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

Lecture – 07
Action Potential – Part 2

So, welcome to this class on Neuroscience of Human Movements. So, we will continue with our discussion on an Action Potential. So, this is part 2 of our discussion on action potential.

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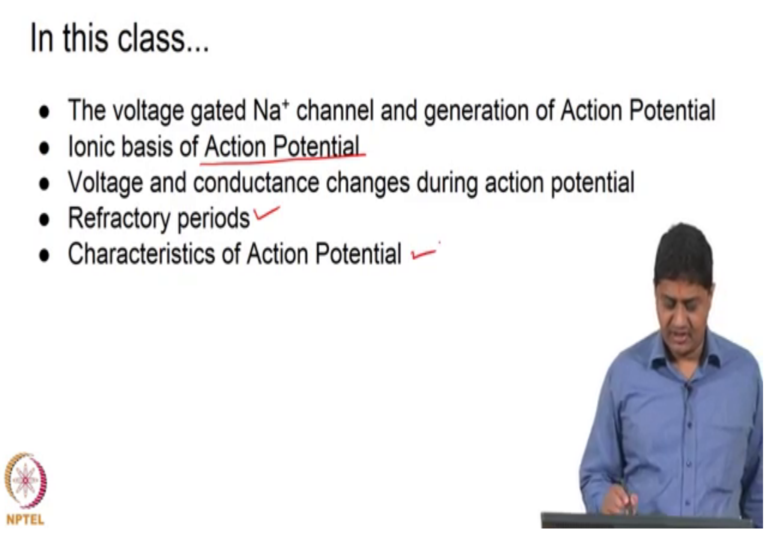

In this class we will discuss the special case of the voltage gated sodium channel and how action potential is generated. And we will discuss the ionic basis of action potential. And how conductance changes during action potential, and we will discuss refractory periods and we will discuss import characteristics of action potential.

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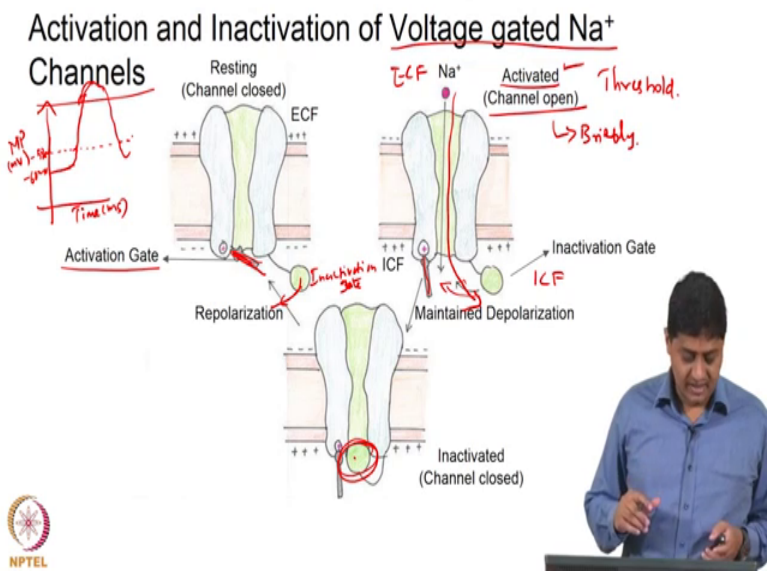

We discuss the case where there is a stimulus that causes slight depolarization of the membrane, or when there is a stimulus whose strength is small then the response is going to be a small.

And if the stimulus strength is larger than the response is also going to be larger. We saw this earlier. This we called as graded potential there is this is usually cost the grated potentials are usually cost by what are called as a stimulus sensitive sodium channels right. In addition you have what are called as voltage gated sodium channels, these channels are depolarization sensitive. They depend on the membrane potential for their opening and closer depending on the value of the membrane potential they will either remain open or closed right there is a particular point at which this voltage gated sodium channel we will open this point is called as threshold.

Essentially this is the threshold at which this channel is going to open. But in general when we say threshold is reached action potential happens. In general, we use this as if threshold is reached for the entire membrane. What is actually happening threshold is reached for this particular voltage gated channel. It turns out that there are 2 gates that this particular channel has these are the activation gate and the inactivation gate ok. So, there are 2 gates, that each voltage gated sodium channel has. One is the activation gate, and the other is the inactivation gate in general at rest the activation gate remains close like that, and the inactivation gate is open like that all right. In general, the activation gate disclosed and the inactivation gate is open.

Suppose threshold is reached at some point the threshold is reached what happens is that, the activation gate and the inactivation gate both receive come and to change from theirresisted. So, let us remember, what is the original configuration at rest. At rest the activation gate is closed and the inactivation gate is open both of the must change from their current configuration. When the threshold is reached, when the threshold is reached; that means, the activation gate will open like this and the inactivation gate will close; however, it turns out that the activation gate opening, that process is a relatively rapid process is a very fast process.

As soon as the command is reached the activation gate immediately opens quite immediately. Whereas, closer of the inactivation gate is relatively slow process so; that means, there is going to be a relatively brief period during which both the activation gate and the inactivation gate remained open. The activation gate immediately opens and the inactivation gate is trying to close, but not completely closed. In that state the channel we will remain open for a brief period of time for a relatively brief amount of time the channel will remain open note.

This is the extra cellular matrix and this is the intra cellular fluid. Since a lot of sodium is present outside the cell a lot of sodium we will defuse through the channel too the inside of the cell right. So, this is the activated state of the voltage gated sodium channel during which the activation gate is open and the inactivation gate is also open, but is in the process of closing right.

After sometime what happens the inactivation gate completely closes like it happens here. In this state sodium can no longer come inside this cannot happen so; that means, there is going to be no more sodium entering inside the cell. Now what would happen essentially for the membrane potential in this case at this state, this is time in say milli seconds this is membrane potential in milli volts. So, that is resisted right that is restricted at that say, for example, some small stimulus is taking it to threshold the let us say that is the threshold. For example, that threshold will open that gate and close that gate, but this opening is a fast process this closer is a slow process. We saw that, because of that reason there is going to be a brief amount of time during which this is going to remain activated or open.

During that time lot of sodium will come and take the membrane potential to a very positive value. Note this is about say minus 60 milli volts this is about say minus 50. For example, some numbers typical numbers right. So, it is possible for the membrane potential to actually cross 0 and become positive, because this channel is going to allow a lot of sodium to enter inside, during that brief period, but at are all after some time this inactivation gate is closed and no more sodium is going to enter, at that time right that potential is reached and after sometime the potential will actually come down. Where does it come down is something that we will have to see in the future slides right.

So, this is the mechanism by which the voltage gated sodium channel functions and depolarizes the membrane.

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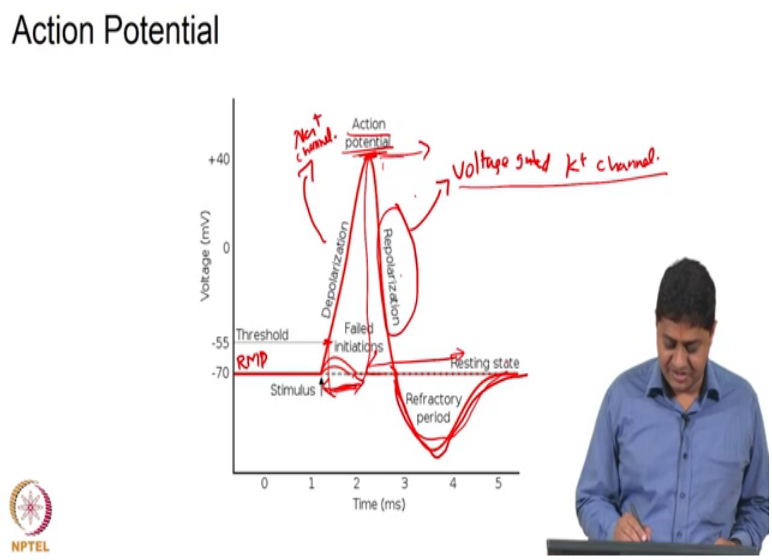

So, when the threshold is reached for example, here there is going to be a rapid depolarization. And this is called as the action potential are the raising part of the action potential right, but after sometime the membrane potential quickly comes down, actually going way below the resting membrane potential, this is the resting membrane potential actually it goes way below resting membrane potential and then comes backs to rest.

Right, it is clear wide depolarization is cost while depolarization is cost in action potential that is because of the action of sodium channel or the voltage gated sodium channel. We saw that earlier right. Why is repolarization cost we said at this point at this point what happens, but approximately that point the inactivation gate closes; that means, that no more sodium cannot can enter inside right; that means, it is all it is possible for the membrane potential to remain at that value, but that is not happening it is not remaining at that value it is coming down like that something else must happen.

So, what is that something else? That something else is at around that potential what happens is, voltage gated potassium channels open. Now voltage gated potassium channels, if it opens we know what could happen because potassium is present in relatively large quantities inside the cell when compared with the outside the cell right. So, when a potassium channel opens a lot of potassium is going to leave the cell; that means, the cell will become less positive or more negative.

Essentially, bringing the cell back to resting membrane potential actually this voltage gated potassium channel remains open for a relatively long period, when compared with the voltage gated sodium channel which is remaining open for a relatively brief period, say for example, that period right in comparison voltage gated potential remains open for a long period that it takes the membrane potential below the resting membrane potential right like that.

So, this is what is called as a action potential.

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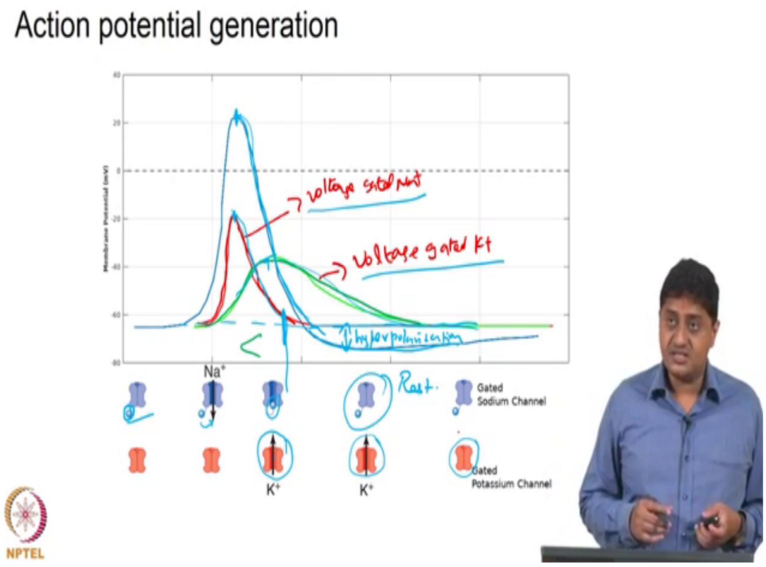

What causes this one more time another way of viewing the same thing right. So, the plot in blue here is action potential. So, that is action potential, this is the action potential plot. What you see in red and green here are the conductances of the voltage gated sodium and voltage gated potassium channels respectively. So, that is the red one is the voltage gated sodium, and the green one is the voltage gated potassium channel. Now what I mentioned earlier, the sodium channel on the sodium conductance remains a only for a brief period of a time and immediately comes down.

Whereas, the potassium channel it is conductance increases and remains elevated for a relatively long period of time. Note the amount of period for which the potassium conductance remains high right. Membrane potential goes below the resting membrane potential note the resting membrane potential in this case is are on that value is it not of erase on this.

So, that is the resting membrane potential approximately. So, the higher conductance in the voltage gated potassium channel causes this hyper polarization right. So, note this means that depending on the changes and conductance of the voltage gated channels you can describe the action potential curve itself.

So, this is the peak of the conductance curve for the voltage gated sodium channel. And the peak of the action potential is approximately at the same time right. And as soon as the conductance starts to follow of the action potential curve also start to follow of. And note actually the falling period of the note that the fall of the potential from the peak is due to multiple factors due to the increase of the potassium conductance and the decrease of the sodium conducts. The combination of factors come in to the picture.

So, what happens is it addressed the voltage gated sodium channel is at resisted basically the activation gate is close and the inactivation gate is open like this right. As soon as threshold is reached the activation gate is open leading to a lot of sodium entering the cell right, but slowly the inactivation gate is trying to close at around that point that happens at around, that point right the inactivation gate is close after this time after some time the voltage gated sodium channel goes back to resisted this is the resisted right, but when does the voltage gated potassium channel open that is approximately at that point right.

So, for example, so, that is approximately the time when the voltage gated potassium channel opens and it remains open for a relatively long period of time like that. After sometime it goes back to it is resisted ok.

So, a combination of this factors cause action potential right.

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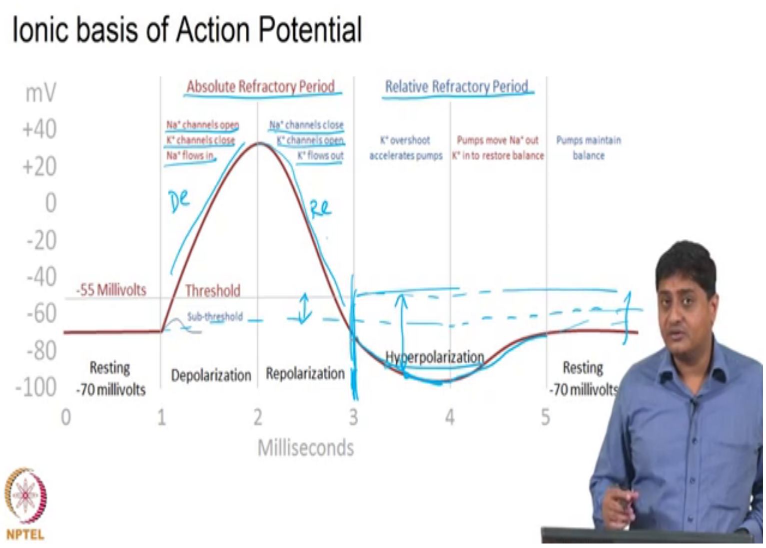

So, some terms one more time looking at the same thing in one other way and defining some terminology one more time. So, at this stage the sodium channels are open, the potassium channels are close and the lot of sodium flows in; that means, the membrane is depolarized. At this face the sodium channels are close and the potassium channels are open and potassium flows out that means, the membrane is repolarized. This is depolarized with the d this is repolarized with an R.

There is a period during which you cannot cause one more action potential why? At around this time the inactivation gate of the voltage gated sodium channel is closed. So, whatever you do you cannot activated during that period you cannot cost one more action potential by raising the membrane potential that period is called as absolute refractory period.

But at around that point say for example, that point what happens is that the voltage gated sodium channel goes back to resisted. What is the resisted? The resisted is that state at which the activation gate is close and the inactivation gate is open. When the voltage gate at channel is at resisted it is possible to cause one more action potential, but already let us compare the potential at this point when compare with the resting membrane potential. Because of extended potassium conductance this region is at repolarized state or a hyper polarizer state right.

So, because of this reason the membrane potential is below the resting membrane potential, but the threshold does not change according to that. So, the threshold remains here. Earlier it was sufficient permit to produce that much stimulus to cause an action potential. Now are if you are here for example, if you are at that point you will have to produce a much larger stimulus to cause an action potential. At this stage an action potential can be cause, but it requires a larger amplitude. The period during which a larger stimulus can cause an action potential is called as relative refractory period. You can cause an action potential, but you need a larger stimulus than usual right.

So, that is called as relative refractory period. So, this is due to you know potassium over should this is due to extended potassium conductance right. After sometime rest you rate to mechanisms bring back the membrane potential back to the resisted or the resting membrane potential. Once at around that point your back at rest. So, one more cycle of action potential can be half rested at around that point, you can actually start an action potential from here, but you need a larger amplitude.

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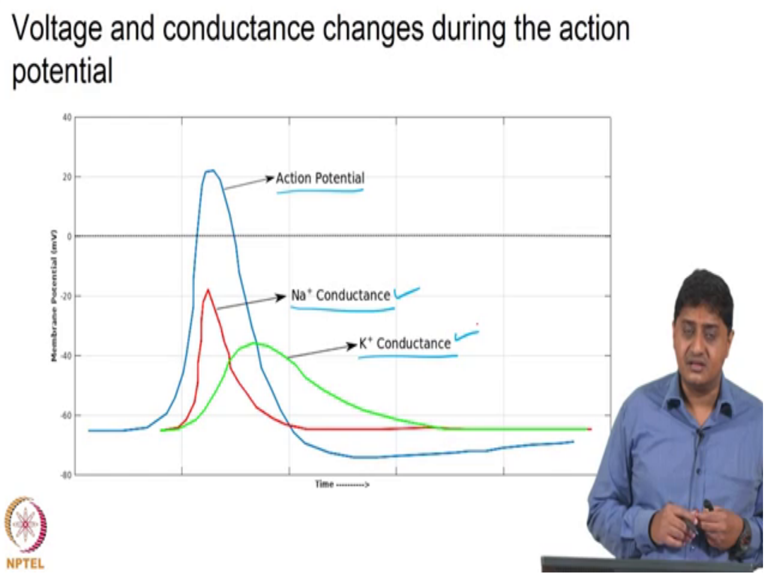

So, once again showing so; that means, this is cause by sodium conductance potassium conductance and the action potential is basically a combination of these, actually there are other factors not just these there are other factors that is the reason by combining these, you will only get a vague action potential not the actual action potential, there are other factors that are not included in this discussion ok.

So, changes in conductance of the voltage gated sodium and potassium channels dictate to a large extent the changes in the action potential curve right.

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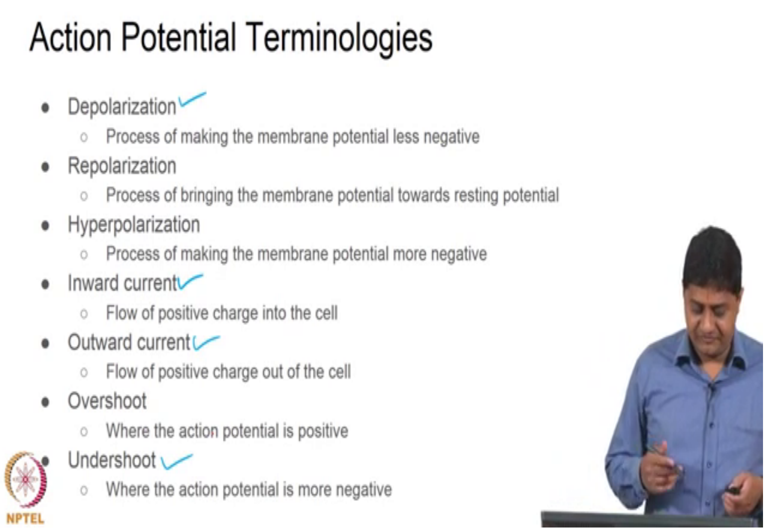

So, we already saw just depolarization is the process of making the membrane potential less negative, depolarization is the process of bringing back the membrane potential from more positive value. Hyper polarization is making the membrane potential more negative say when compared with the resting membrane potential flow of positive anions into the cell is called is an inward current. And flow of positive charge out of the cell is called as an outward current overshoot is this period when the action potential remains positive and undershoot is this period, during which the action potential is more negative.

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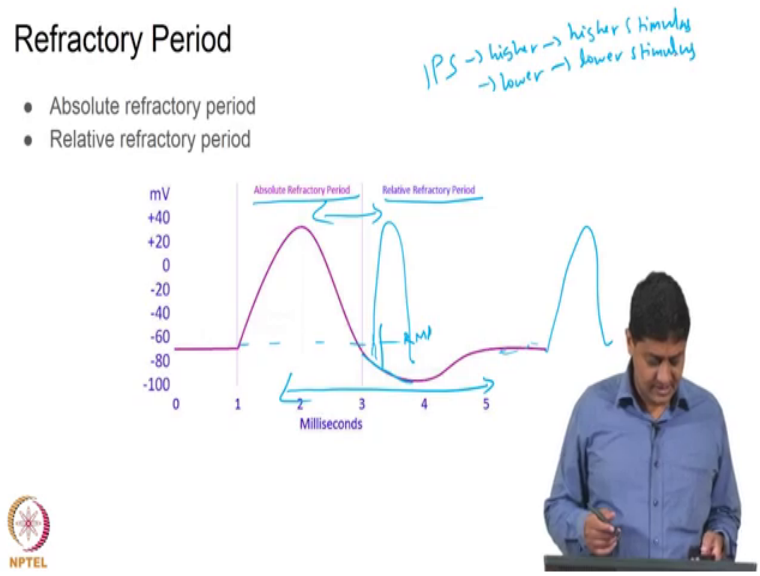

And we also defined absolute and relative refractory period absolute refractory period, if this period during which you cannot cause an action potential low matter the strength of the stimulus. Because the inactivation gate of the voltage gated sodium channel is closed. Relative refractory period if this period during which you can cause an action potential, but with the higher amplitude stimulus, this is because the voltage gated potassium channels have taken the membrane potential to a more negative value when compared with the resting membrane potential. This is the reason why you need a higher amplitude stimulus for causing an action potential.

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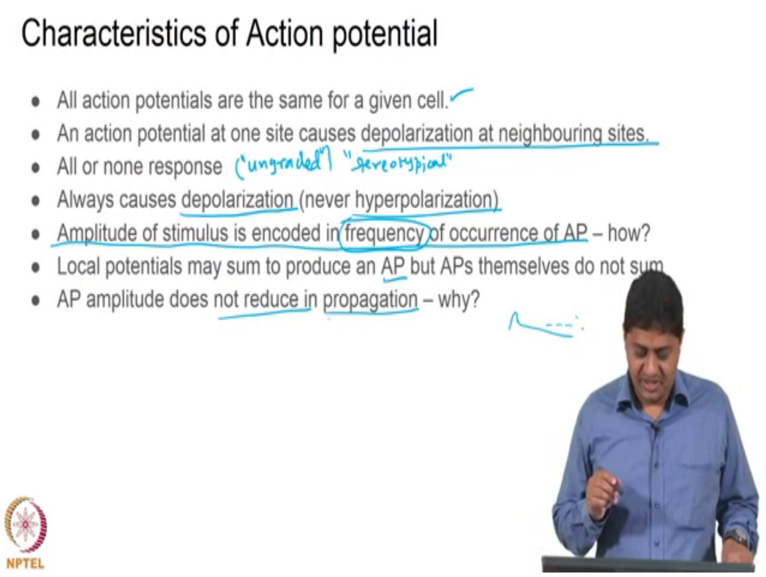

Importantly the following are to be noted. Turns out that all action potentials are same for a given cell and an action potential at one site has the ability to cause depolarization at neighboring sites. This is the crucial characteristics of action potential. There is just a lot of sodium entering inside that diffusion of this sodium causes the remaining areas or the neighbouring areas to be depolarize or the neighbouring parts of the membrane to be depolarized and the neighbouring voltage gated sodium channels are reaching threshold.

So, that they also open and a lot of sodium enters inside. So, action potential of one side causes depolarization at neighbouring sites. And note action potential is an all are none response either you have an action potential or you have no action potential. So, it is not possible for you to have half action potential. Once you cross the threshold you have a full action potential. In that sense what you are having is an ungraded response. So, this is binary, either you have one action potential or you have 0 action potential. There is no such thing as gradation depending on the strength of the stimulus. As long as a stimulus strength is above the threshold it will cause an action potential.

For whatever stimulus strength action potential characteristic will be the same right. So, it is an ungraded stereotypical response ok. So, action potential is an ungraded stereotypical response. A note action potential always causes depolarization. Compare this with graded potential we said earlier that graded potentials can also cause hyper polarization. So, and note 2 graded potentials can some to produce a total potential change, where is to action potentials cannot some. Once the threshold is reached or crossed one action potential will be caused. And in the mean value if you increase the stimulus strength it is not going to cause any change to the action potential characteristic, why because you are at the refractory period.

So, it will and also and it will not cause hyper polarization. Only graded potential will cause hyper polarization. Action potentials will not cause an hyper polarization, it will only cause a depolarization the hyper polarization period of that action potential curve exist, but you cannot selectively cause positivity or negativity it depending on there is no such thing as, or in other words there is such thing as negative action potential. Action potentials are always depolarizing right the amplitude of the stimulus how is it encoded is the question right. It turns out that the amplitude of the stimulus is encoded in the frequency of occurrence of action potential. How?

We said earlier that this is the relative refractory period right. Suppose the stimulus strength is relatively high, that can cause an action potential as soon as the relative refractory period is reached because stimulus strength is higher, than it will cause one more action potential here.

So now instead of it going so much distance back so much time, taking so much time to go to resting membrane potential, and then have one more action potential. If the stimulus strength is high, there will be 2 action potentials relatively closer to each other in time. So, the number of pulses or the impulses per second will be higher for a higher stimulus, higher strength stimulus. It will be lower for a lower strength stimulus.

So, in graded potentials we saw that the response amplitude is what in graded potentials; we saw depending on the stimulus amplitude the response amplitude changes in action potentials the response frequency or the number of pulses per second changes in the response to stimulus amplitude change. So, the amplitude of the stimulus is encoded in the frequency of occurrence of action potential.

Several local potentials are graded potentials can sum and cross the threshold on produce an action potential, but 2 action potentials cannot add with each other. And action potential amplitude does not reduce during propagation. Importantly graded potentials started one point and in the neighbouring say it is amplitude slowly reduces. Action potential amplitude does not reduce as it propagates. The reason is because you have strategically placed voltage gated sodium channel on the membrane. Such that that action potential in one of the voltage gated sodium channel will cause an action potential in the neighbouring voltage gated sodium channel. Because of this reason the amplitude of the action potential does not reduce.

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So, for their contribution to the discovery concerning ionic mechanisms involved in excitation and inhibition, the peripheral and central portions of the nerve cell membrane basically describing action potentials and ionic basis of action potential Hodgkin and Huxley and Eccles, if you the Nobel prize in physiology and medicine in 196 3 it.

So, they has come to be known famously as the Hodgkin Huxley model. So, much of what was discuss in today's class was from the original Hodgkin Huxley model except that it is a very simplified version.

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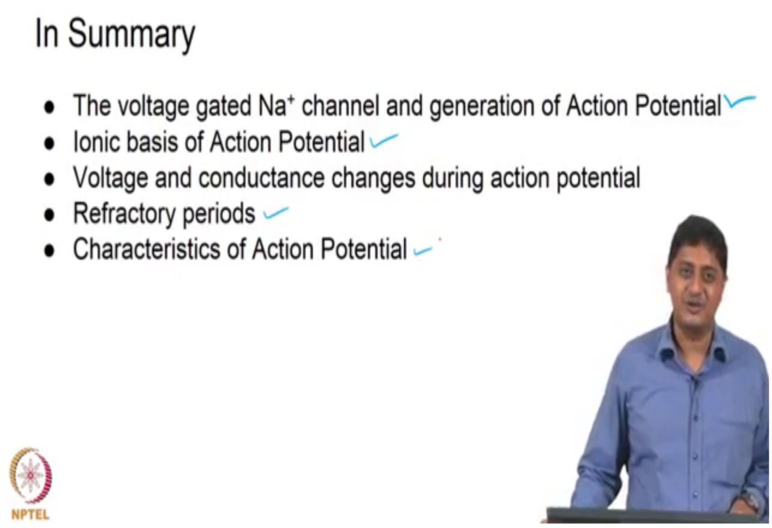

So, in summary what we saw today was the action of a voltage gated sodium channel on the generation of action potential. And the ionic basis of action potential and how the sodium and potassium conductance dictates the action potential voltage and refractory periods and we discuss important characteristics of action potential. With this we come to the end of this lecture, we will continue with the different future class.

Thank you very much.