessary to know that you know it is more a matter of curiosity as to how these things act.

So, you have shaped the entire molecule, it changes its shape and froms a closed conformation to open conformation. So, conformation as I told you is formation is the 3D shape of proteins.

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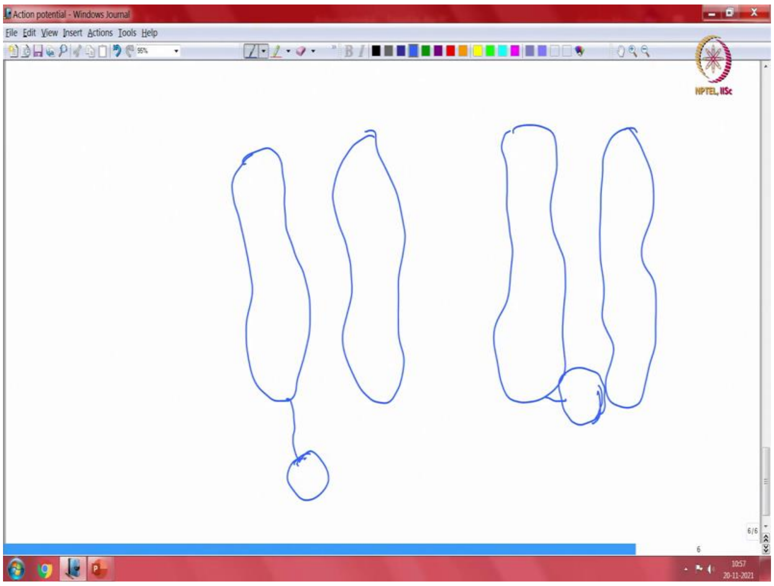

So, the third method is more interesting than this one, in which there is a part of the protein which is free and that part of the protein actually can act as a gate or as a door and then it forms open and closed systems. So, this is more for the matter of curiosity that I am describing, but they are very interesting if you consider that you know these are just chemical molecules which are very large organic molecules which have this very interesting property of being sensitive to voltage changes.

So, part of the molecule is subjected to change in voltage. The entire molecule does some funny stuff and that forms a gate between two entities. So, here we are looking at the cell membrane of the entire cell. It can also be more subcellular structures say for example, endoplasmic reticulum or a mitochondria, which are subcelluar structure. So, this form is a very common method of logic at various kinds of cells.

Now, this forms the first basis. So, we have voltage gated channels which are very specific for things called as excitable cell. So, you have excitable cells. Excitable in the sense that you put an input to the cell, the cell does something funny and that is directly related to the kind of excitation which is put on to the cell. We here restrict to voltage but do remember that we later on in sensory system, we have pain, pressure, temperature sensations you know these are sensation.

So, when there is a particular input given to that particular set of receptors, which basically is still a cell, one of these things happen. So, there are specific channels over there which are linked to other molecules and then they do the same stuff. So, the method of logic implemented continues to be the same. So, these are fundamental methods by which the nature takes care of implementing logic within cell systems. So, these are the kinds of ionic channels, and we move on to pumps.

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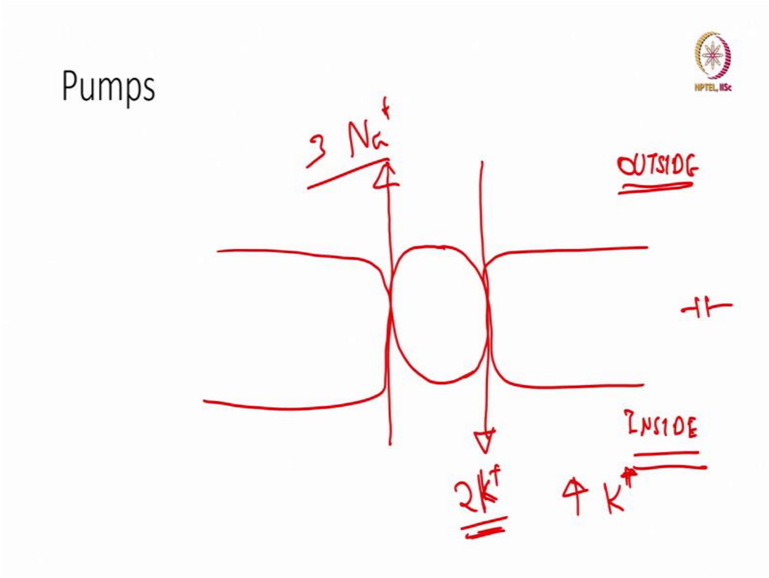

So, yesterday I told you about pumps and the most important of these pumps is the sodium potassium pump. So, it exchanges ions again in two directions across the cell membrane. So, the cell membrane is the important capacitor. So, it is basically a capacitor. So, you have outside and inside.

So, sodium and potassium, at the outset it would look like a very straight forward transaction one ion out one ion in, but it is against the gradient. So, 3 is to 2 and then you are generating charge. So, you are basically generating charge within the cell and that is a very important function as I told you and we will see why this is so.

So, you should remember that when you keep on continuously, even potassium which is the lower of the two ions you have very high intercellular potassium. So, there is higher concentration of potassium within the cell as opposed to outside of the cell and higher sodium concentration outside of the cell when compared to inside of the cell. So, we established concentration gradients because of this pump across the semi permeable membrane along with the charge.

So, these are three independent things. You have got a semi permeable membrane which is very fundamentally important which is a capacitor and you have charge distributions on either side of the capacitor along with that you have a pump. So, basically you can think of the pump as a battery.

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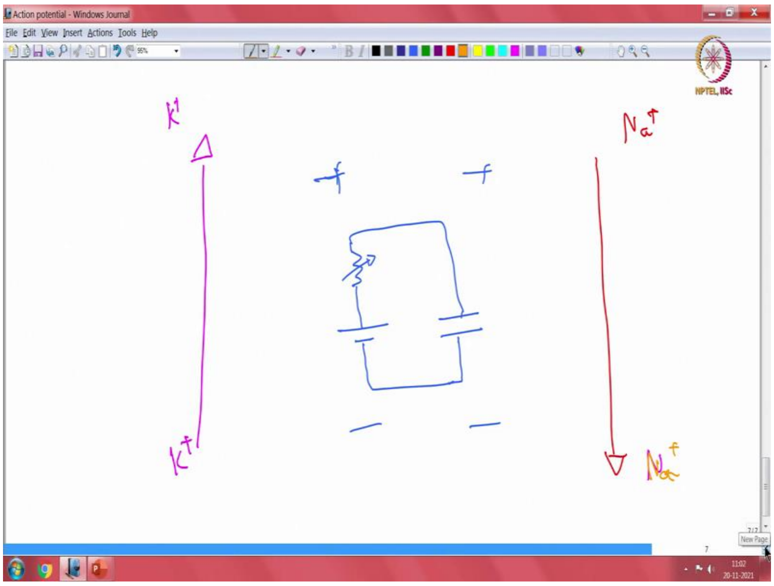

So, to replicate the whole thing you have a battery and you have a resistor or this one which varies with time and so, this sort of forms of the entire equivalent circuit for the system. So, the pump generates electromotive force by which you have negative on the inside of the cell and positive on the outside of the cell along with a concentration gradient.

So, concentration gradient for sodium is towards the inside, concentration gradient for potassium is towards the outside. So, you have charge which is there and ionic concentrations which is here. So, these are the two things which you would need to remember for the next part of the story.

So, sodium and potassium and this forms the building block for the action potential. So, once we have established this, now we will just look in sequences though. Once we have established this logic, we look into the next sequence of what actually happens when you apply a voltage across the cell membrane.

So, cell membrane, now, actually we should understand that cell membrane in this context refers only to neuronal cells and excitable cells.

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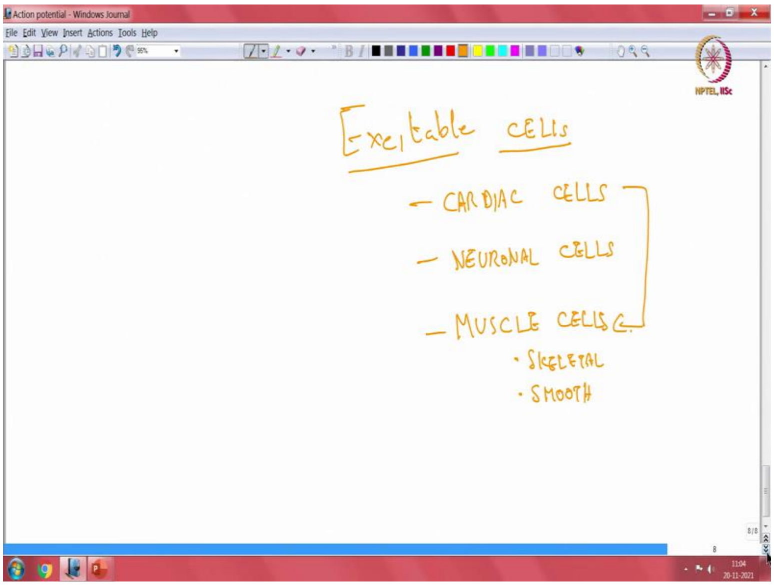

So, excitable cells are cardiac, neuronal, then you have muscle cells. Of course, cardiac is a subbranch of muscle cells. There is also skeletal. We need to look at these things later on in some detail. I would not bore you with medical terminologies and medical data, but in order to understand the higher-level functioning of stuff you always need to have a strong basic and that is basic foundation and that is essentially in be it whatever branch of science.

So, skeletal, smooth just look at these, I hope they are not rigorously medical terminology, but they convey a lot of things. So, you have excitable cells, which basically indicates that they have voltage gated channels on top of the cells and these channels are very specific to changes in voltage. And they have this property of changing their resting membrane potential, I think that is something which I am going to introduce now. So, what actually is an excitable cell?

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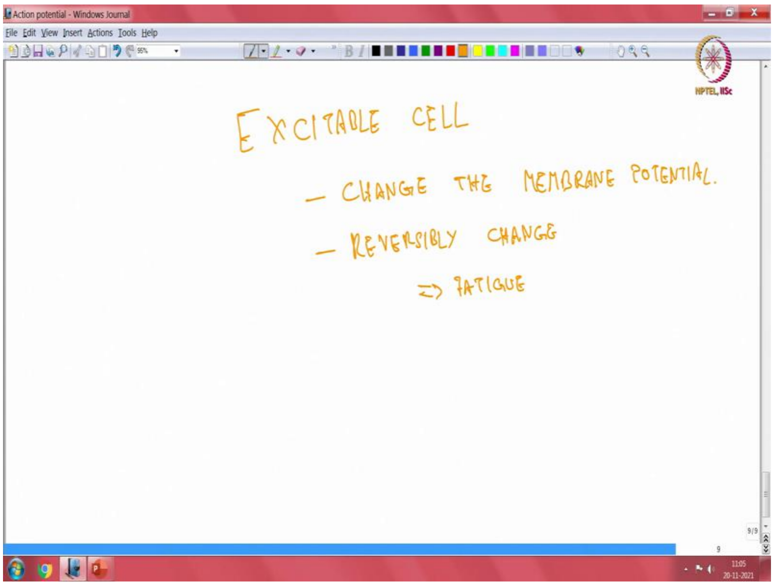

So, the fundamental property is it can change the membrane potential. Second thing is it is can reversibly change which is very important which also indicates these two would infer that they have some process called as fatigue. So, during which the functioning of the cell becomes sub optimal. So, there is an interesting physical property. Physical in the sense that anybody knows that when you work hard or think hard, you get tired.

So, there is a fundamental logic or fatigue built into it. Of course, there are various kinds of fatigue we would complain of or feel, but at the cellular level there is an entity called fatigue which happens when the things go really high frequency. So, excitable cells have the property of changing the membrane potential and reversibly change and there is this entity of fatigue. So, these are things which you should remember. So, now, we go into the actual thing called as a membrane potential.

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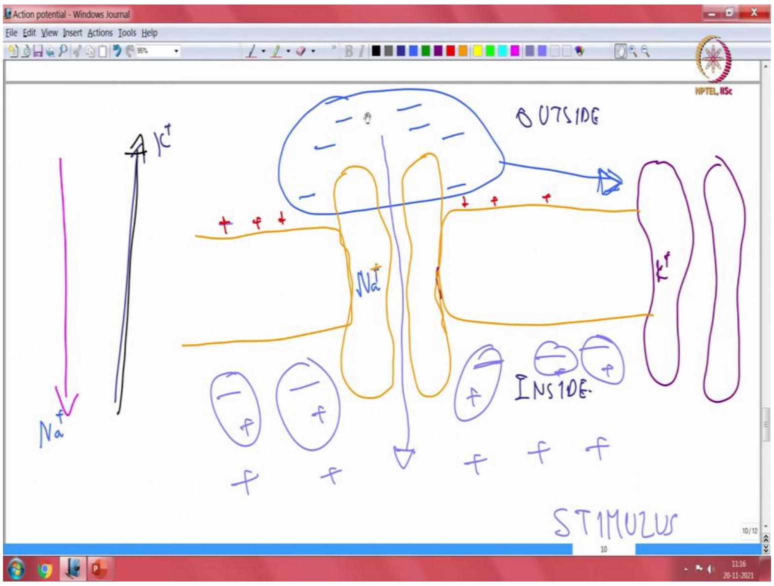

So, here again, we start with our membrane and here we start with just the sodium channel. So, this is the sodium, and we will also incorporate the potassium channel for later reference. So, this will be the potassium channel. Now, the conventional way of teaching is you apply something called as voltage to the outside of the membrane and that is how the fundamental studies have been done on and they form the basis of our understanding.

But here I think I will digress from the conventional method and then I will try to tell you what actually happens when this when the voltage changes. So, we come to the understanding that once we change the voltage there is the gate opens. So, the sodium channel opens when there is a change in voltage.

So, when there is negative charge around this for whatever reason we will come to the reasons later on. So, you have negative charge, what would happen? So, we had come to the conclusion earlier that sodium was a net inward gradient and potassium was a net outward gradient, I think I should use consistent methods of labeling.

So, there is sodium and potassium and so, that is what happens. So, when you put voltage on the outside of the cell, we know that the there is a change in the sodium channel. So, according to the change the channel just opens. Now, there is a concentration gradient of sodium from outside to inside. This cannot pass potassium through the same channel; the channel does not allow potassium through that.

So, what happens to sodium as a single ion is it moves inside. So, when sodium moves inside, we had inside and then negative charge on the inside of the cell membrane which is the capacitor and this is positive. So, basically it neutralizes ok. So, you lose charge. Now what happens is the concentration gradient of sodium is so high that it just does not neutralize it, it actually builds up a positive charge.

So, if we look at the next step of the story, what has happened so far is; I will label this as the stimulus phase. Stimulus phase we have applied charge on the outside of the membrane, there is a sodium channel. The sodium channel opens up, it allows sodium across its concentration gradient which is from outside to the inside and yeah.

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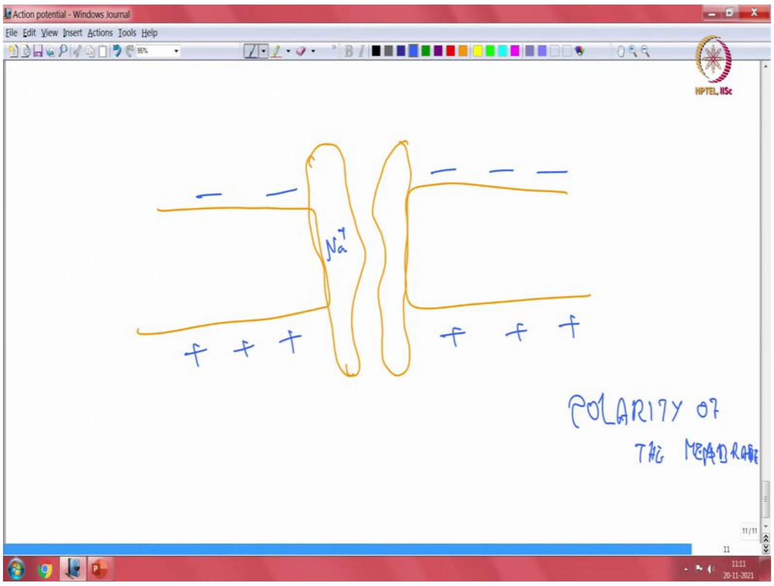

So, now what is the picture? So, picture has to be redrawn. So, we have membrane. We have an open sodium channel. So, what color was my sodium channel? Sodium channel was still brown. So, we have an open sodium channel and what has changed is there is positive charge inside. Positive charge inside because the concentration gradient is sodium is so high that not only it has neutralized charge on the immediate vicinity of the cell membrane vicinity of the channel, but it has also reversed the potential.

Now, reversal has happened because you already got negative charge on the outside because of the stimulus and positive charge because of the excess of sodium which has gone into the cell. So, this forms the first part of the story. So, we have seen this stimulus and that has caused a specific a membrane potential change which is basically reversing the polarity of the membrane.

So, polarity of the membrane is changed from positive to negative; positive to negative on the inside of the cell and negative to positive on the outside of the cell. So, this is the first part of the story. We spoke only about the sodium channel in the beginning. Now, the same voltage which cause the change on the sodium channel also causes the change in the potassium channel. So, we will look into what happens to the potassium channel.

Now, this is in isolation. Remember in the first part we had shown this to be in quite near vicinity, you know it is not that they are very far apart. They are so they are very closely placed within the across the capacitor which is the cell membrane. So, you have sodium channels and potassium channels which are closed to each other. And so, whatever change has happened to the whatever change has happened to the sodium channel also influences the potassium channel.

But interestingly the potassium channel does not react at the same time, it takes a lag of lag there is a time lag and that change incidentally also causes the potassium channel to open.

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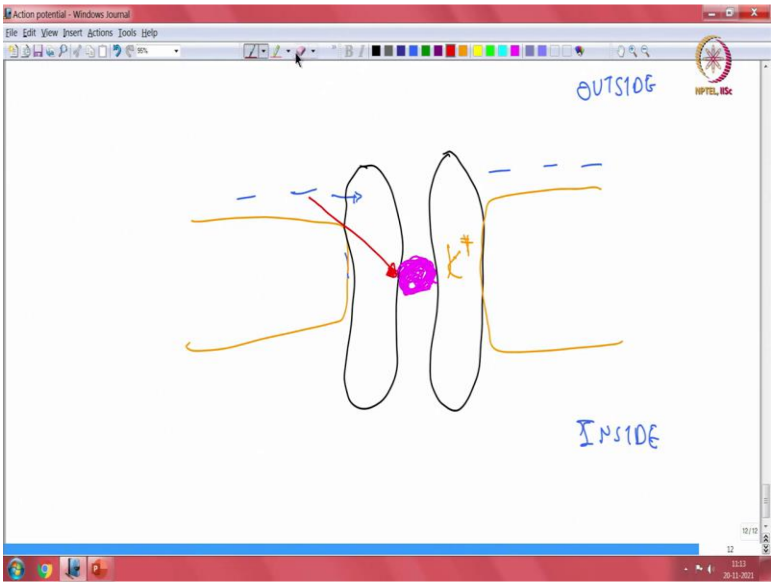

So, we will see what is happening to the potassium channel. So, we are back in the potassium channel. We have label this as potassium and we look at the scenario here. So, when we look at the potassium channel, we it is the same charge issues which were happening. So, this is the outside again, this is the inside ok.

So, there is negative charge which is built on the outside. And potassium as this negative charge has in fact cause the conformational change in the potassium. So, what was initially closed? So, what was initially closed? The, I have a shortage of colors here. So, I will use red.

So, the negative charge causes this thing to get opened. So, it is open, so, now, what happens to the potassium? So, potassium goes along as concentration gradient. Now concentration gradient for potassium as we have discussed in the previous slide or board or whatever is like this. So, you have potassium which is outside from inside to outside of the cell.

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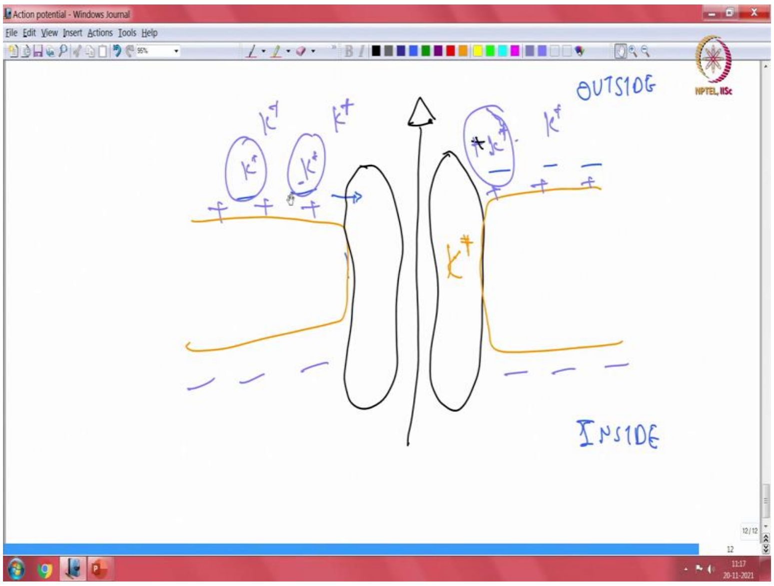

So, potassium goes along the gradient from inside to outside of the cell ok. Now, potassium is positively charged and so, what happens is the potassium changes the charge again. It is going on along its molecular ionic concentration. So, a concentration of potassium within the cell is much higher than the concentration of potassium outside of the cell.

So, when it goes out of the cell what happens is the charge reverses. So, loss of positive, so, the each positive potassium ion comes back outside neutralizes potassium outside neutralizes potassium outside neutralizes and in the process it you are restoring the negative charge inside ok. Now, again here there is a it is not that you know the it is just neutralization, you have excess of potassium beyond the ionic equilibrium and that results in the positive charge.

So, to revise, so, what we started with was this stage in which you had negative charge sorry we had positive charge outside in the beginning then the stimulus are supplied. So, stimulus is applied which is basically a negative charge on the cell. The cell causes a change in the configuration. So, first this sodium channel gets affected, sodium moves along the gradient, neutralizes the charge within the inside of the cell and also goes a overshoot of that resulting in a positive charge on the inside of the cell.

Now, as after this particular phase we have the this is the stage which happens at the end of the sodium channel activation which is negative charge on the outside and positive charge on the inside. So, polarity of the membrane gets reverse. Then it goes into the next phase in which the sodium potassium channel opens. Potassium moves out of the cell from the inside that causes change in the potassium exactly in the as in the first phase of the story.

So, there the not only neutralization of the charge happens on the outside of the cell, but also positive charge builds on the cell. The loss of potassium also causes the negative charge to come back on the inside of the cell. So, I think we will stop at this and then look at the whole picture in the next session.