Neural Science for Engineers
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Lecture - 05
Action Potential - II

So, in the previous class we saw the first part of the action potential. So, we saw how proteins are sensitive to changes in their environment which is basically the extra cellular environment and due to whatever reason that there is a change in the voltage proteins also changes the channel, which is the sodium gated channel, potassium channel. So, sodium channel they change their conformations and allow ions across their concentration gradients, these ionic gradients have been built by pumps prior to the event.

So, the resting membrane potential is the stable state of affairs and then there is an inciting stimulus which happens and then because of that stimulus there is a reversal in the polarization of the membrane. Now not only that the reversal is timed, in the sense that you have a change which is reversed after a certain period of time, but both of them also happening in sequence, it is not that both require independent stimulus.

So, you have one stimulus which produces the entire change. So, what we saw earlier was how the changes are happening in the membrane potential due to the concentration gradients and now we will look at the larger perspective.

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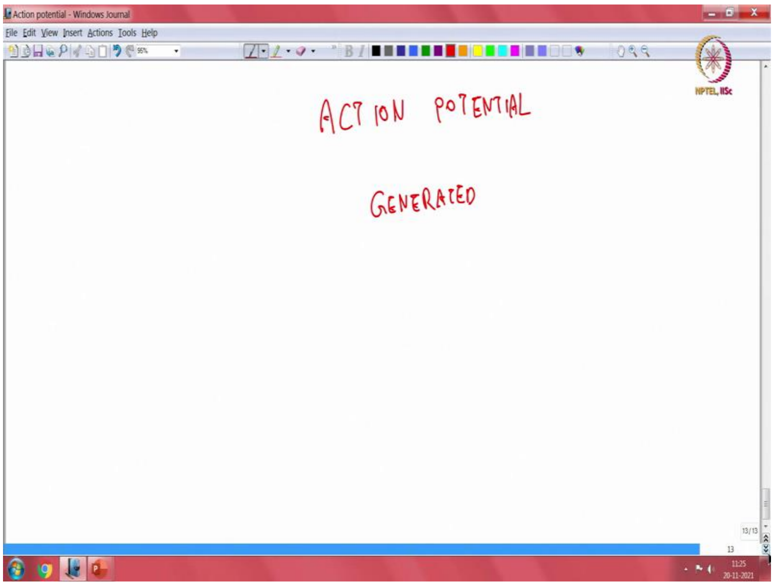

So, we have so far seen the generation of the action potential now the action potential is what is being discussed. So far we have seen how it is getting generated.

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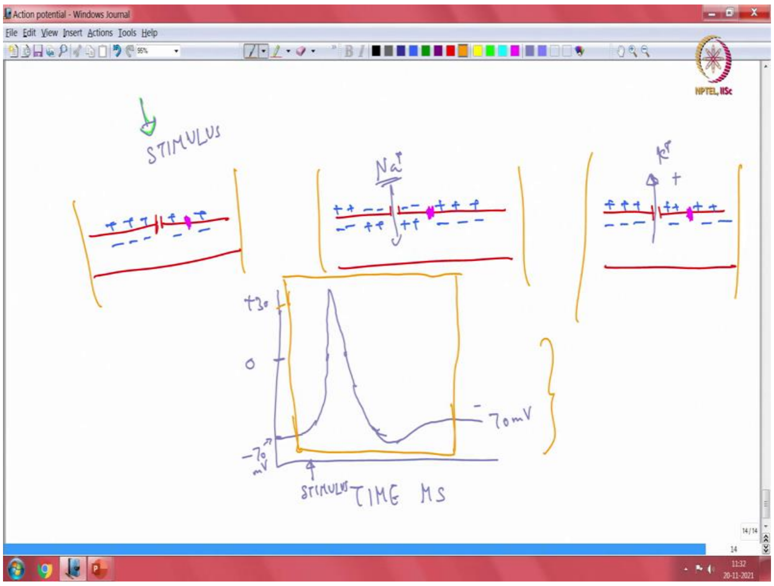

So, to summarize again what has happened within the last class. So, we have a different depiction of the cell. So, you have initially positive, positive, positive, positive, positive, negative, negative, negative, negative, negative. It changes to positive, positive, negative, negative, negative, negative, positive, positive, positive, positive here because of the sodium, which is not there across the cell membrane, it again reverses back due to the potassium channel.

So, here you know this will be visible. So, here is the stimulus. So, there is stimulus which is applied and then there is or sodium which goes in potassium which goes out, so that is the story so far. So, now if we plot the voltage changes on a graph which is what is a current activity.

So, we start with something called as around 70 millivolt, then you have 0 here and you have +30 over here. So, we will set the basic ground frame framework for describing the action potential. And time in milliseconds I suppose. So, we have a stable resting membrane potential at 70 and you give a stimulus over here. So, what happens at the stimulus is the sodium ions get into the cell that causes a reversal, it causes at first a neutralization of the charge.

So, it goes up to 30 it goes up to 0, but it continues along the concentration gradient changing the potential to +30, next what happens is the potassium channels open. So, that causes a reversal in the charge. So, first it goes to neutralization that is up to 0 and then the potassium builds up, as potassium goes outside at a greater extent reversing the potential actually it just does not reversal it goes below the 70 it goes up to 80 or 90 and then the membrane is restored back to -70 milli volts ok.

So, this entity seen here, this entity seen here forms the action potential. It is the language of the brain, it is the fundamental method of communication of intelligent organisms. And by which, I mean anything above which has got anything above multicellular organisms which has got a nervous system.

So, the action potential is so fundamental that it has to remain the same across various organisms including us and with all of frontal lobe and all our thought processes imagination, language, fine motor skills, launching rockets, seeing DNA and what is that gluons and stuff and everything is mediated by this fundamental action potential.

So, the language of the brain is composed of alphabets which is basically the action potential, and this single wave form is what is replicated and what we are subsequently going to discuss is how this waveform is used to communicate between cells and how it is developed along the cell. See we so far discussed the controlled event in which one set of sodium channels and one set of potassium channels and nothing else, you are not connected anything else to this fundamental entity.

But it is important to understand is it has a fundamental entity to which all other stuff gets added upon. So, action potential is the basic alphabet of the nervous system and that is something which you should remember I have tried to simplify as much as possible, I do not know whether it is an over simplification or not, but I would believe that people in the audience would need to know at a very fundamental level, you can read this from lot of places, but what happens is when you read stuff the sequence of events may not be all that obvious.

And one of the liberties of having a class such as this is that you can literally explain to the finest granular detail without being concerned about the time frame of a class. So, I have made use of that opportunity please do excuse if it is too laborious or too boring, but a good understanding of this step is necessary because all other as I told you all other discussion is based upon this. Now where do we go from here. So, we go from here to the two depictions over here.

We have seen a section of the membrane and we have seen the electrical representation of the same. So, first time we have seen how voltage changes across, and this is in a localized area of the cell membrane. So, now, generating a change in a local area is interesting because you know you have something called electricity which is changing a biological entity which is basically this one. So, there is a lot of electronics built into this package, but completely ionic.

I think that is the beauty of the whole system and for all the advances which we have done in electronics which is electron based and maybe quantum coming up now. This biology did not think it worthwhile to deal with electrons you know, it thought its going to deal with concentration, its ionic concentration, ionic manipulations, there is a lot of evolutionary background behind each of these proteins and you know they have been solidly transmitted across various living species.

Anything which has a nervous system has the same mechanism. So, if we go back to the introductory class where I spoke about mechanisms of information transfer and biological systems genetic. So, you should remember that the same set of genes for the sodium channel and potassium channel responsible for the action potential has been conserved from very low organisms to very high organisms. So, you can imagine the amount of error checking and redundancy which has been built into the genetic framework.

And that is something you know we already speak of, you know floppy disc became obsolete, CDs became obsolete, blue ray discs not to be seen, we have hard disc and that is all within a span of 40 years. So, these the data for sodium channels potassium channels is genetic which has been conserved over the past couple of million years or billion years I think of life. So, we started with local area, so how do you make it useful?

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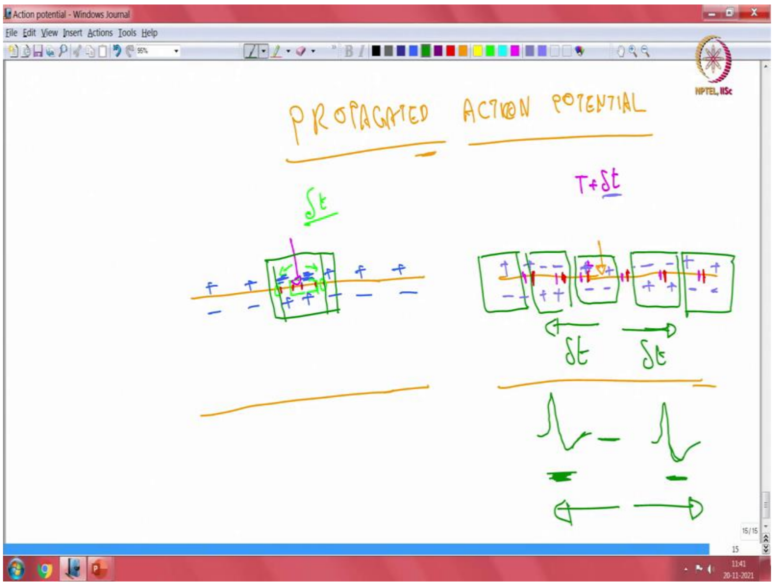

So, that is something called as a propagated action potential. So, only when the action potential is propagated, propagated means you know if it is a travelling wave does it form the entity of communication. So, there is some information which is generated in some part of the cell which needs to be propagated to some other part of the cell, so we will see the mechanism. So, this part is easier once I have set the groundwork in terms of the action potential and the basis of its generation.

So, we started with section of the membrane where we had this, there is a particular stimulus. So, stimulus needs something, so stimulus is basically the change in charge. So, there was negative charge over here and we had positive, positive, positive, positive otherwise. So, the action potential is locally generated. So, locally generated what happens is you have the sodium coming in. And so, that causes local change over the potassium and then there is a local change which in the outside also.

Now, what happens is this particular change just does not influence sodium channels over here which I will represent with red sorry. So, these are the sodium channels which I spoke about, but incidentally it is not the membrane has a rich density of sodium and potassium channels so as to say.

Now, there are also sodium channels all over here and they are a little bit further away from this particular stimulus now what local change in current which has happened is yeah. So, local change in current gets transmitted slightly out because of all the voltage changes which are happening and then what happens is after duration of time small time you have neighboring channels which are affected.

So, first set of channels is this set and then it progresses on to the next set of channels which are lateral. So, what happens the same cycle gets repeated. So, effectively what actually happens is that you have same membrane a point stimulus which was there at that point of time, but the changes the action potential gets transmitted.

So, transmission in the sense that you have, I will exaggerate the sodium channels and also keep the potassium channels for understanding. So, the orange ones are the sodium channels, the pink ones are the potassium channel. So, when this stimulus, this is after time t, $T + \Delta t$ ok. So, what happens at $T + \Delta t$, is this places after the stimulus. So, these changes have happened and then the membrane potential has come back. So, what has membrane potential come back to? We have again positive charge on the outside negative charge on the inside.

But after Δt we have the neighboring potassium sodium channel which has become activated. So, what does that do that causes a negative on the outside and positive on the inside negative on the outside and positive on the inside. So, this is local to this particular set of channels. So, negative and positive, but still much lay distally you will find distally in the sense farther away from the stimulus, you would find the native thing which is negative inside and positive, positive, positive, positive and negative.

So, we will analyze this picture. So, at the onset of stimulus the change was localized to this small area you know not even this small area, this small area. So, this is the area in which there is a local change at the end of the particular stimulus meaning at the end of the first action potential which is this one. So, there is you know it has come back into normal, but it has caused the change in the adjacent areas right. So, this is normal laterally.

Now, all this is happening because of the same set of sodium and potassium channels, but only due to local changes in voltage. Now the first change in voltage was due to an external stimulus which has been applied, but when it goes away from the stimulus that is because of the local changes in voltage which has caused this particular sodium channels to open much further. So, stimulus is one, but the effect continuous across the cell membrane on either direction we will find out that it is not so uniform.

And of course, obviously, neurons do not get simulated from external sources all the time you do not get shocks in your body at points to you know do your work. So, we will understand that stimulus as a different context in the body and we will. So, for the time being we understand that there was an external stimulus which was on some part of the cell membrane and then that cause the local change which is an action potential, and the action potential actually moves on either direction.

So, it has moved to this direction in time Δt. So, the membrane is like this if we look at the potential change which is happening over here over a small period of time. So, it is there is an action potential here and then there is an action potential here exaggerated of course, so this is the action potential. So, what effectively it means is that what action potential was in this particular area is actually traveling.

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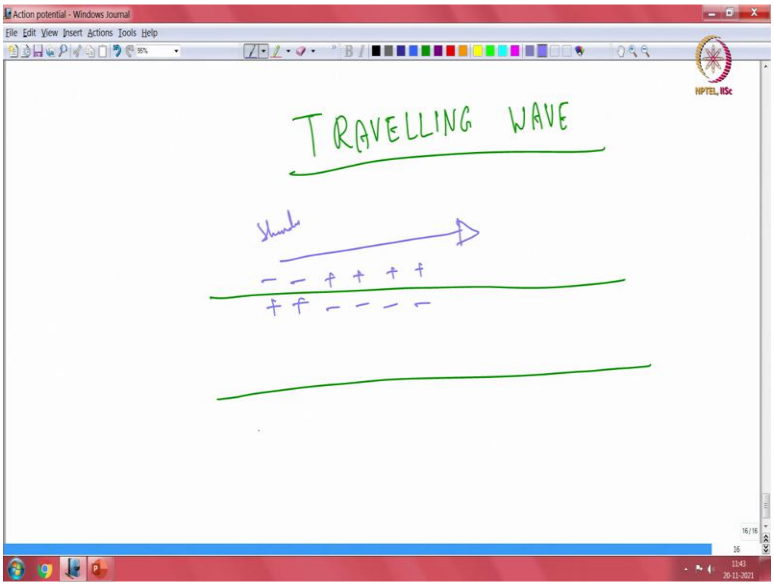

So, we have a travelling wave so as to say and that brings in wave dynamics into picture. So, what started initially as changes in potential due to unique properties of the membrane which we discussed earlier from the Gibbs-Donnan where the restring membrane is there to the excitable cell. Because of the presence of these excitable channels which are voltage gated channels we are now seeing that those fundamental properties are responsible for having an electrical wave which started from a single stimulus which is like a pebble in the water or so.

And then that is getting propagated across the membrane in both directions. Now, this is the basis of most biomedical applications and things like that you have travelling waves which are travelling across a membrane and it is directional. So, you have a direction and you have changes in the membrane.

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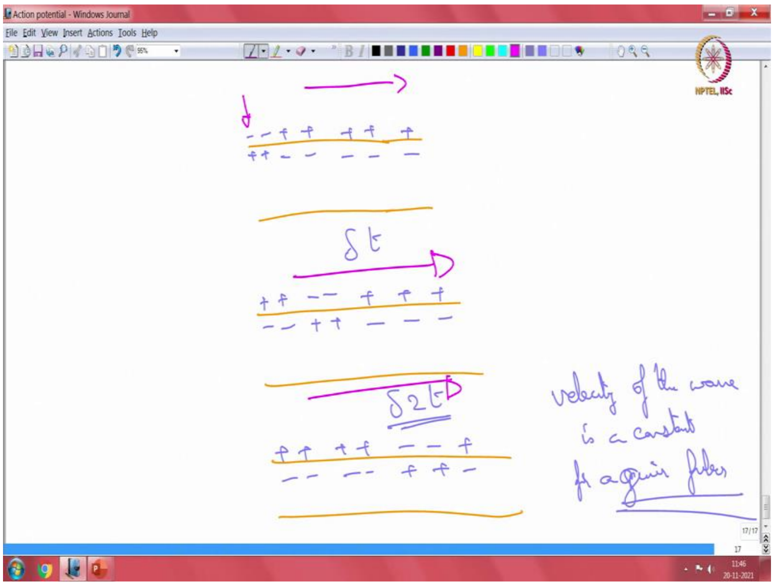

So, we use consistent marking. So, stimulus starts over here and you change, change, change, change ok. So, at the end of the action potential over here we have positive negative again back, but it has transmitted distally time t ok time 2t. Yeah 2t is important because velocity of the wave as a constant for a given fiber, is a particular fiber transmits the wave only at a particular velocity and it does not accelerate. There is acceleration, we will come to that later.

But acceleration not in the mechanics type of acceleration. So, if you have a given axon it transmits the signals. Now, we have come to signal. So, we started with potential changes, then we came to a particular wave form, then we came to a particular wave and the wave gets propagated. So, we have got a propagated wave across the membrane and now we need to find the properties of the wave. So, I will discuss it as wave function.

So, I think this should be clear. So, we for us given stimulus the wave transmits travels across the membrane, and it takes a finite amount of time to go across that it is in milliseconds. So, obviously, all this stuff which we do is in under a second. So, a couple of milliseconds of transfer across, but we will later realize that how difficult and how complex and how rich the system is that to account for various velocities across various neuronal entity neuronal and neuronal structures.

And how the brain is able to compute in spite of having so much of limitations in terms of speed for the kind of things which we do in our life. So, yeah so start with wave discussion.

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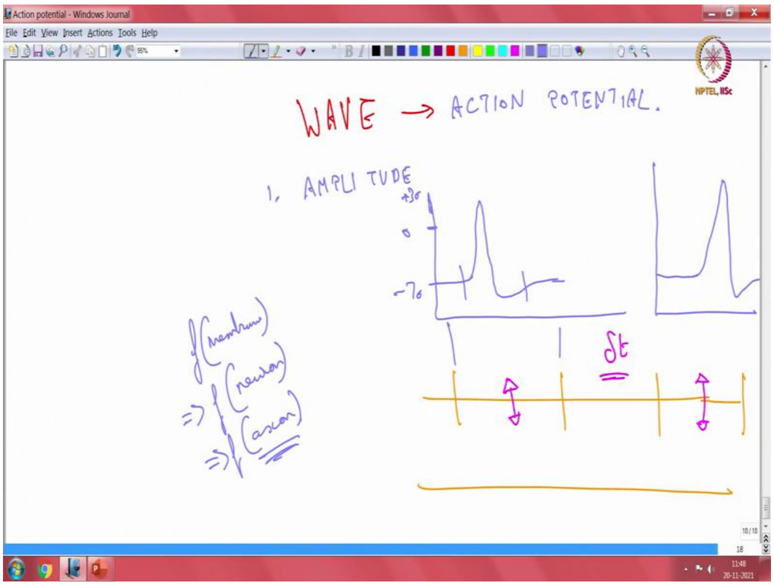

What are the properties of the travelling wave? Which is basically the action potential. Now the first property is the amplitude. So, amplitude I showed you that it goes like this, go comes down back and then it goes like this back. So, -70, 0, +30, now this is in a segment of the wave segment of the membrane ok.

Now, if you look at the membrane per se, if we take this is from this segment of the membrane, if we evaluate the wave function at a different segment of the membrane and plot we essentially understand that the dynamics remains the same that is the density of sodium channels for the membrane remains the same the voltage gradient across this membrane remains the same the sodium and potassium concentration gradients across this membrane remains the same and its only the time which has changed.

So, basically what I am trying to convey is that the amplitude of the wave function remains the same. So, that is very important. So, when we are looking at an action potential the time duration of the action potential is a property it is a function of the membrane. Membrane which implies that it is a function of the neuron, or it is a function of the axon specifically. So, axon is the part of the neuron we have not studied the parts of the neuron. So, we will come to that subsequently.

But we what I am trying to say is that for a given neuron basically all human neurons you have the same wave form which is replicated across the board for different kinds of neuron. So, whether you have cranial neurons you have a spinal neurons amplitude remains the same because the voltage gradients which are maintained remain the same and they are conserved genetically, and it is very important for the body to have that same set.

So, when we discuss an action potential amplitude remains the same, but it changes when we look out look at compound action potentials and eegs, an emgs and various kinds of biological data which you see where there is amplitude changes and. So, it is very important to distinguish between an action potential analysis versus a compound action potential analysis which we will come to later. So, we are still discussing amplitude, now one thing which I told you about is the concept of fatigue. So, what is the concept of fatigue in channel terms ok.

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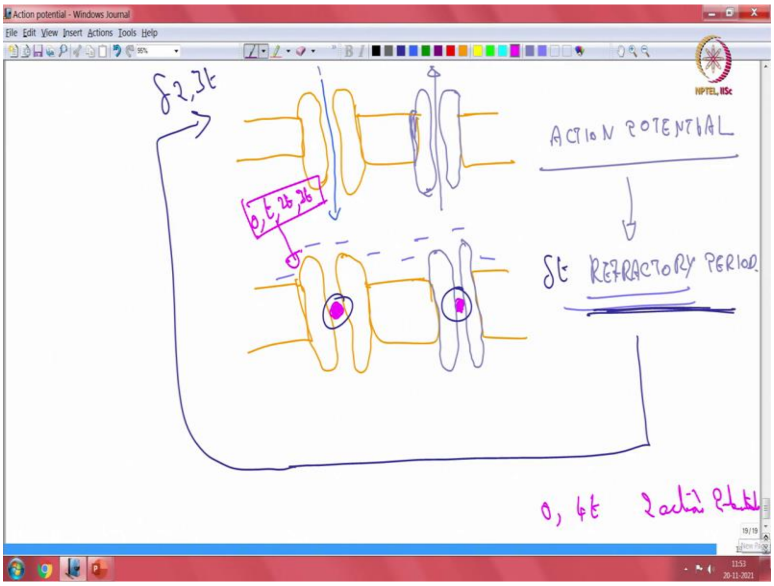

So, I need both the channels, so we start with the sodium channel which is here and the potassium channel which is here ok. So, stimulus applied you have sodium which comes in potassium which goes out. So, that is in the, so this is in the action potential time. So, that generates the action potential now there is something called as refractory.

So, what happens here is during this phase the sodium channel remains closed, potassium channel remains closed this is the native state of the membrane, but the key point to be understood is if even if you put a stimulus you know you put in negative charge there is no change in the block.

So, there is a particular time of after an action potential when there is recovery of the cellular parameters, we see we have been discussing all these things in isolation none of these things ever work in isolation. They are part of a huge complex mechanism of several kinds of systems which are running literally and parallel. So, concurrency problems have been solved by the cell millions and billions of ages back we have solved concurrency I think it is still not solved to be frank.

So, these are problems which have been taken care of a long time and maybe somewhere down the evolutionary pathway somewhere it was realized that you need to have a refractory period. So, a refractory period is a time when you cannot activate the channel like it is supposed to get activated. So, you wait for some period of time and. So, this is after say some period of time T Δt and after some more time Δ2 or 3 t you can again stimulate the cell.

So, even if you apply a continuous stimulus. So, you know you have stimulus applied at 0, t, 2t and 3t you do not have responses within the cell. So, it is only after say 4t. So, 0, 4t you will have two action potentials, look at it graphically.

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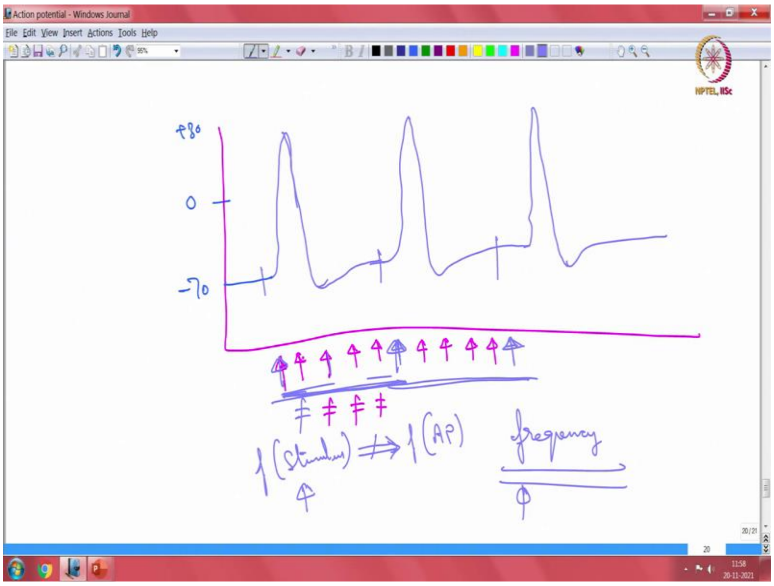

So, resting membrane -70, 0, +30. So, we first started a stimulus over here then that produces an action potential see this curve is not so symmetric it is not symmetric. Because the potassium and sorry sodium and the potassium channels are not very symmetrical electrically. So, the changes which happen are slightly asymmetrically, sodium up upstroke is far sharper and steeper than the.

So, the slope of the sodium part of the story is steeper than the slope of the potassium side which is more slack and that the overshoot which comes back to its more it takes a lot more time. So, they are not very linear. And that is why this particular wave form has a very specific shape and that shape as I told you is conserved for a given set of neurons and even set of species.

So, you imagine that we when we given this stimulus, we given one more stimulus what actually happens, nothing happens, we give another stimulus over here nothing happens, give another stimulus over here nothing happens. Another stimulus over here I will not compound this, there is something else which can happen over here, but I will not include in this current discussion.

So, after the membrane potential has reached back to normal and you apply a stimulus which is of course, the sequence of stimuli which is happening over here the action potential is generated again. Same neuron, same membrane different time periods single stimulus same amount of stimulus ok. So, stimulus is the same response happens only from 2, same thing.

So, we continue that further no response, no response, no response, no response then there is a response. So, the response is another action potential and then it goes over here. So, what I would like to convey is that particular membrane segment can give a particular frequency and that frequency can is in multiples of course, we have a continuous stream of stimuli assuming that we have a continuous stream of signal stimuli the freak function of stimulus does not correlate to frequency of action potential ok. So, it does not correlate to that and function of action the action potential in turn is.

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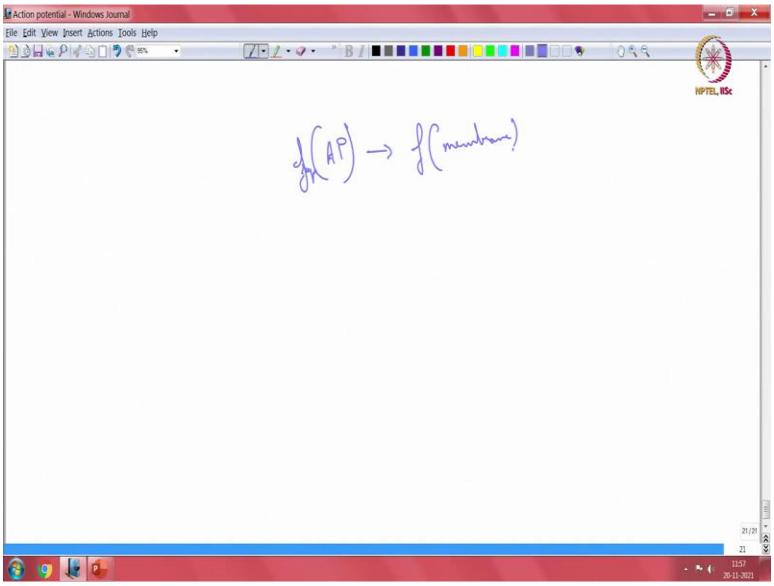

The frequency of an action potential, this frequency of action potential is a function of the membrane. So, both these are important things. So, for a continuous strain of stimuli frequency depends upon the membrane more than that of the stimulus, but if you look at it there is a particular thing which has to be understood as that.

Suppose your frequency of stimuli itself is only here, then frequency of input is equal to frequency of output that is stimulus to action potential is equal to 1, if it is lesser, you increase the increase it further. So, you have got only stimulus over here, still it is you know the membrane can generate the same output frequency as the input frequency.

So, actually the frequency actually depends upon the membrane and the rate at which the stimulus is applied to the membrane, the action potential amplitude remains the same. So, that concludes this part of the story.