Demystifying the Brain
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Lecture – 06
Neural Signaling: Molecular and Cellular Basis

Welcome to lecture 3 segment 2 of this course Demystifying the Brain. So, in the last lecture we talked about brain structure and this lecture we are going to talk about neurons and neural signaling.

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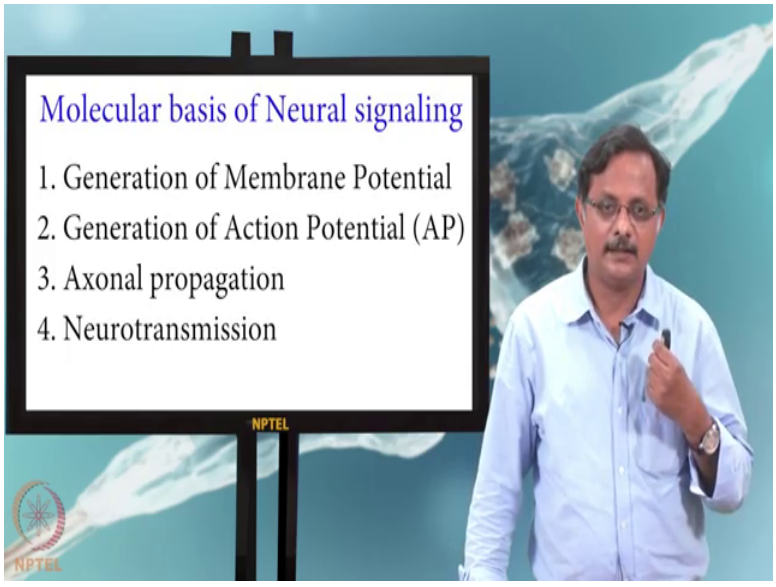

In the previous segment of this lecture we were talking about different signaling components and neuron we said there are four components, there is a generating process then the summation the soma then there is axonal propagation and finally, there is synaptic transmission or neurotransmission. We simply describe these signaling processes, but we did not describe what is the cellular and molecular basis of this signaling processes; how are this process generated.

So, that is the subject of the current segment. So, in this segment we will talk about how is membrane potential generated; how does a neuron generate this electricity right. Then we will talk about how does an action potential form, how is generated and then will talk about axonal propagation and neuron transmission. And we will basically talk about the molecular basis of all these four signaling processes.

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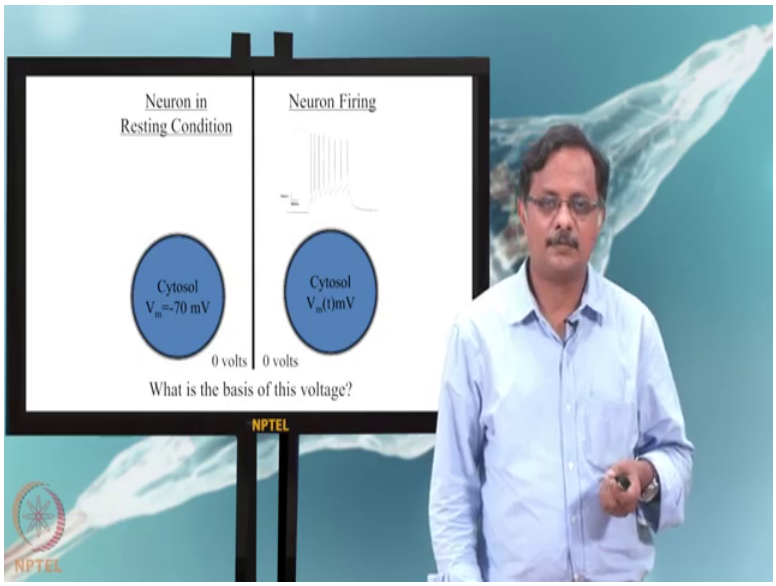

So, we have described in the last segment that neuron can live in two states; there is a resting state where the membrane potential is at constant value of about minus 70 millivolts. And then there is a excited state where the membrane potential exhibits this fast by packing activity that called a action potentials.

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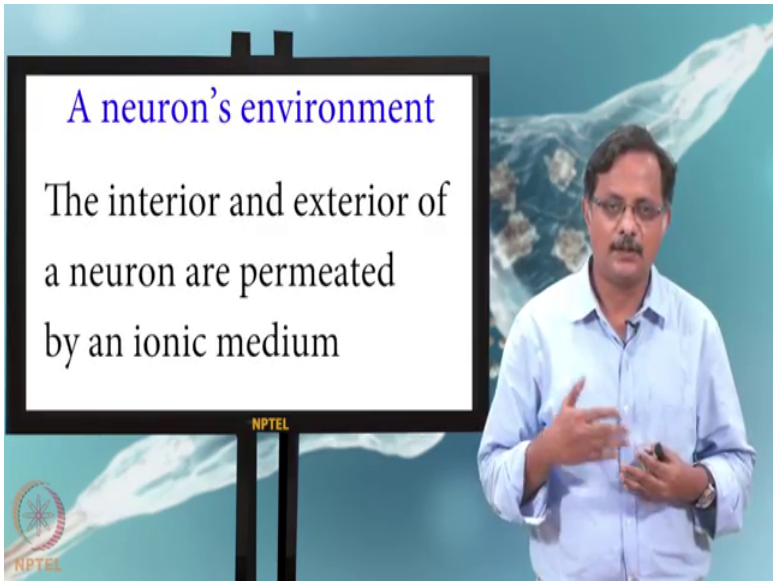

Now, where is this voltage coming from? Now we must remember that any cell red and neuron 2; lives in a environment which is full of ions it is a it is ionic medium both the

interior and the exterior of a neuron all right is permeated by an ionic medium and this medium consists of ions.

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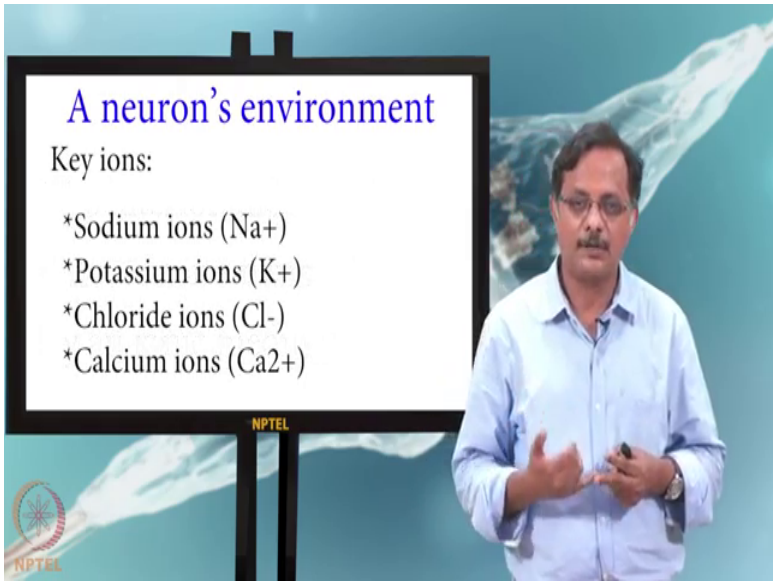

Like sodium ions, potassium ions, chloride ions and calcium ions.

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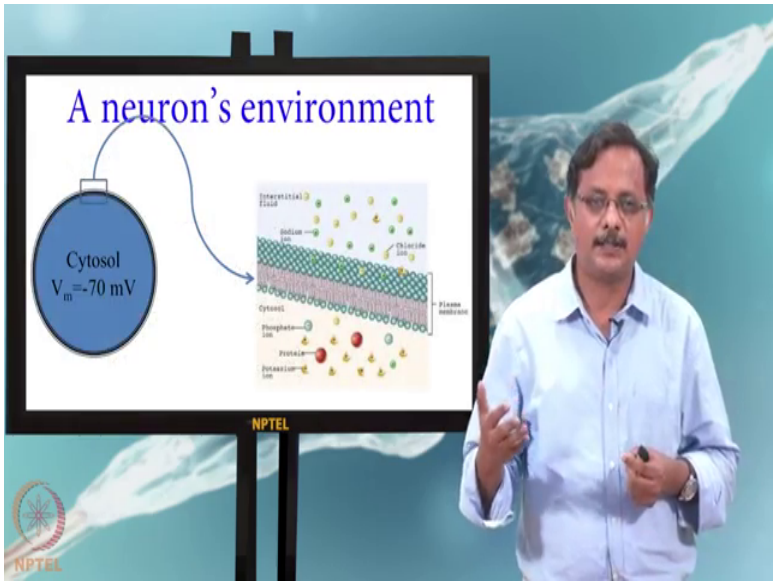

And these are separated by the cell membrane or the plasma membrane which consists of two sheets of lipids or fatty molecules and they separate this two medium.

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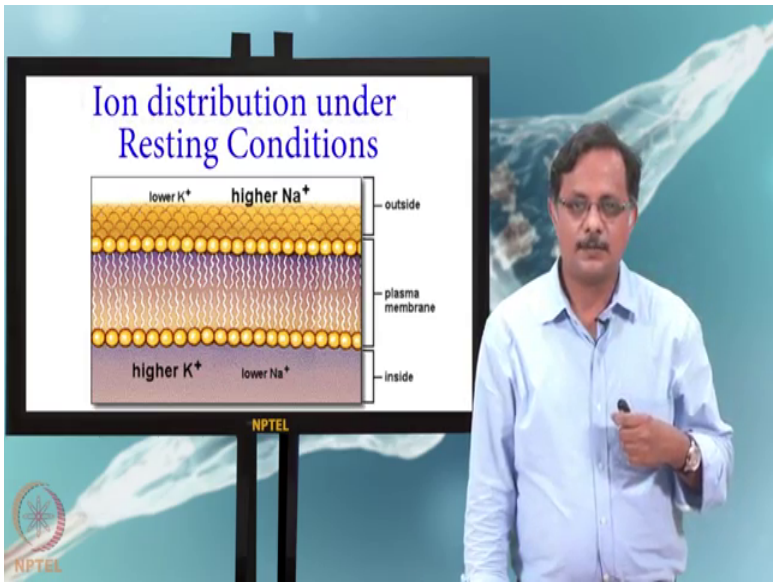

And these ions are distributed differently both in inside and outside of the cell.

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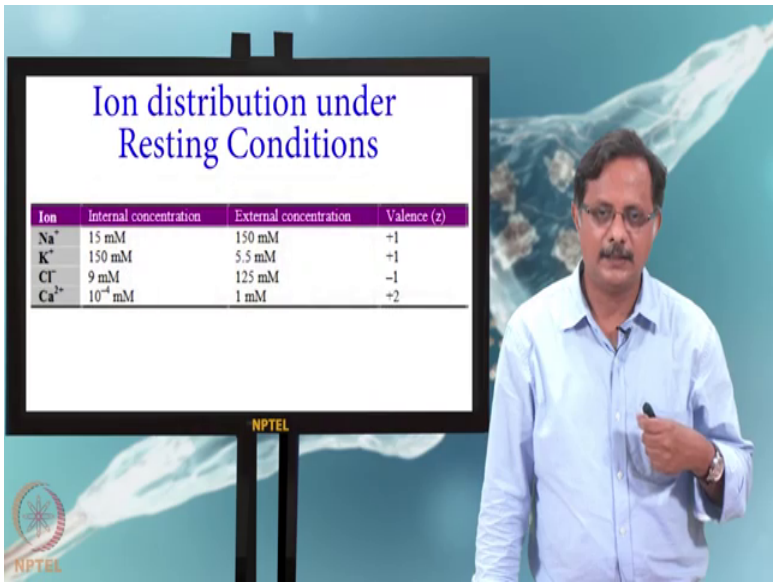

So, for example, we look at the table given here the inside of the cell the sodium concentration is low and outside it is high. And potassium concentration is a high inside and low outside and they similarly chloride is low inside and high outside and calcium is high outside and low inside. So, the thing is the four kinds of ionic species of distributed differently between inside and outside of the neuron.

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So, addition to ions then there is a membrane there also the structures called ions channels which are like holes set inside the inside the cell membrane the plasma membrane and these are actually large protein molecules which have some kind of a you know passage in the middle of them this passage allows ions to move from inside to outside.

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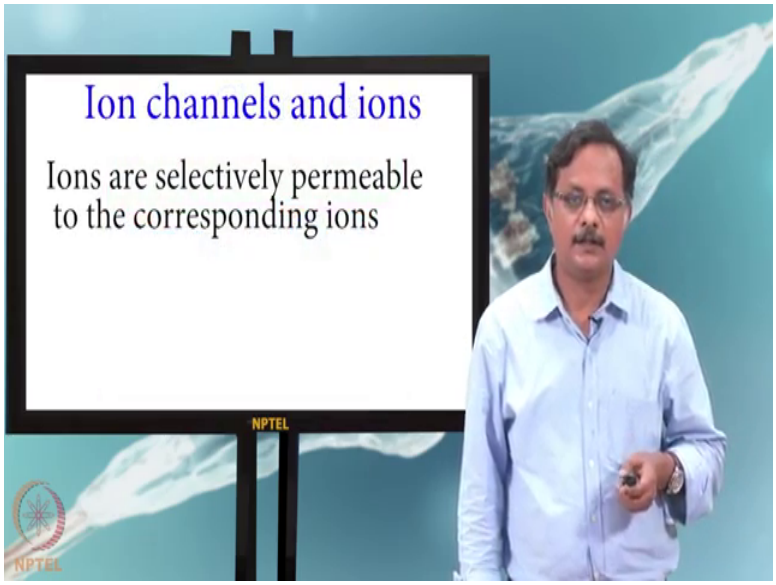

And there are many different kinds of ions channels and very often these channels are specific to certain kinds of ions.

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So, for example there are sodium channels which allow passage of sodium ions or there are calcium channels which allows passage of calcium ions and so, on and so, forth. A lots of channels are mixed they can allow a multiple ionic species, but typically channels are specific to certain kinds of ions.

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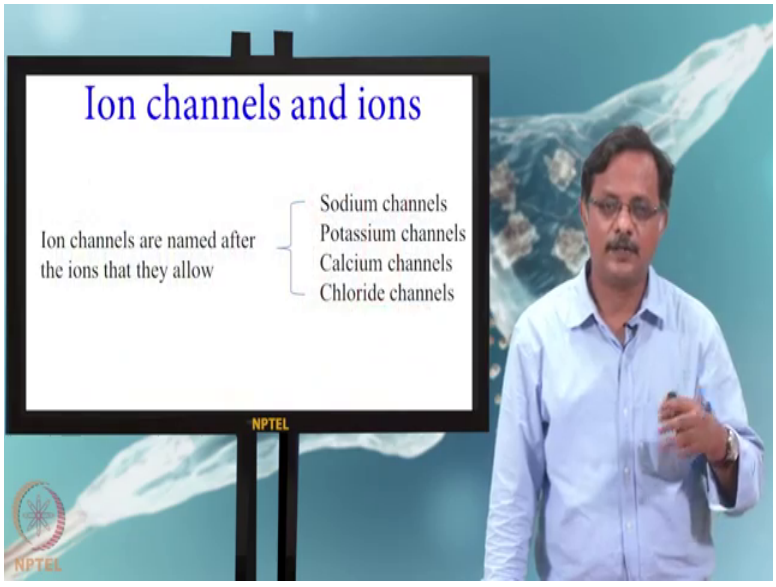

So, very often the channels are named after the ions if they have allowed. So, that you can have a sodium channels, potassium channels, chloride channels and so on and so, forth.

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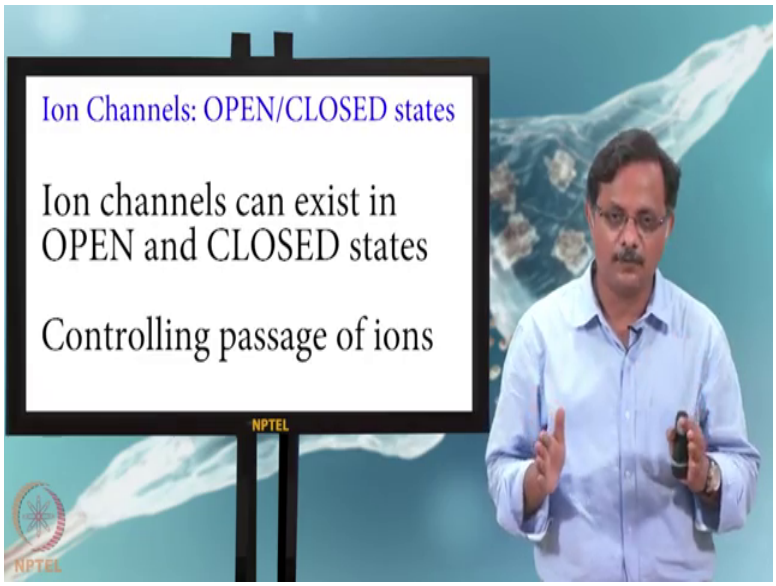

Now, what is most interesting and important about the channel is that they are gated. So, they are so they the passage can be closed if you want right or left open if you want.

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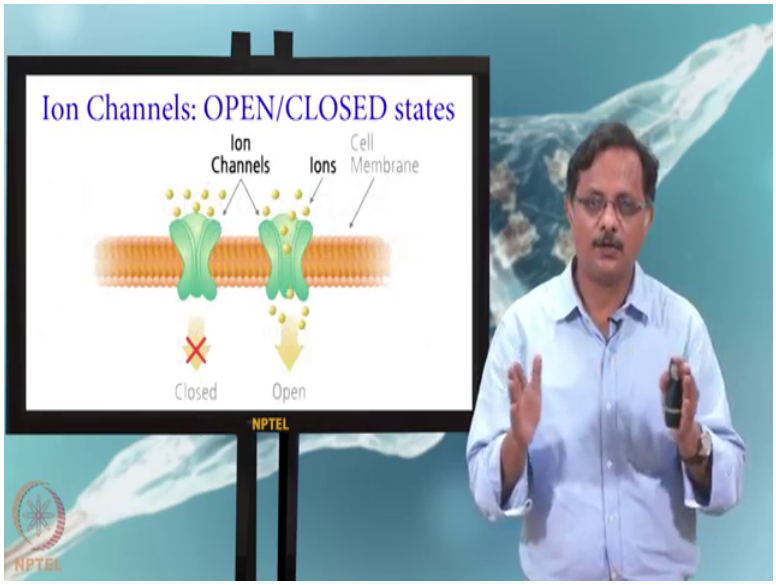

So, this opening and closing activities of channels can be controlled by many factors. So, this; so, the ion can exists in open or closed states and therefore, flow of ions to them can be controlled by various processes.

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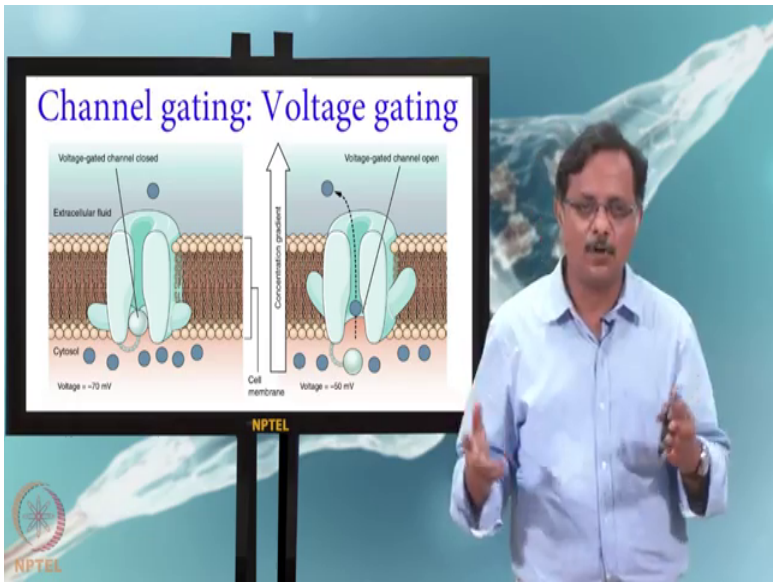

So, this the process by which a channel can be opened or closed is called gating all right; controlling the gating activity of channels is called is called gating. And there are several kinds of gating mechanisms we will talk about only two in this current lecture; the other two are not relevant to the current discussion.

So, there is something called voltage gating where by changing the membrane potential; you can change the open closed of state of the channel. Example in this slide you can see on the left a channel is closed or you can see a kind of a ball like structure which is blocking the passage and there is also kind of chain there; actually this is only a pictorial presentation; I mean in the real channel, you do not have balls and chains and stuff like that; it is just a conceptual representation.

So, on the left side we see a channel which is blocked and ions are not able to go through that. And then you increase a voltage then that opens a channel then the ions are able to pass ok. So, this kind of a gating is called voltage gating.

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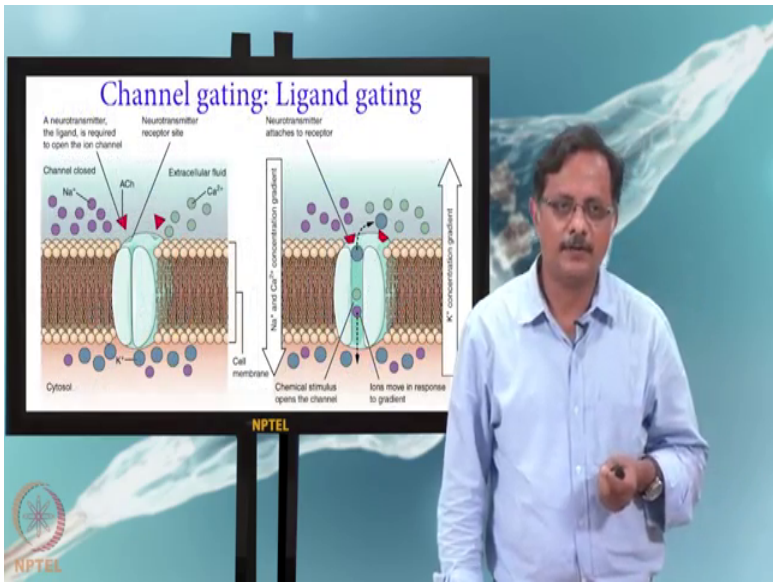

In this another kind of gating, which is very important for neurotransmission in this case the factor that opens a gate of a channel is not voltage, but a chemical of which is called a ligand.

So, this kind of gating is called a ligand gating. So, in this figure you can see that on the left side of the slide, you can see the channel is in the closed state. And on the top of the channel you see a couple of red objects hovering on top of the channel these are actually a molecules of a neurotransmitter called as the colin ok. And in the in the left figure, you see the as the colin is not yet is not yet come in contact with the channel. And on the right you see that the as the colin molecule as it come into contact with the channel and actually bound with the channel receptor of the channel and as a result of that the channel opens and then it close passage of ions.

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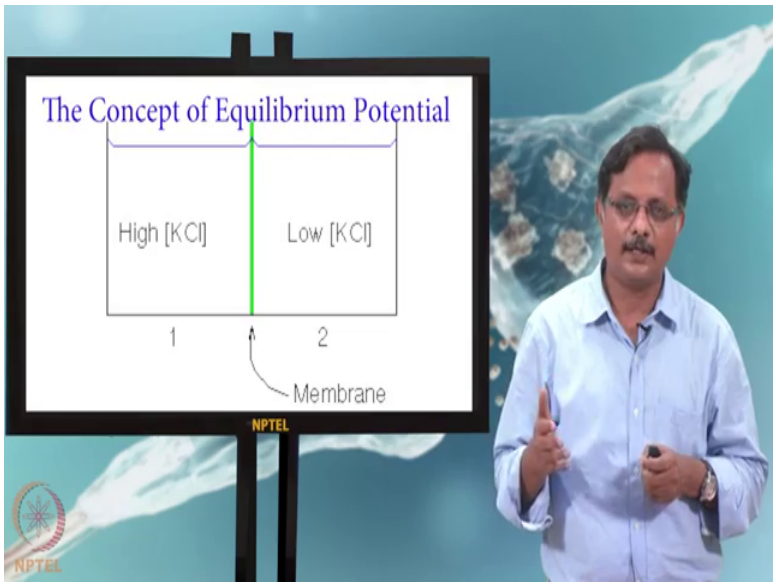

So, this kind of a gating which is mediated by a molecule or a ligand is called ligand gating. So, we just talked about some other cell a molecule machinery in the in the neuron which are responsible for relatical activity of the neuron. But exactly how do you control this molecule machinery to control the membrane voltage and produce neural activities like action potentials?

So, let us start from basics. So, we need to first look at the concept of equilibrium potential or some of this concepts you might have heard, you might have become familiar and your high school electro chemistry; so, let us quickly revise that. So, imagine there is a compartment which has a you know there are a vessel which has two compartments left and right. And both compartments are filled with you know potassium chloride red solution on the left side the concentration of KCl is high; on the right side it is low.

And the two compartments are separated by a membrane which is permeable to both potassium and chloride. So, as you know that because there is a concentration gradient from the left to the right; a both potassium and chloride ions move to the right ok.

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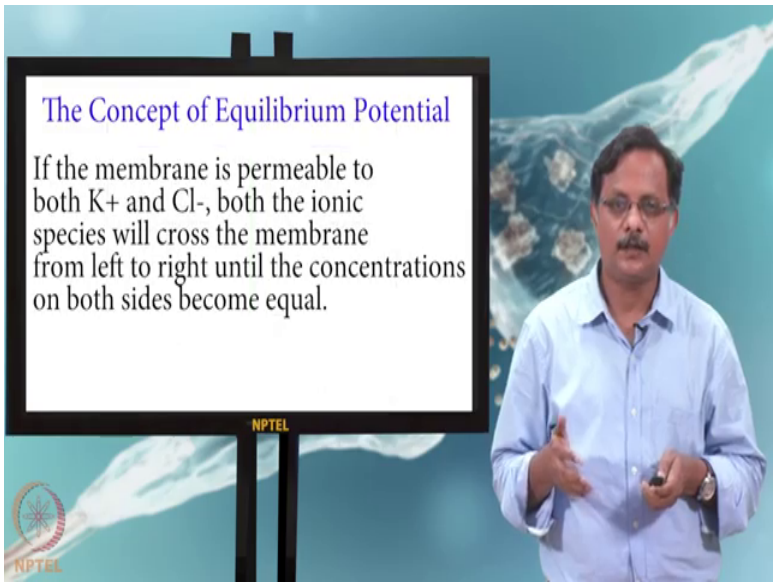

And so, this process keeps continuing until a concentration of the KCl on both sides are equal. So, at the end of we will just have a vessel in which both compartments have equal amounts of a KCl. So, nothing very interesting happens in this case.

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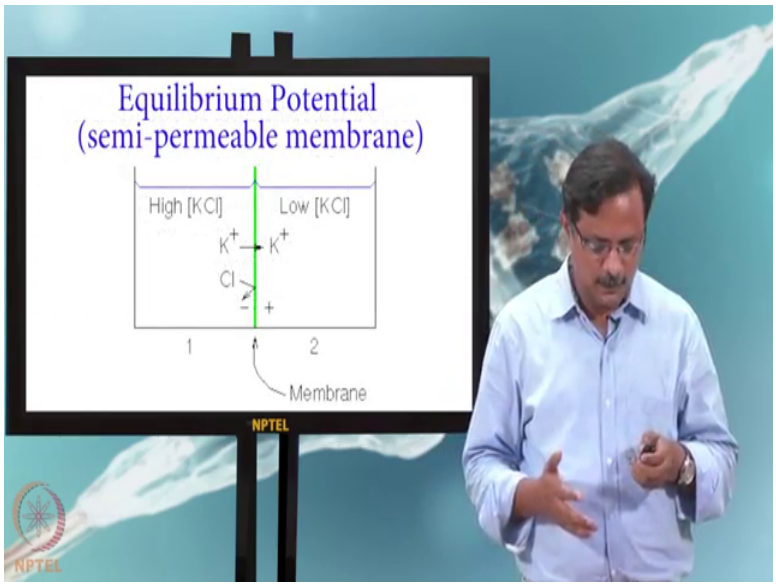

Now, let us take a slightly different situation where you have a beaker and that the and there is a high concentration KCl in the left side and low concentration KCl on the right side like before. But this time the membrane that separates the two compartments is semi permeable that is it allows only potassium to pass, but not chloride.

So, in this situation since potassium is allowed to pass and is potassium is of high concentration on the left side and low on the right; potassium from left starts more defusing towards the right and crossing the membrane, following the chemical gradient because chemical concentration is high on left and low on right

So, the chemical gradient right driving the flow of potassium from left to right, but as this keeps happening the potassium ions keep building up on the right side and creating the partial chart and therefore, increasing the voltage on the right compartment. As this keeps happening the voltage on the right compartment keeps increasing; there by creating an electrical gradient which counters the chemical gradient which was preexisting. So, at some point the chemical gradient and the electrical gradient exactly counteract each other and analyze each other. So, at this point there will not be any further flux of potassium from left to right. So, system would have re equilibrate at this point.

So, in this state you still have a voltage; a higher voltage on the right side compared to compared to the left. Initially we solve of with with this with the configuration where both the compartments are neutralized electrically neutral, but because of the presence of a semi permeable membrane and differential in the concentrations of the solution right; we have ended up with the situation where there is higher voltage on the right compared to the left ok. And this voltage that you get is equilibrium potential of the system; it is calculated by a formula called a Nernst potential ok.

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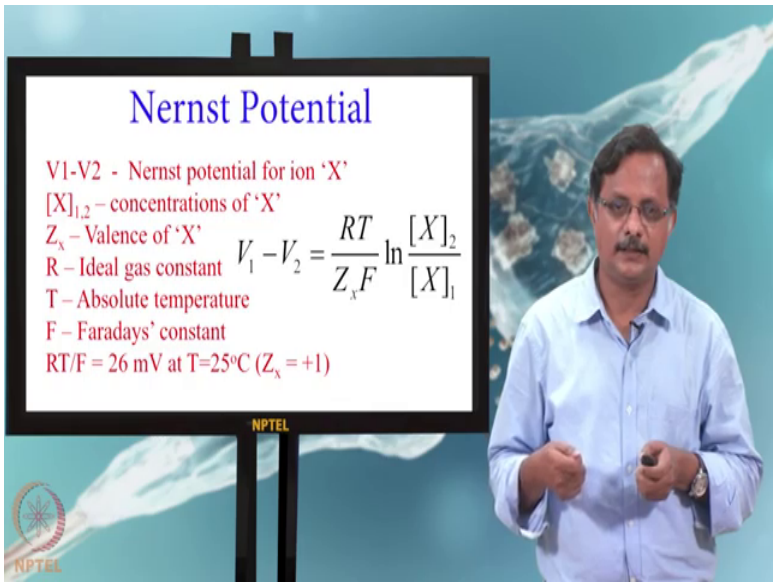

So, in this formula gives basically the relationship between the concentrations of the ion that we are interested in this case a potassium ion right and the ratio of the concentrations between two compartments and the voltage difference between two compartments these two quantities related by this formula. So, you see that in this formula on the right side we have capital R which is the ideal gas constant. Then the capital T which is absolute temperature then the Z x is the valence of the ion.

So for example, sodium as valence of plus 1 production was the balance of plus 1 and so, on so, forth F is the Faradays constant. So, at room temperature of 25 degree centigrade the RT by F for valence equal to plus 1 turns out to be 26 milli volts and that can be used for simplifying your calculation of Nernst potential. So, and then you have this is this is the factor then you have long which is a natural logarithm of the ratio of the concentrations on the right side or X 2 by X 1. So, see that the voltage difference between compartment 1 to 2 is related to the ratio of the concentrations between compartment 2 to ok.

So, if you remember that will calculate some of the Nernst potential of various ionic species in a moment, ok.

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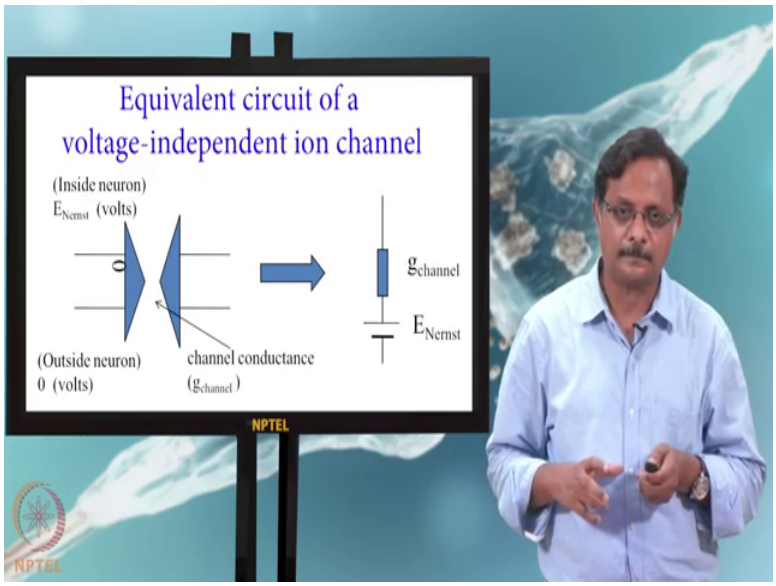

So, each ionic species whether it is sodium or potassium creates a kind of a Nernst potential depending upon the ratio of concentration of these ionic species between inside and outside of the neuron. So, we already have described that each of these ionic species has certain ratio; have certain differential distribution between inside and outside. So, because of this each of the ionic species produces a certain Nernst potential.

So, therefore, given channel can represented by a kind of a battery which is the whose voltage is equal to the Nernst potential of that channel. And also the channel itself has a conductance because it allows ions which is a current. So, the structure allows passage of current therefore, it has some conductance; so the whole ion channel; iolitically speaking kind a represented as a series of a conductance and a battery.

So, this is the represented on the right slide as a series circuit of a conductance g channel, which corresponds to the conductance of the channel and E Nernst which corresponds to a Nernst potential of that channel and the corresponding ionic concentrations. So, so, basically you can represent a channel as a series of a conductance under and battery which is Nernst potential.

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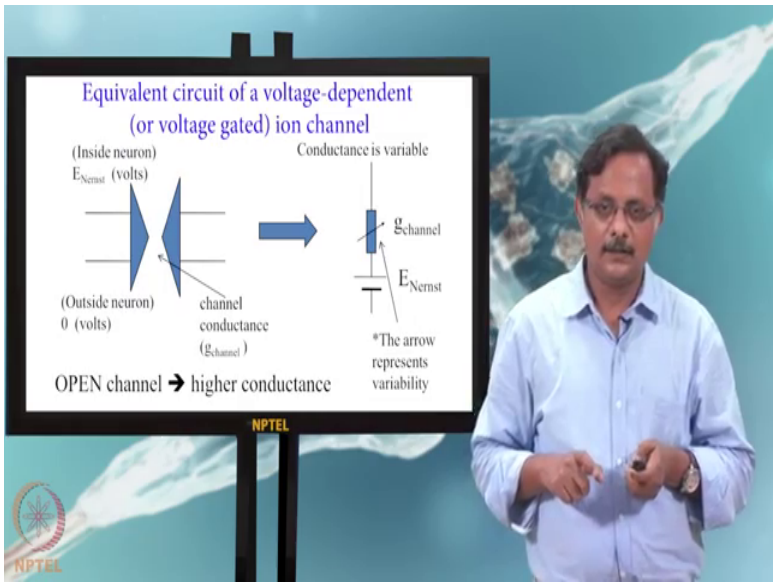

Now, here we have two situations. So, we some channels which are voltage dependent where they have voltage gating and there are channels which are not voltage dependent. So, they have voltage independent.

So, the channel is voltage dependent then; that means, it can open or close by a function of voltage of membrane voltage. So, therefore, the conductance of the channel can be variable because open channel means, it can allow passage of ions more easily which means it has higher conductance. So, whenever you represent a voltage dependent ion channel; the corresponding conductance is a variable and that variability is denoted by that arrow which cuts across the conductance as shown in the figure.

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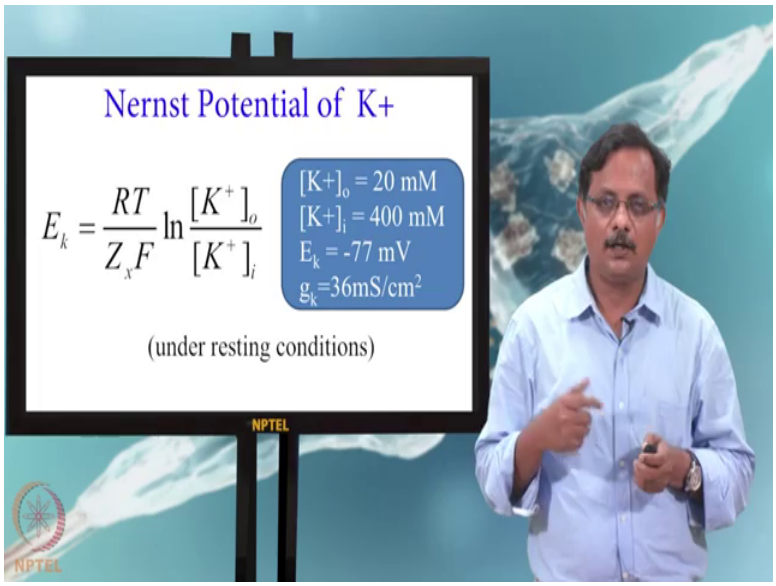

And so, now, let us look at the Nernst potential of potassium. So, potassium like we describe before is low in concentration outside and high in concentration inside and if you plug in this two values; so, it is outside it is 20 milli molar, inside it is 400 milli molar; if you plug in these values, you will get a Nernst potential of potassium E K as minus 77 mile volts. And below that you have g K which is a conductance of potassium channels under resting conditions. So, that is 36 millisiemens a per centimter square.

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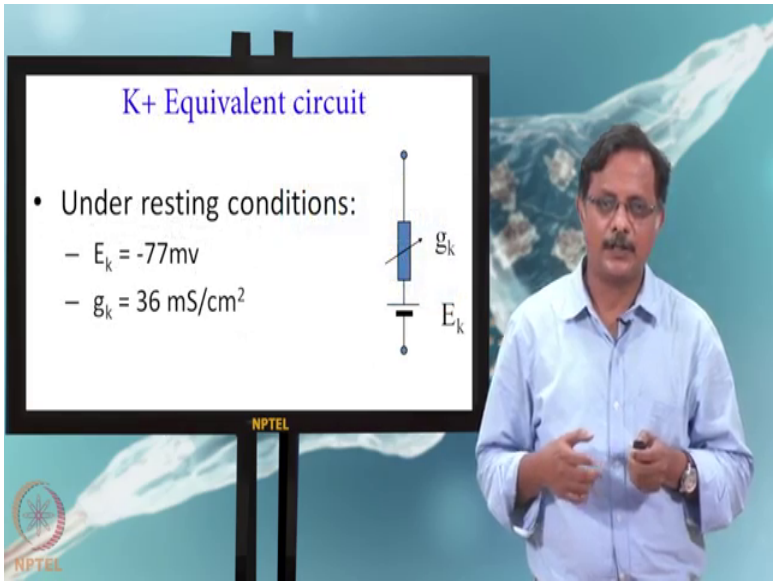

So, therefore, potassium equivalent circuit can be represented by a series of a conductance g K alright and battery E k.

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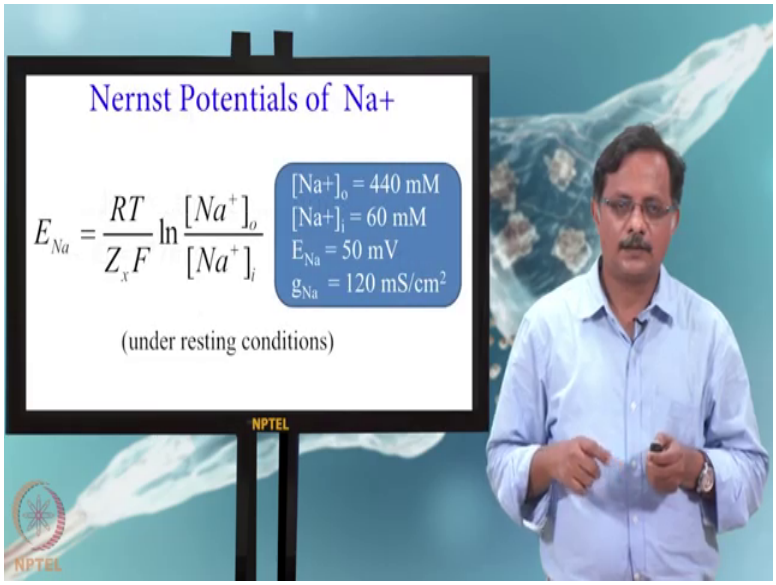

So, now let us calculate the Nernst potentials potential of sodium. So, sodium is high outside for a milli molar and blow inside 60 milli molar therefore, if you plug this numbers into the formula right you get an E N a value of 50 milli volts. So, sodium Nernst potential is a positive value and then g N a; the conductance of sodium channels under resting conditions is 120 millisiemens per centimeter square.

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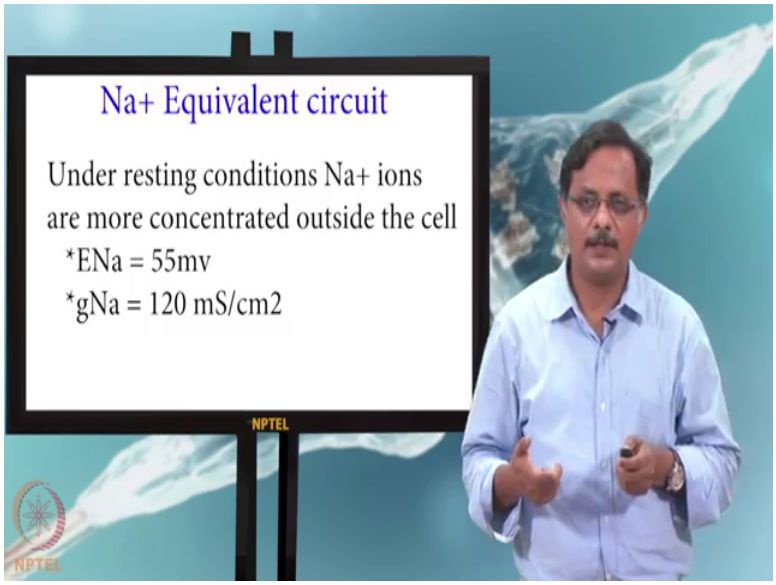

So, therefore, the sodium equivalent circuit can be described as a series of a conductance under battery where conductance is g N a and the battery is E N a.

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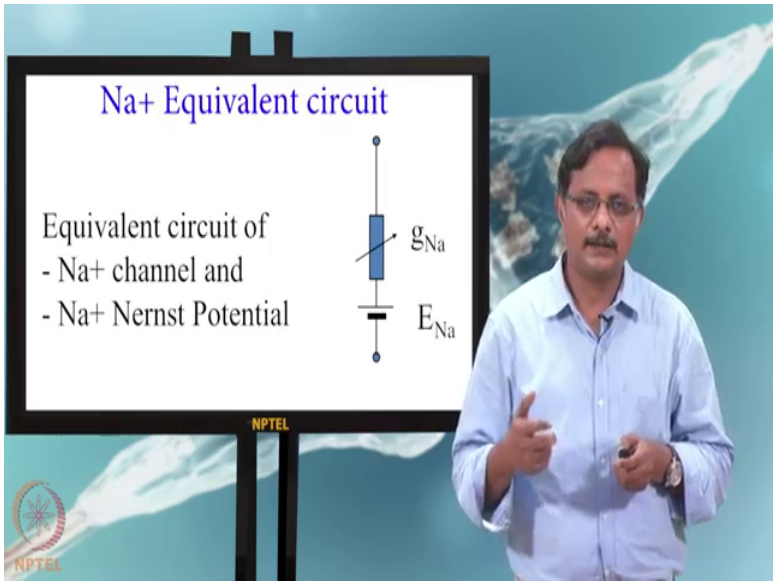

When there is a; so, we have like I said two kinds of channels membrane voltage dependent and voltage independent.

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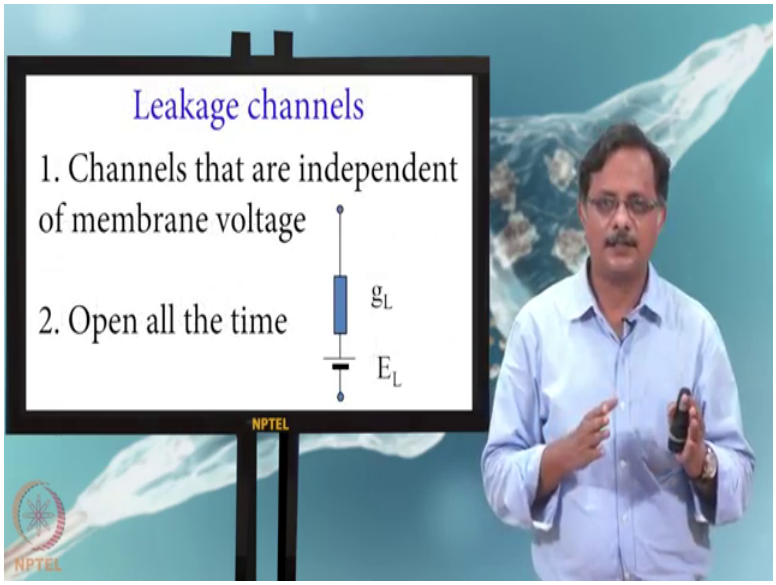

So, voltage independent channels are kind of open all the time the; they do not they are not a controlled by a voltage. So, therefore, they are called leakage channels because the kind of imagine that the leaking ions all the time from inside to outside. So, these

channel can be represented by a constant conductance. So, they are they are not variable and in series with a battery which is called the kind of called a Nernst potential of the leakage channels.

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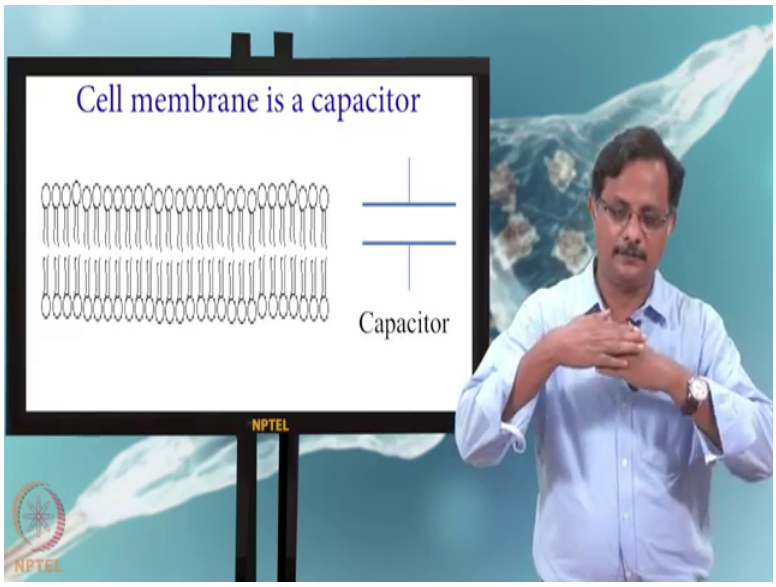

So, there is one more electrical element in a neuron membrane which we have to consider if you want to in order to understand the electrical activity of the neuron that element is the cell membrane itself.

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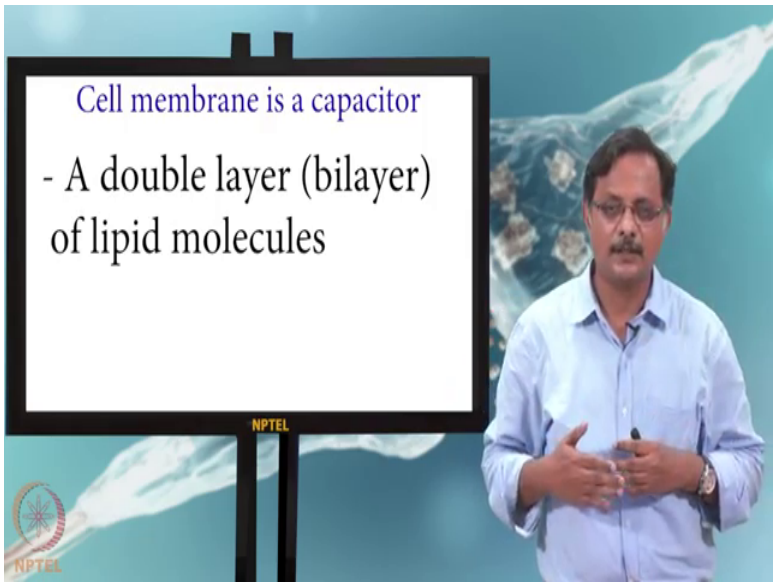

So, we have described before the cell membrane consists of two sheets of lipids or this fatty molecules right and these two sheets form kind of insulating sheets right insulating cover for the neuron.

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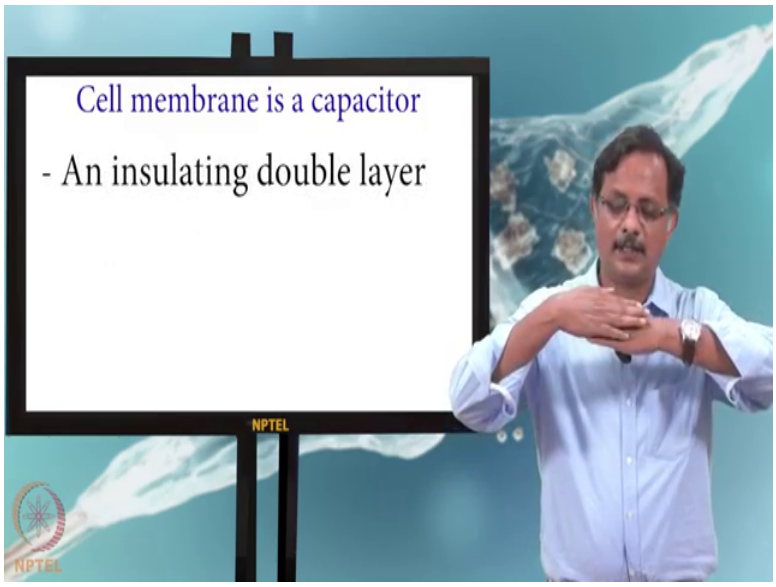

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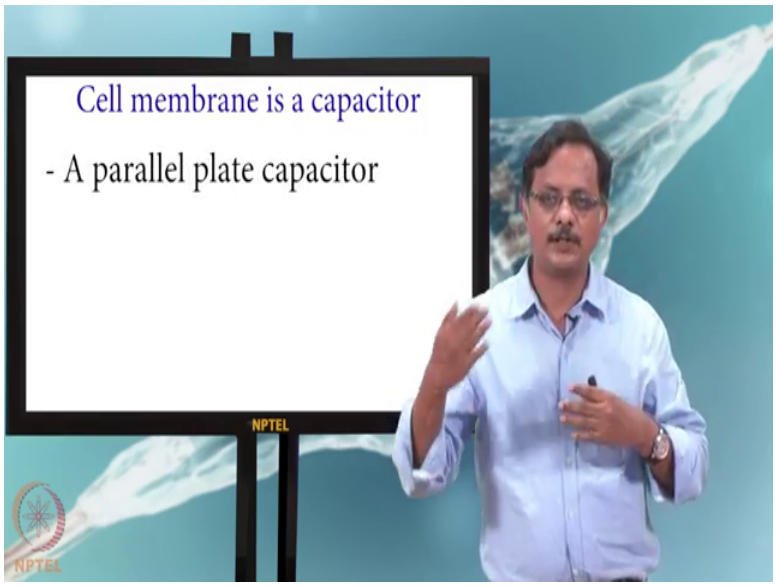

And the y can be compared to a what is called a parallel plate capacitor which you might have studied in your high school circuit theory ok. So, we can represent the membrane itself as a parallel plate as a capacitor.

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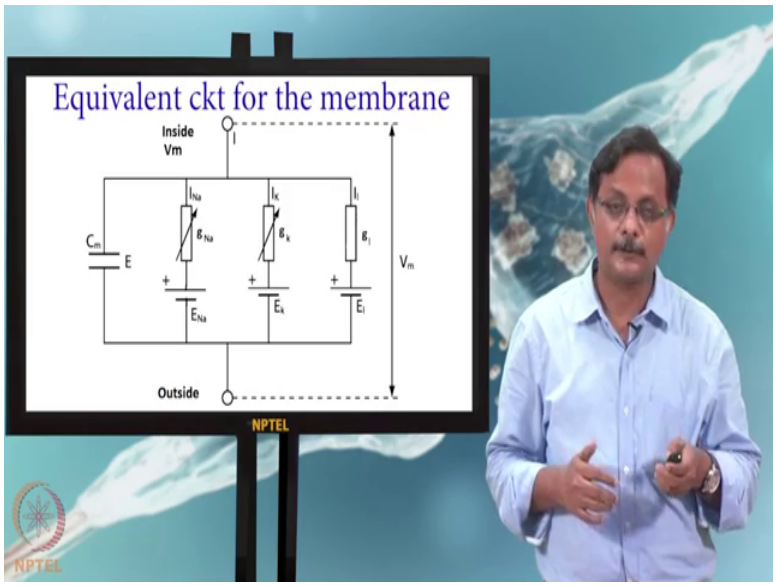

So, if you combine all these observations; you can construct a kind of a circuit model of the neural membrane. And this circuit model consists of a capacitance which represents a cell membrane itself. And then I have one a conductance and battery branch which represents sodium channels, then the next one represents a potassium channel and the last one represents the leakage channels. So, this whole thing as a circuit model of red of a neuron membrane.

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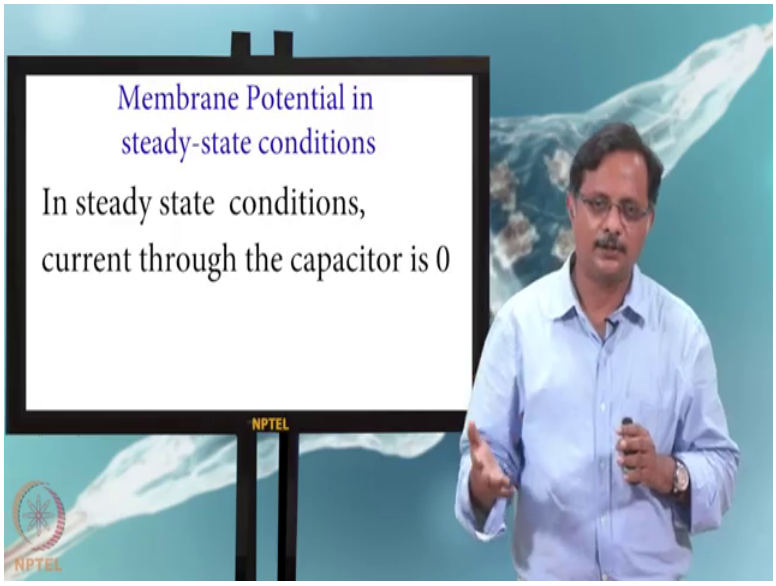

So, now let us consider what happens in this circuit under ideal condition under steady state conditions. So; that means, there is no nothing is changing in the in this circuit and you know currents are all constant and voltage is constant right. If you consider that kind of a situation, you can do some simple analysis from your circuit theory.

And I am not going to into the details of these calculations.

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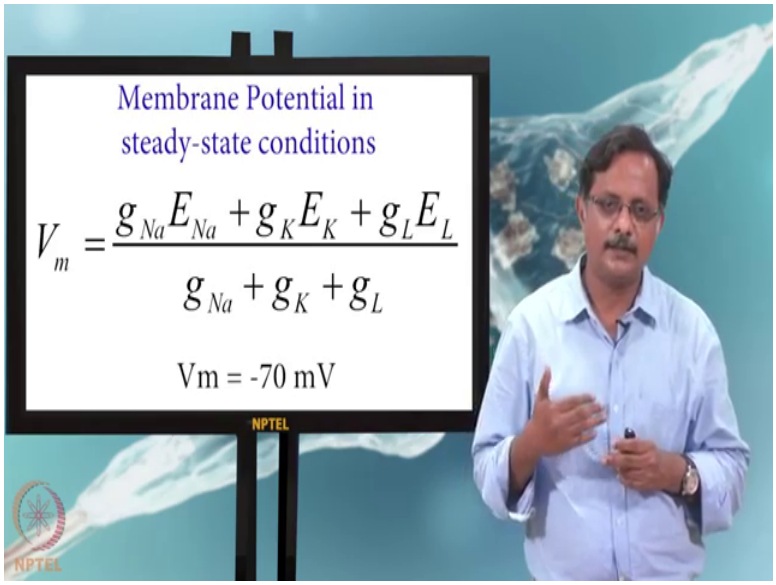

But it is sufficient just to you know understand that this is the formula that gives you the relationship between the conductances and the Nernst potentials right under membrane voltage. So, it goes as V m is equal to g N a; E N a plus g K, E K plus g L; E L divided by g N a plus g K plus g L.

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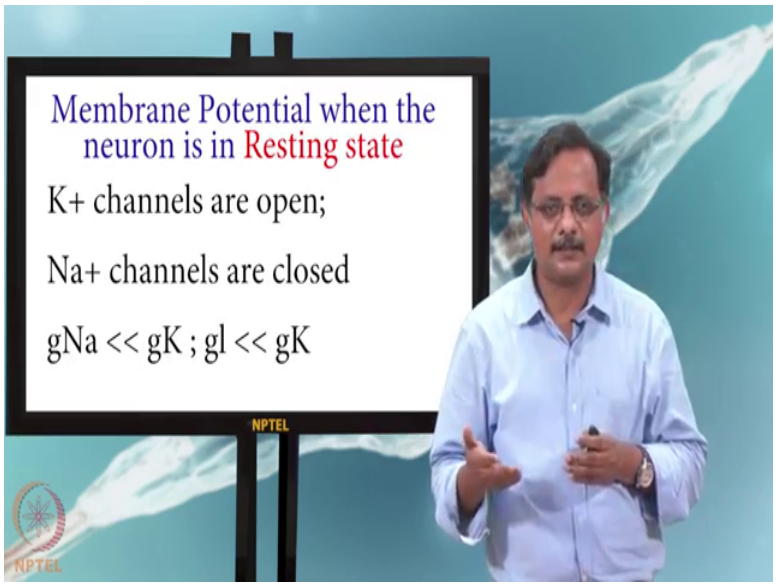

So, now under resting state let us see what is the V m value that we get. On the resting state it so, happens that potassium channels are open and sodium channels are closed that is the that is how these channels work in resting state. What; that means, is sodium conductance is much lesser than potential conductance and typically leakage conductance is generally very low.

So, that is also taken to be much lesser than g K. So, g K dominates the formula right in under resting state. So, if you plug in these conditions into the formula here right in the numerator g K, E K term becomes dominate; the denominator g K terms becomes dominate.

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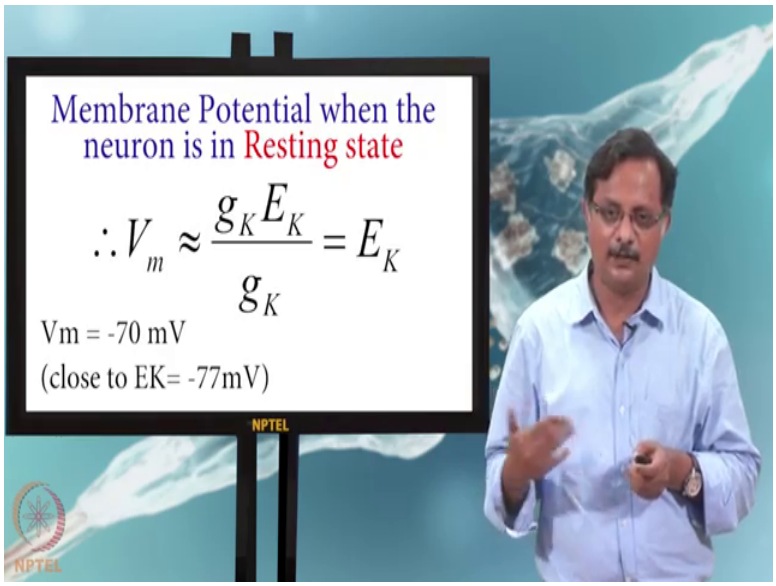

So, if you make this approximations right you get V m is approximately equal to g K; E K by g K which is equal to E K. So, V m is approximately equal to E K and E K we already calculated to be minus 77 milli volts; actually V m under resting conditions is is about minus 70 milli volts. So, it is kind of close to the E K value of very low negative value of minus 77 milli volts.

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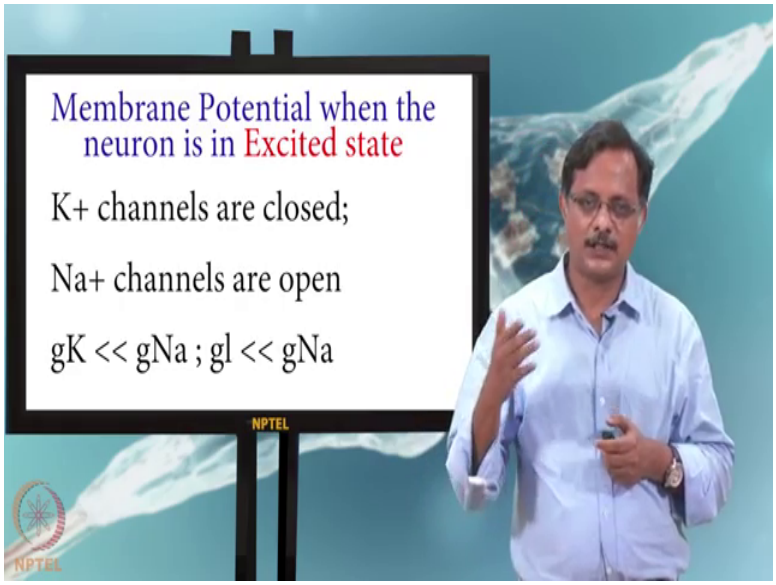

So, let us consider what happens under in a excited state. So, in a exited state it turns out that potassium channels are closed and sodium channels are open so; that means, in this case g K is a is is much lesser than g N a and g L is also much lesser than g N a.

So, if you plug in these condition into the formula here.

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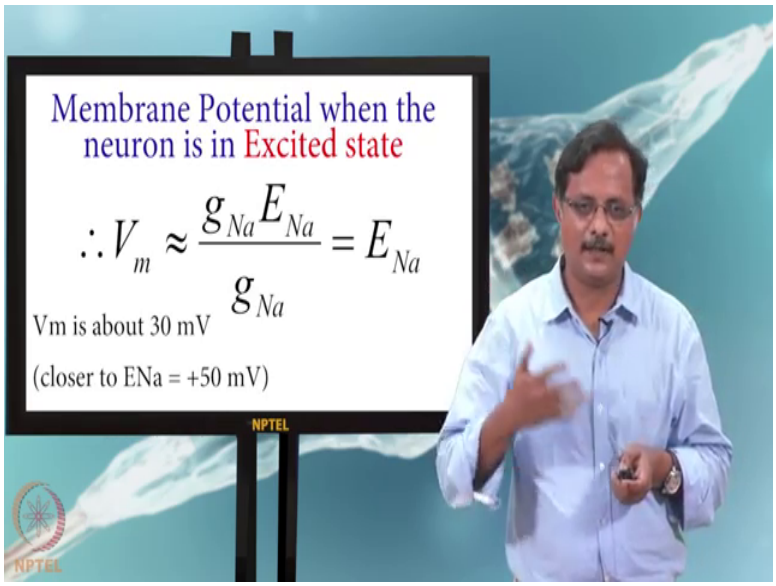

And then and the numerator you have g N a; E N a which dominates the expression in the denominator it is a g N a dominates a whole summation. So, if you if you assume that then we have the becomes g N a; E N a by g N a which is equal to E N a.

So, therefore, V m in this condition is approximately equal to E N a and E N a we know is plus 50 milli volts. And actually if you do not makes the approximation V m when there when the cell is excited, we will go as far as like you know 10, 20, 30 milli volts which is a positive voltage.

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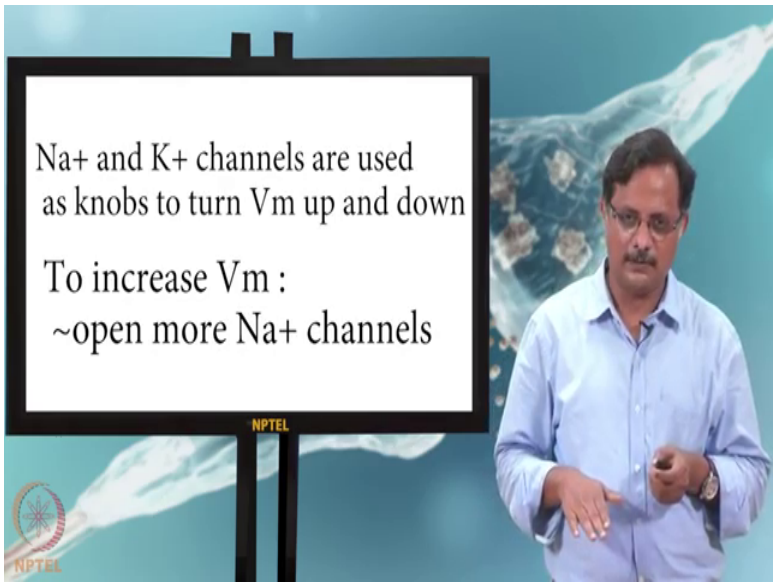

So, basically what we understand from these very simplified calculations is a sodium and potassium channels can be used as to knobs to turn V m up and down.

So, if you want to increase V m basically open more sodium channels and close potassium channels.

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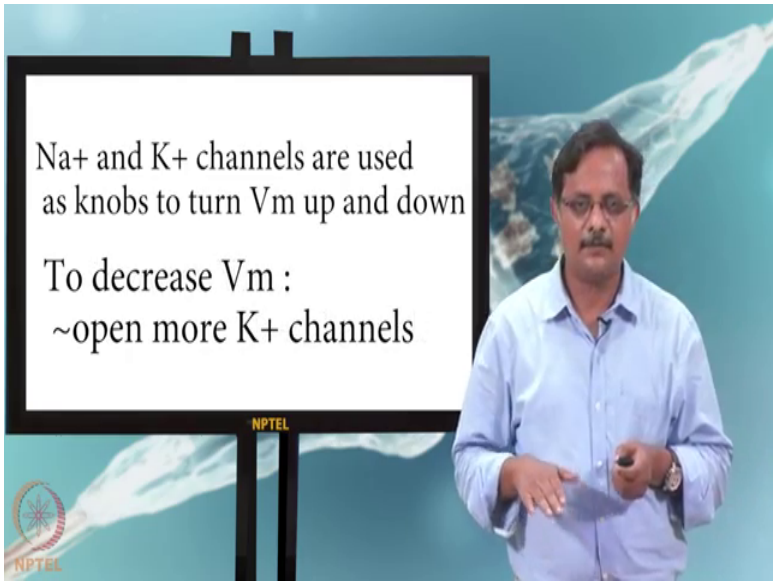

If you want to decrease V m open more potassium channels and close more sodium channels. So, this is like you know two knobs which you can control to turn V m up and down.

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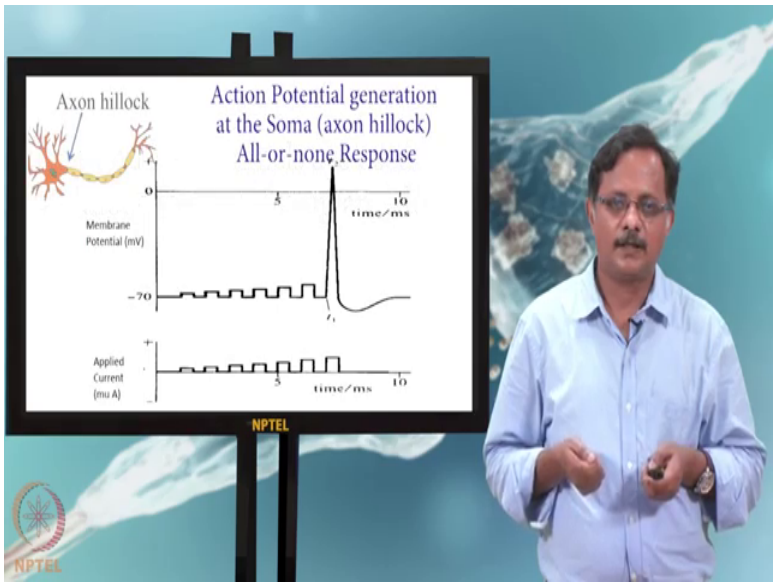

So, with this background now we can understand what exactly drives the generation of an action potential.

So, we have already seen the previous segment that when you give a current pulse to the to the neuron at the pioneer say axon hillock; as you gradually increase a current pulse amplitudes, there will be a threshold amplitude at which suddenly the neuron membrane voltage shows this sharp upward excursion and then which also rapidly falls down and just called the action potential.

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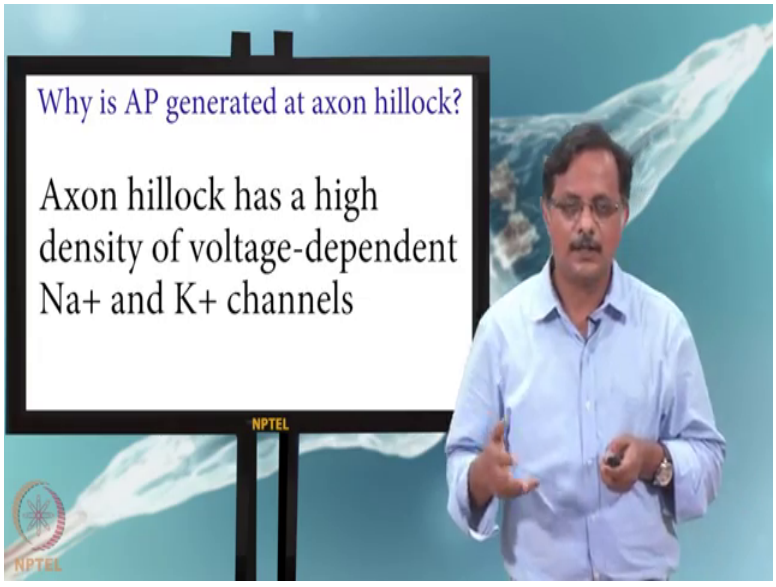

Why is AP generated at the axon hillock? So, main reason is that we have this high density of voltage dependent sodium potassium channels in the neighborhood of axon hillock and also on the all along the axon.

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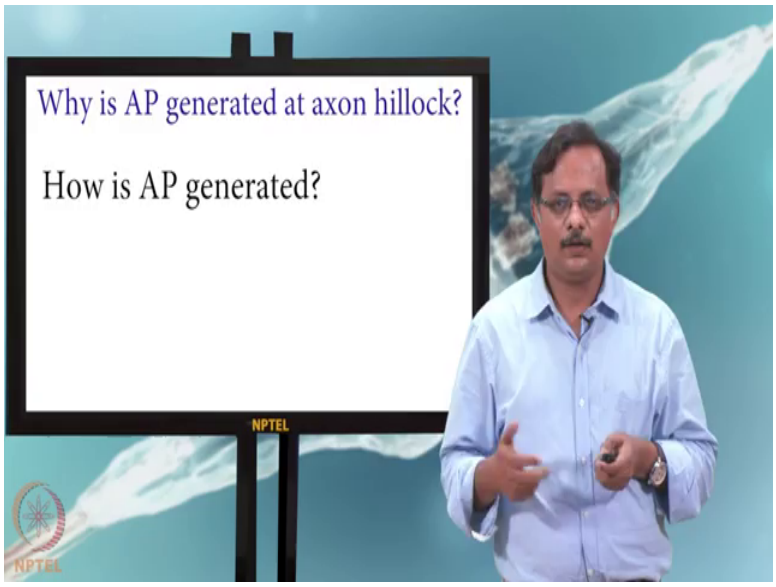

So if that is if that is true then what exactly happens how is AP generated?

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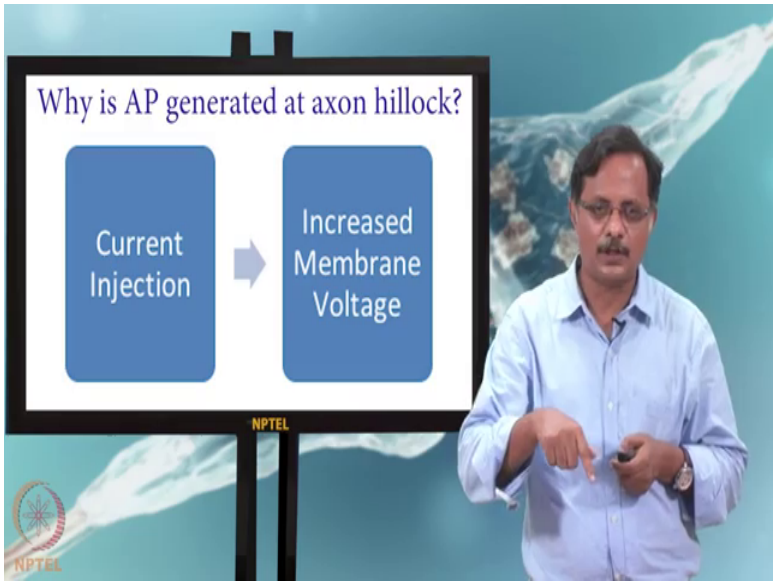

So, basically when you give a current pulse right, you give a current pulse into inject current pulse into the neuron and since you are in putting a positive charge into the neuron that increase the membrane voltage.

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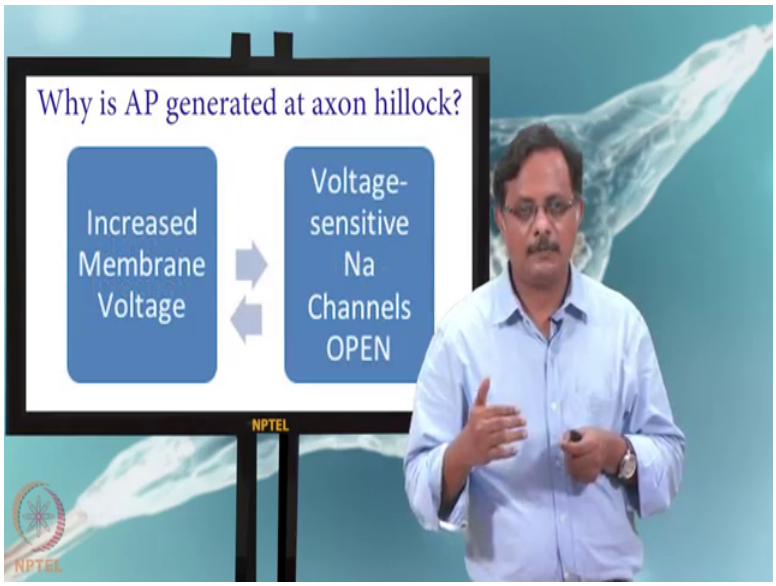

And when the membrane voltage increases towards positive values and because the sodium channels are voltage dependent and they tend to open that when the membrane voltage is increased. So, sodium channels open and we have just realized that when you open sodium channels that tends to increase a membrane potential. So, we have a interesting positive feedback situation here. So, your initial current injection increase a membrane voltage, which in turn increases opens further sodium channels and these in turn increase membrane voltage further and this process goes on a little bit.

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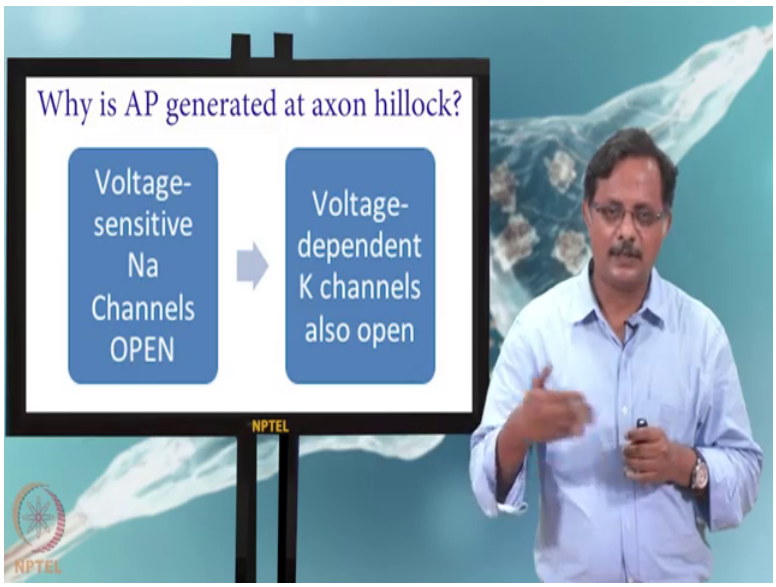

And then about this time the potassium channels also start opening right and then when potential start opening we know that increased potassium channel opening causes rate of reduction of membrane potential.

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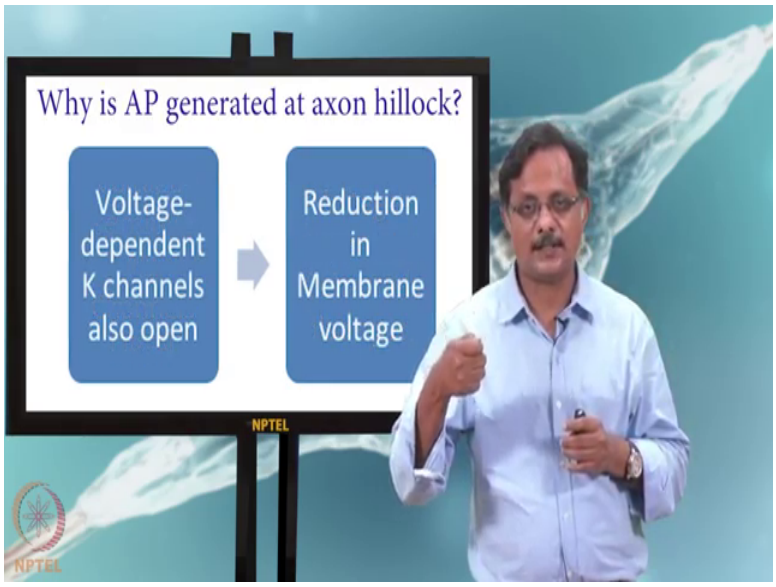

So, so, membrane potential start dropping and it drops back to the resting value and the process ends there ok. So, this can be seen in this series of images.

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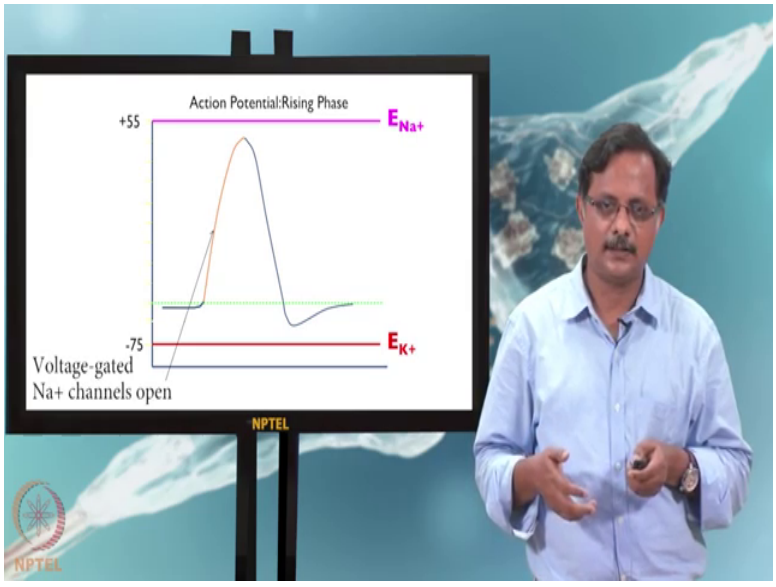

So, this image you see that membrane potential is increasing and this called the raising phase. So, at this point we have the sodium channels opening right and so, sodium channels are opening during this phase.

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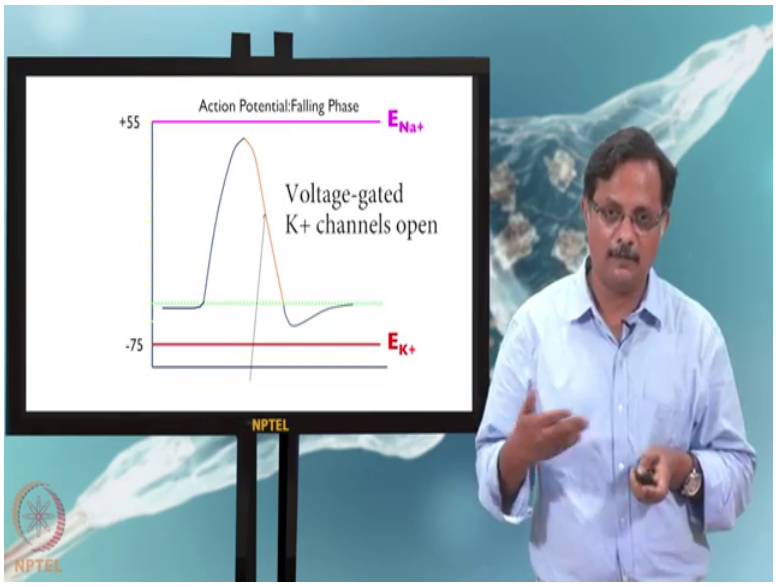

So, then you see that in this figure you see the falling phase of the action potential all right; the voltage is now come back from the peak value to back to the (Refer Time: 21:05) value of a minus 70 milli volts and this is called a falling phase. And during this phase, the voltage sensitive potassium channels are begun to open they are opening.

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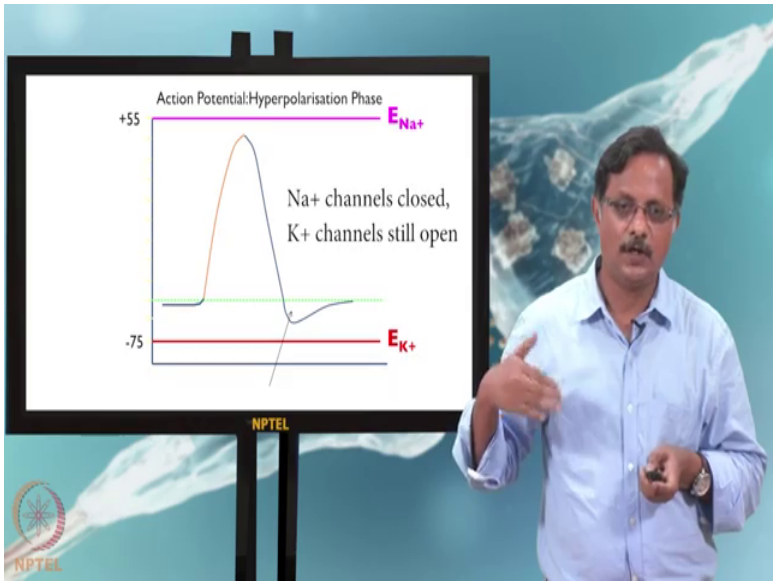

Now, in the third phase which is called hyper polarization phase or in second the part of the action potential where the voltage goes below the (Refer Time: 21:26) value minus 70 milli volts; it is called hyperpolarisation because it is less than the normal base (Refer Time: 21:31) value of minus 70. And during this stage sodium channels have closed now by this time and potassium channels are still open therefore, the membrane potential goes goes very close to the E K value of minus 77.

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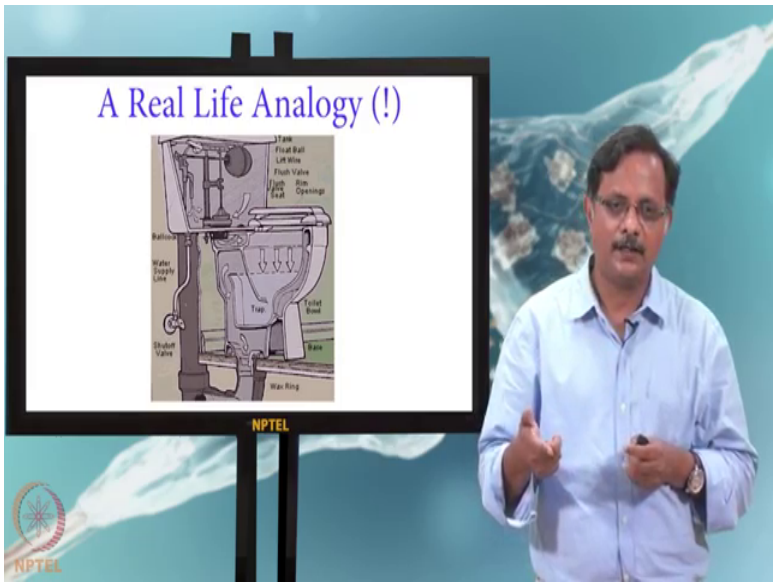

This can be compared to a kind of interesting real world you know system it is kind of disgusting, but it is a very appropriate analogy. Because what happens in action potential is as you if you if you increase your current pulse amplitude, the threshold value act it suddenly membrane voltage shows a sharp rise and a fall in the future action potential. And thus exactly what happens in this very familiar device is called the toilet flush.

So, in a toilet flush when you turn this knob; you give the knob little nudge right you there may be little leakage of water, but nothing much happens. But once you turn the knob as certain critical angle, then kind of whole hell breaks loose and all about water in the tank flows into the flush and then once that is that process begins we have reached a point of no return and you cannot stop that between ok. So, the whole thing has to you know flow before we before it you can flush it again.

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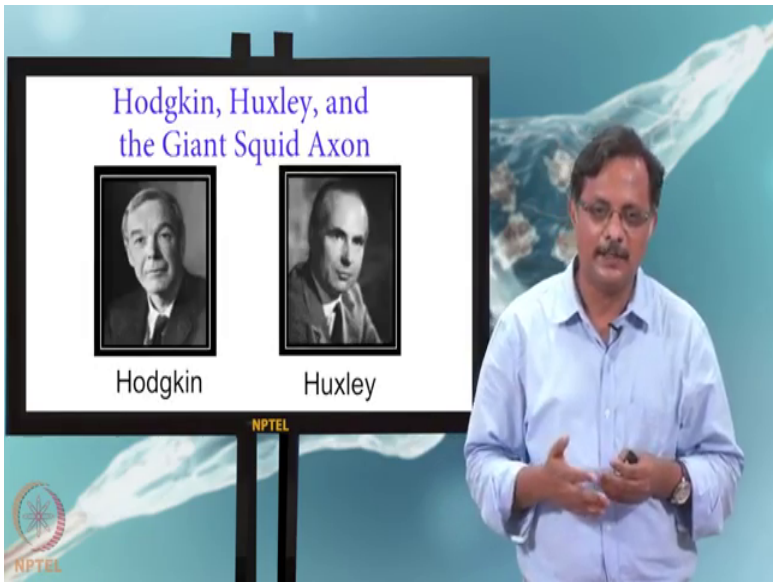

So, so, this is what not the toilet flush, but the whole process of action potential generation and the molecule machinery that underlies the action potential generation.

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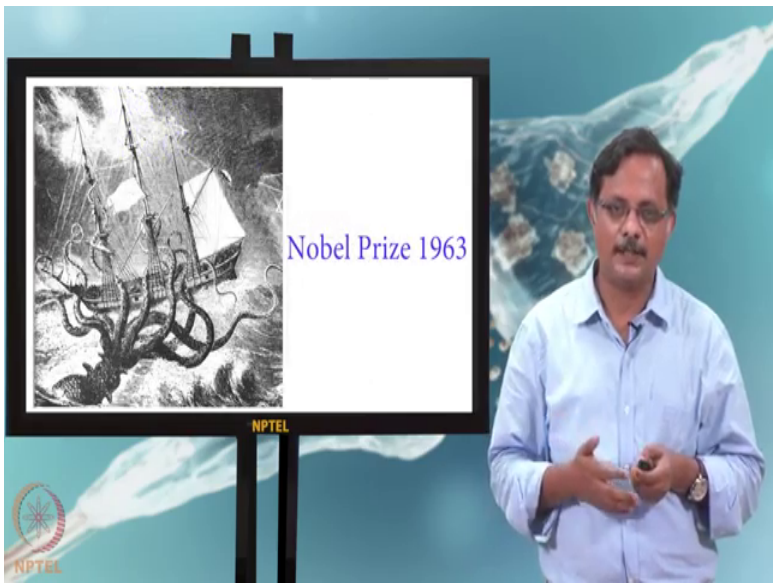

This was developed by Hodgkin, Huxley as we have discussed in the very first lecture and they got an Nobel prize for their a brilliant work in 1963. I want to discuss one more aspect of the action potential generation.

So, if you look at; so, we have seen that as you increase current pulse amplitude, your voltage response also increases and at a critical value of current pulse the voltage pulse becomes abnormally high.

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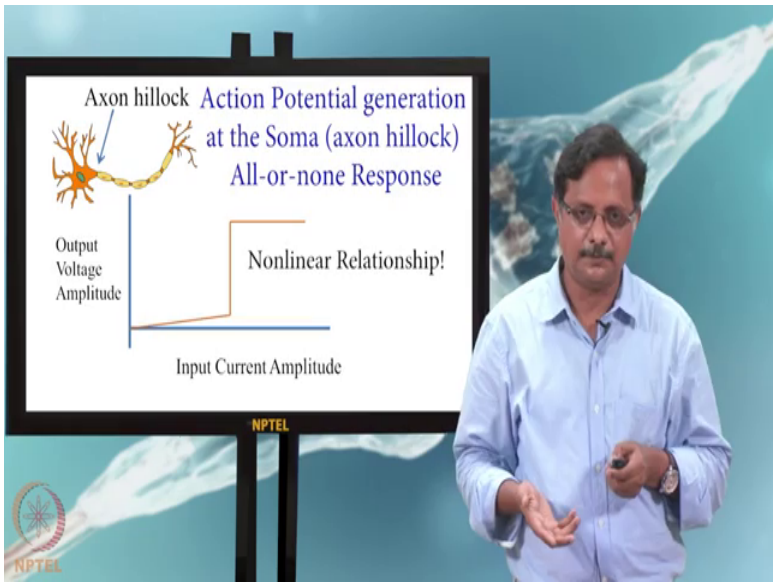

Now, in the right graph on the slide we are looking at the input current amplitude on the x axis on on the y axis its output voltage amplitude.

So, you can see that as input current amplitude increases gradually, up to certain point the output voltage amplitude also increases gradually; pretty much have very much linearly. But once the input current amplitude crosses certain threshold, the output voltage suddenly increases to a very high value. And after that since action potential has fixed amplitude and duration, there is no change in the amplitude after that we have current increase the current amplitude right; there is no change in the amplitude of the action potential.

So, the relationship between output voltage amplitude, input current amplitude looks like kind of a step that which is non-linear relationship ok.

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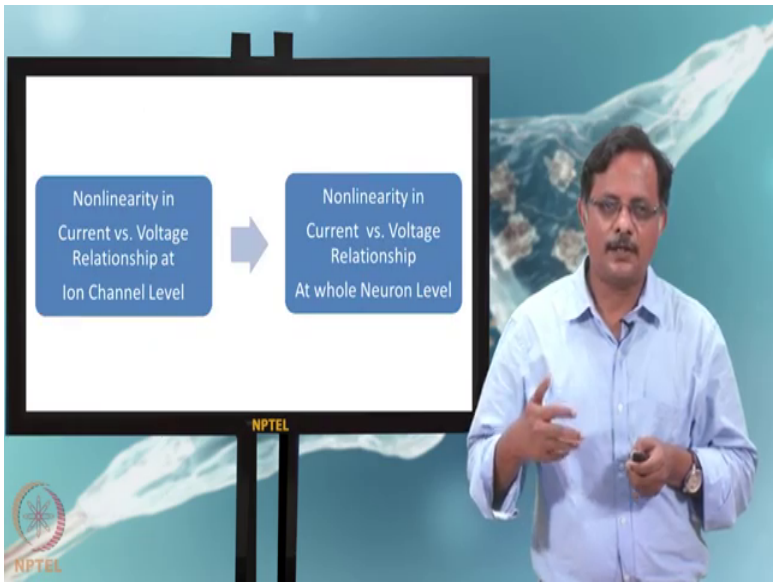

Where is nonlinearity coming from? This nonlinearity is coming from the nonlinearity that that exist at the level of ion channel.

So, therefore, the nonlinearity in the current versus voltage relationship which exists at the level of an ion channel is getting translated into nonlinearity in the current versus voltage relationship; at the whole neuron level which is what we have seen in the previous slide. Now how do we say that the current voltage relationship of an ion channel is non-linear?

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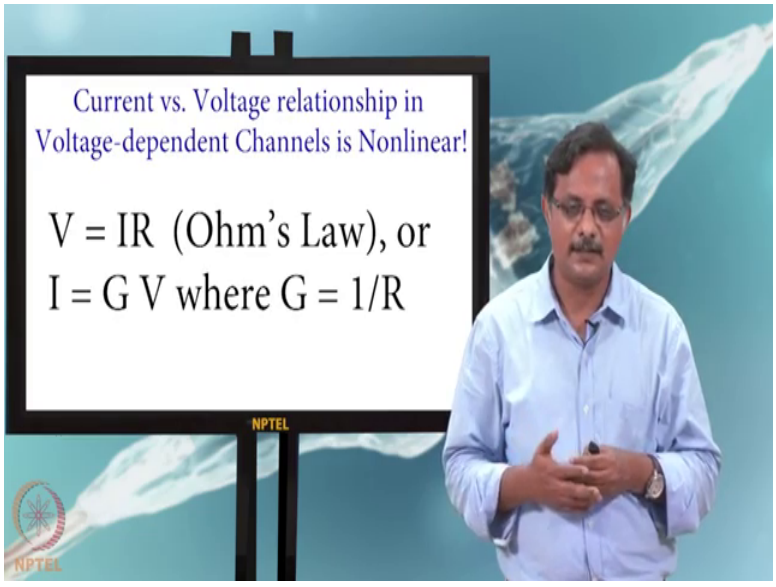

Now, let us go back to our again high school physics and recall Ohm's law. So, Ohm's law says that voltage is proportional to current and the proportional is given by the resistance R; V is equal to IR or this can also be expressed as I is equal to GV, where G is the conductance and; so, G is equal to 1 by R.

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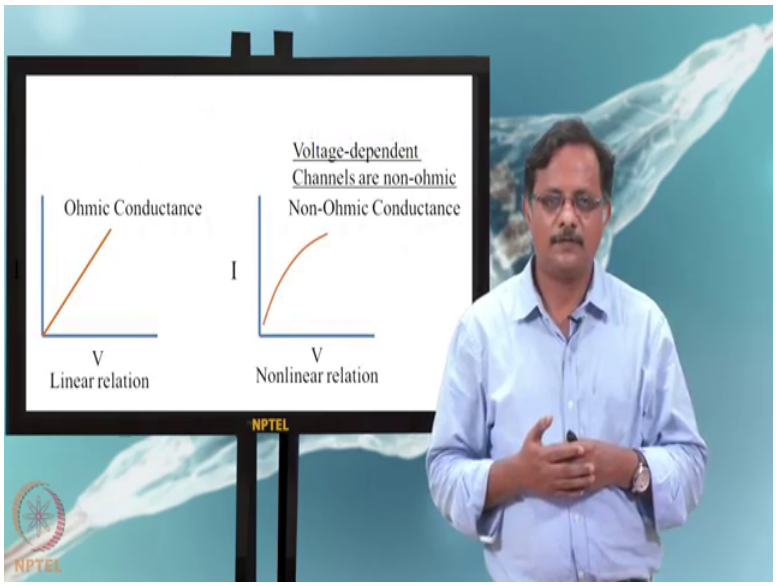

So, therefore, resistances which follow this law Ohm's law are called Ohmic resistances or Ohmic conductance.

So, when we have Ohmic conductance the current versus voltage relationship looks like what you are looking at what you are seeing in the left graph right; voltage is on the x axis, current is on the right axis and the relationship between two is the linear. So, it ims a linear relationship, but suppose G itself is a function of voltage which is like what is happening in case of voltage dependent channels.

The channel conductance is varies as a function membrane voltage so; that means, that G the conductance is a function of voltage. So, G is a function of voltage then the IV equal to IR is no more as the ir linear relationship, the graph that fix range between I and V is no more a straight line it will a some kind of curve. So, the conductance at which follows this kind of a current voltage relationship is called a non Ohmic conductance and the relationship is a non-linear relationship.

So, therefore, the nonlinearity that exists at level of single channels alright translates into nonlinearity in the response of the whole neuron to input current.

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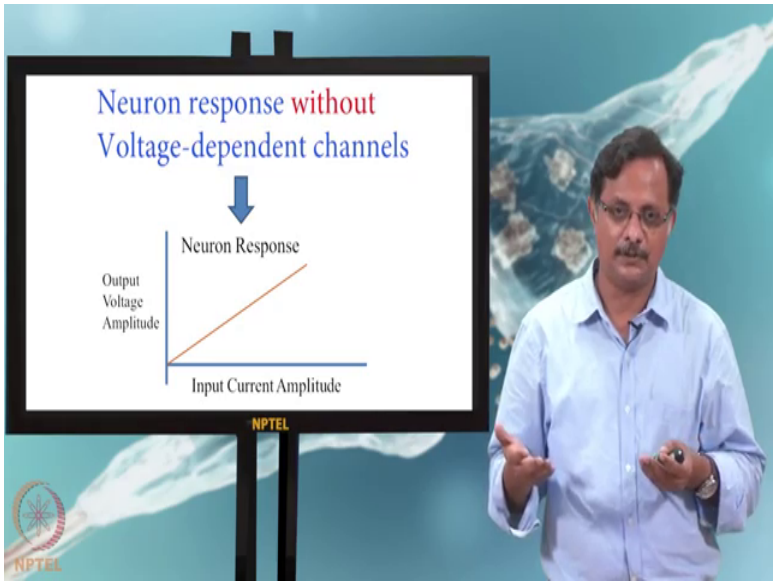

So, so the thing is if did not have voltage dependent channels; if you had only voltage independent channels like leakage channels; the neuron response would be you know linear to input current, you will never have any action potentials right.

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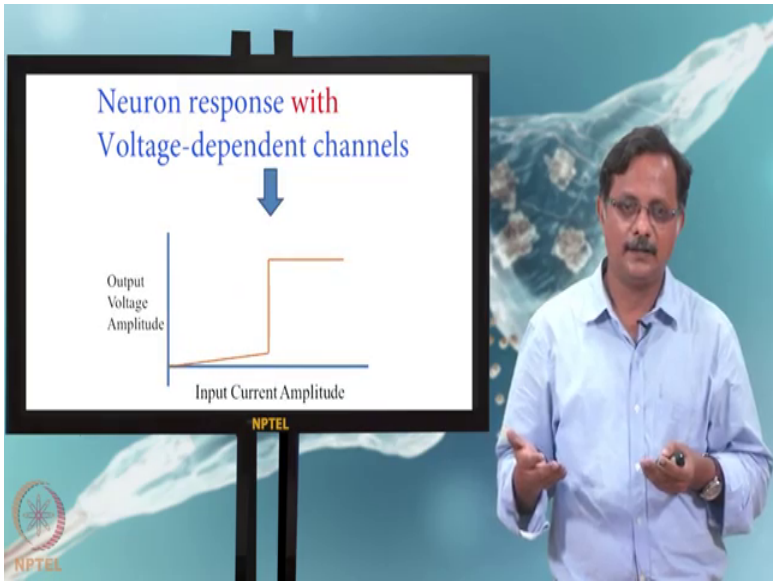

And whereas because of the voltage dependent channels right neuron response is non-linear you have this kind of a step like response in the voltage.

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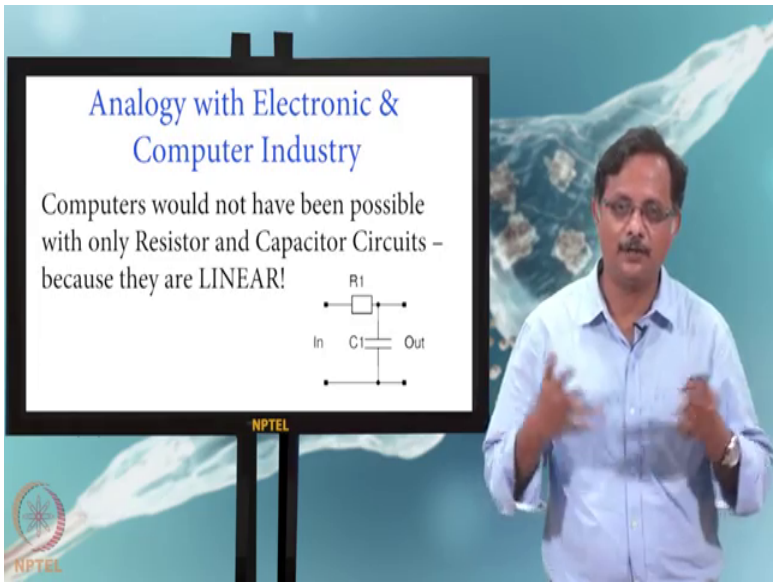

Now, this has lot of significance because it is these voltage dependent channels present in neurons that are making neuron so, power full has computer devices. And it is these neurons that make the brain a very power full computing device. And all this secret of brains intelligence right abilities right have their roots ultimately in this special structure of the neuron and neurons signaling capabilities right ultimately have their roots in this special channels or the voltage dependent channels.

Because the voltage dependent channels are non-linear you know the whole a neuron response is non-linear and makes it a very very power full computing device, whereas, if you had only voltage independent channels then the neuron will be simply be having resistance and capacitances. So, it; so, neuron will then be like a resistance and capacity circuit or a RC circuit and these circuits are linear you cannot build the modern computers with this kind of circuits.

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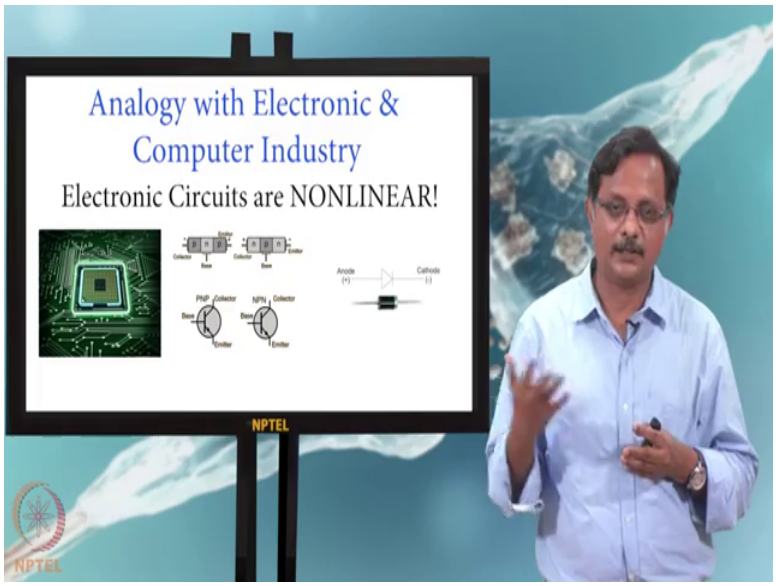

To build a modern computers, we need a electronic circuits which are all non-linear. So, for example, we look at you know diodes and transistors right you know VLSI technology; they are based on non-linear circuits right.

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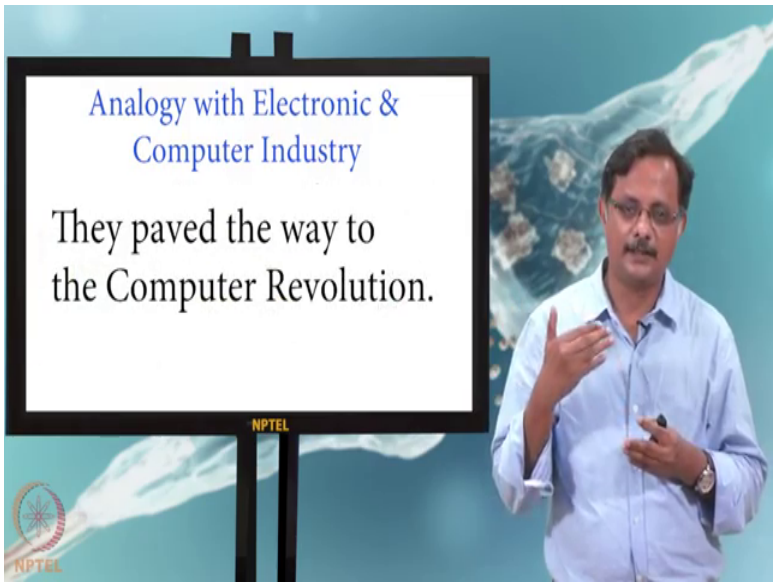

It is this which has assured in the computer revolution. So, just as development of non-linear devices right suddenly brought about a quantum jump right in the computing technology and made computers possible alright and the existence of voltage dependent

channels are very crucial for making neurons power full computing devices and for making brains what it is.

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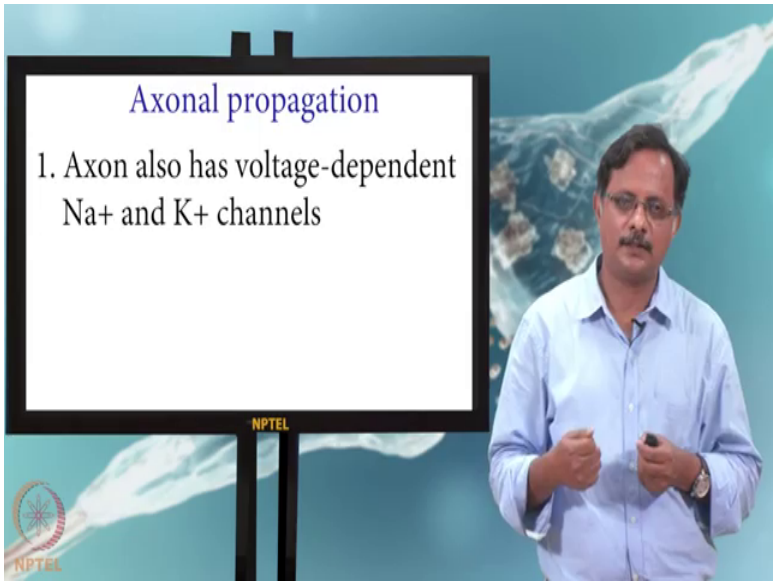

Now, let us go to axonal propagation. So, axons also have voltage dependent sodium potassium channels all along the way all along the length of the axon.

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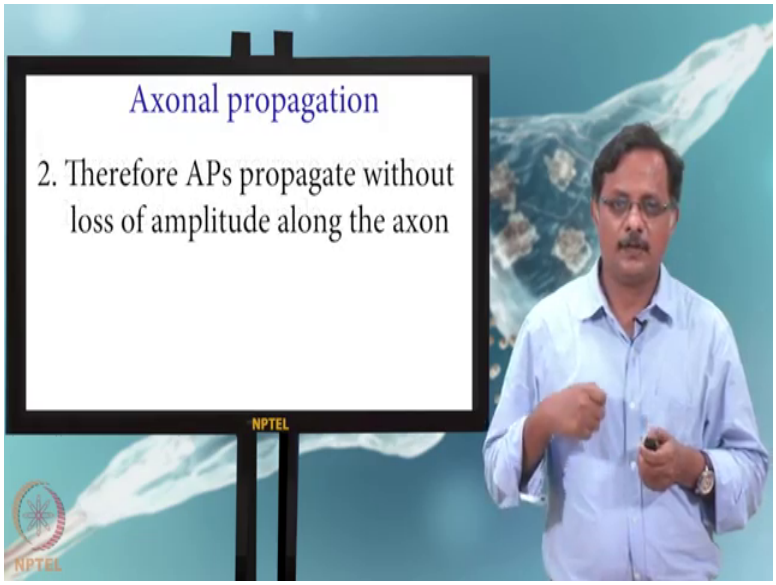

Therefore, action potential propagate without loss of amplitude along the axon.

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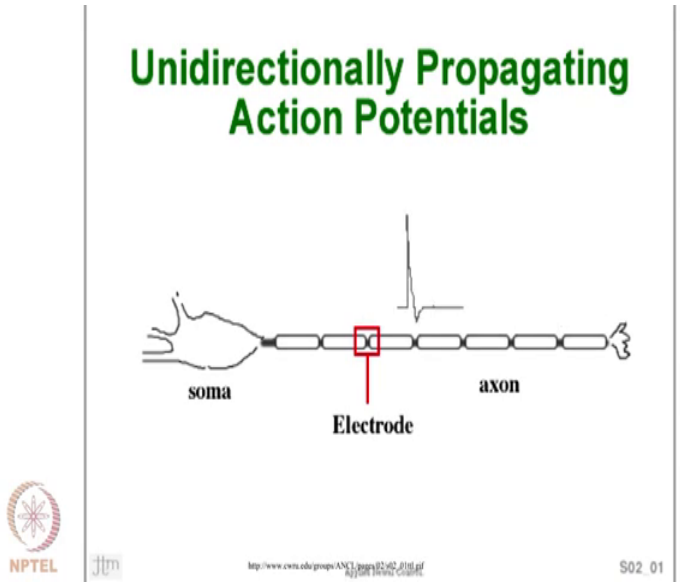

So, we have seen this animation in previous segment so, that is action potential propagates along the axon; it does not loose amplitude, the amplitude intact is width is also does not increase right; the say for the action potential remains intact as this action potential propagates down the axon.

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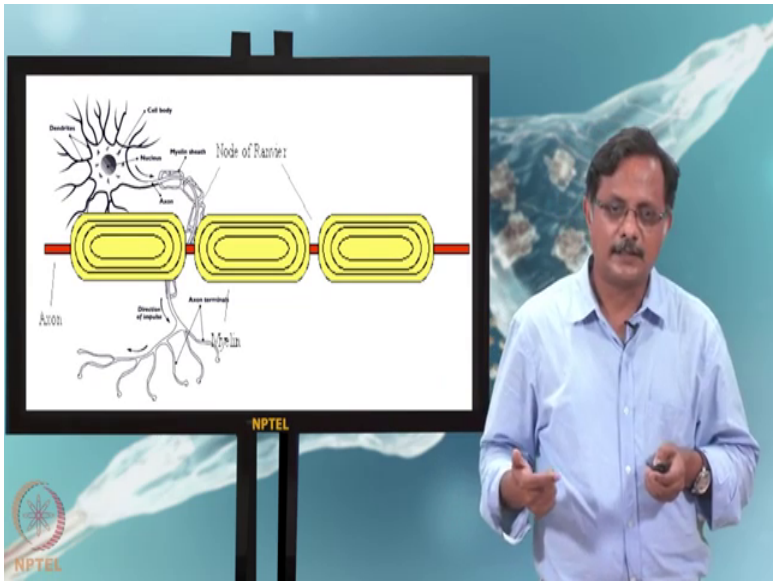

We already mentioned once that so, we have this myelin sheath all right that forms around the axons and that is what gives you increasing conductance. So we have also look at some of these numbers in earlier lecture right.

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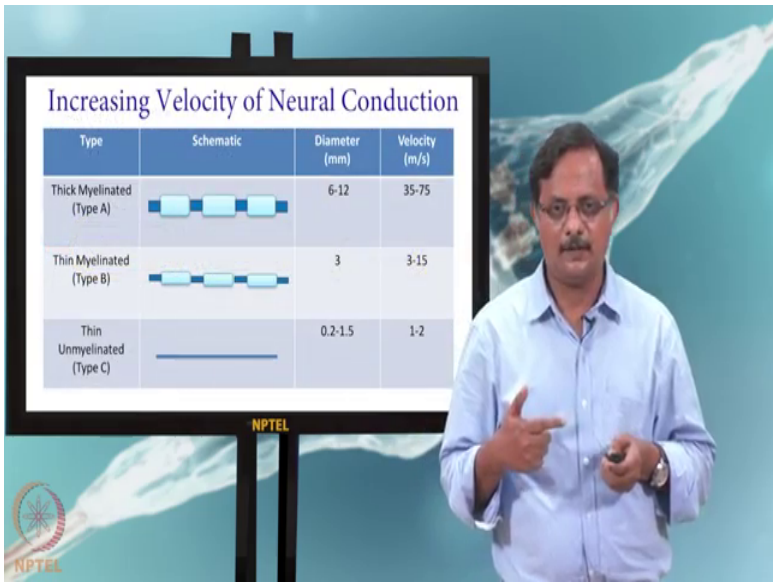

So, we have this thick myelinated axon type a axon which have bigger diameter and higher velocities and unmyelinated axons or type C axons; have smaller diameter and no myelin sheath and smaller velocities ok. So, the way the action potential propagate along an axon is quite interesting.

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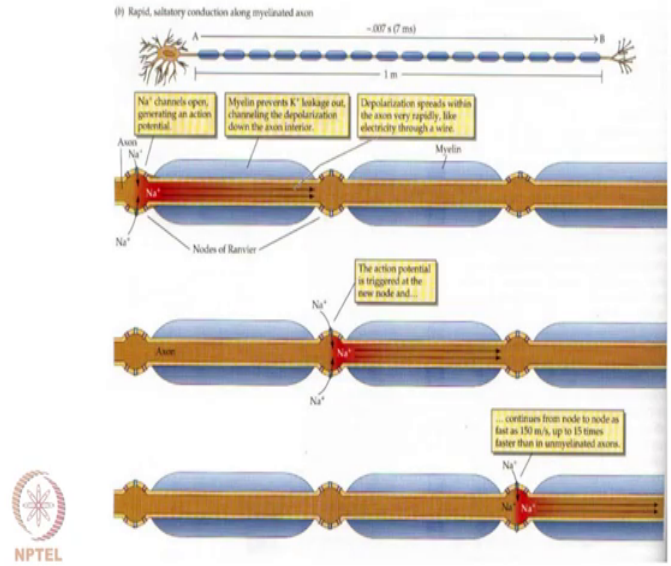

So, myelin sheath is not actually continuously present all along the length of the axon because myelin sheath is as you remember are is supplied by certain kinds of cells. These are the oligodendrocytes in the central nervous system and the Schwann cells in the

peripheral nervous system. So, since they are cells, they only occupy a small stretch of the axon and the so, a series of these cells try to cover the entire length of the axon.

And between neighboring cell there is a small gap on the axon which is not covered by the myelin sheath. So, therefore, myelin sheath gives right because of because it makes the cable thicker it gives you increased conduction velocity. So, as action potential propagates along the axon right and so, while it is propagating in the stretch where there is myelin sheath, it propagates fast.

And then when it comes to these junction point between two successive myelin sheaths right; it slows down a little bit a because they there is myelin sheath and current velocity suddenly becomes a smaller. So, slows on it slows on little bit in this junction point which are actually called nodes of Ranvier. And after that again for the next myelin sheath it speeds up again.

So, if you do kind of a slow motion stimulation of the way in which the action potential propagating. We will see it zipping across the myelin sheath and then slowing down little bit and then zipping across the next myelin sheath and slowing down and so, on and so, forth.

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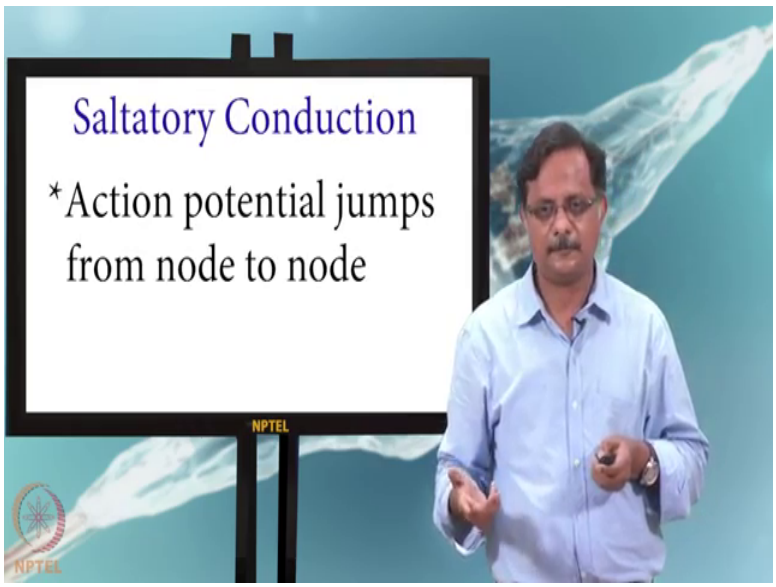

So, it looks as if the action potential is jumping from node to node; one node of ranvier to next node of Ranvier this kind of a conduction is called salutatory conduction.

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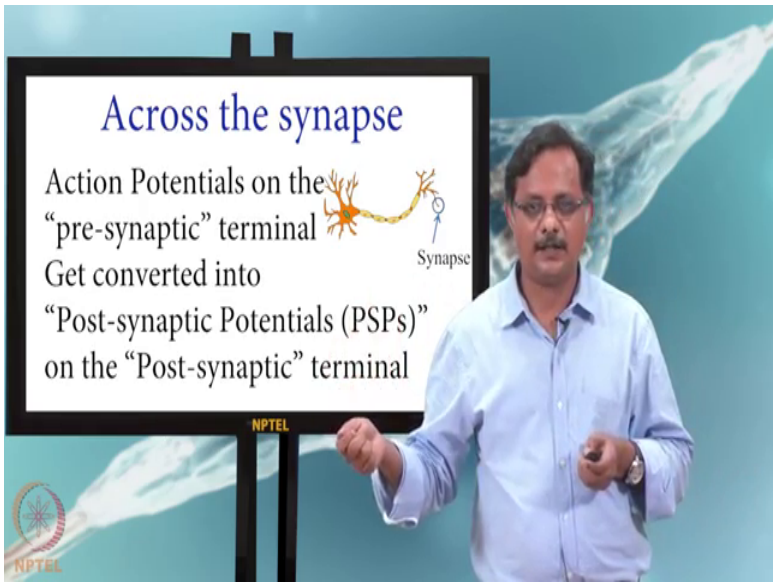

Now, let us come to the final step which is synapse. So, we already seen in the previous segment that the signal transmission at the synapse is a is a chemical step and. So, where the chemical is released by the pre synaptic terminal which is recognized by the post synaptic terminal and converted into an analytical signal called the post synaptic potential.

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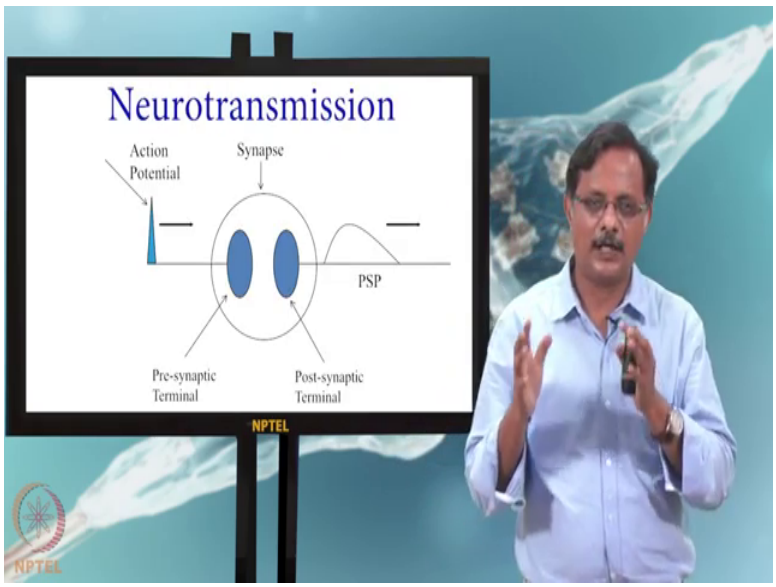

So, let us see exactly what happens. So, here we have a simple synaptic of a synapse; you can see a pre synaptic terminal and the post synaptic terminal. And action potential

from the axon of the pre synaptic neuron arrives at the pre synaptic terminal right and under which produces on the post synaptic side post synaptic potential.

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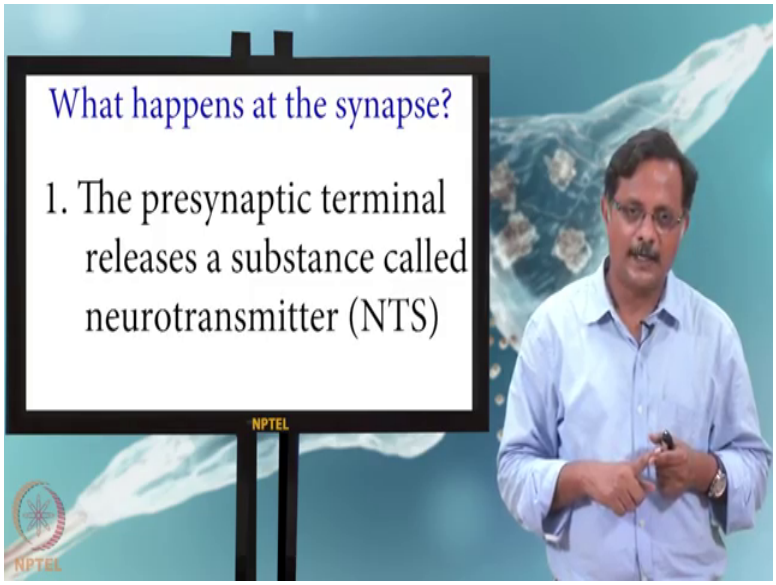

So, what exactly happens at the synapse? So, the pre synaptic terminal releases a substance called neurotransmitter.

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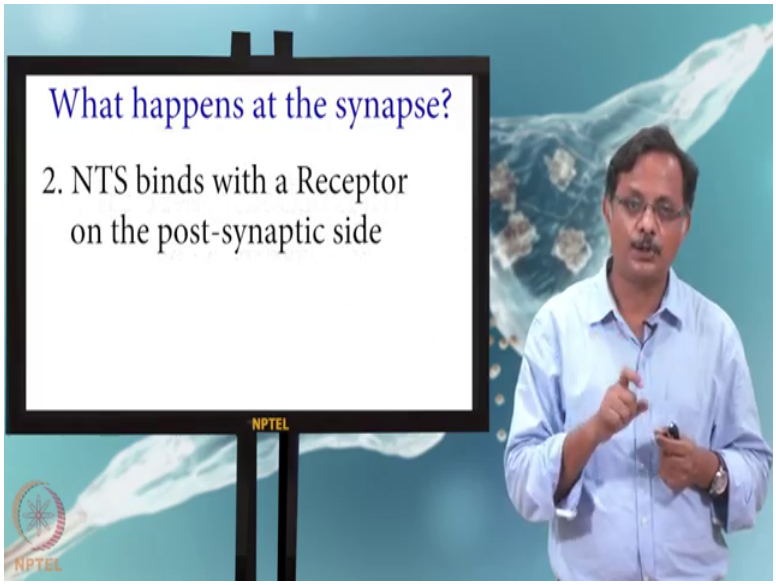

And this neurotransmitter substance or molecule binds with a receptor on the post synaptic side.

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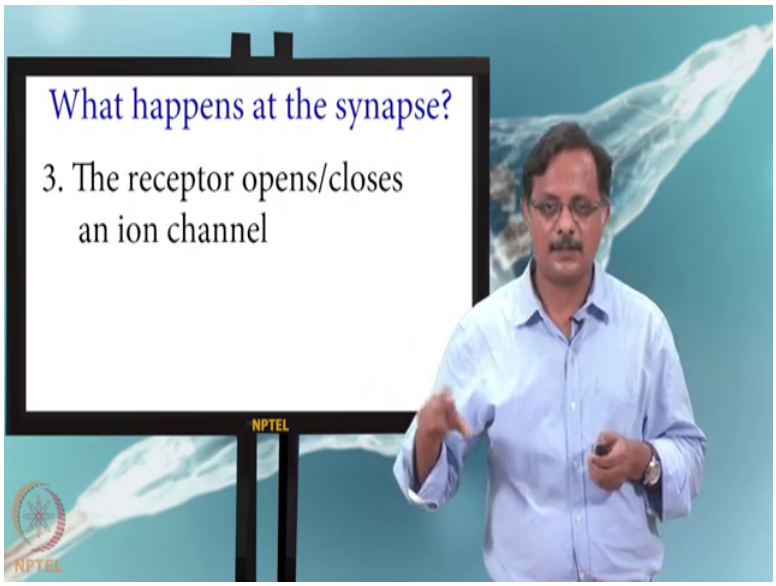

And because of this binding event the receptor opens or closes an ion channel. So, you can see in this picture.

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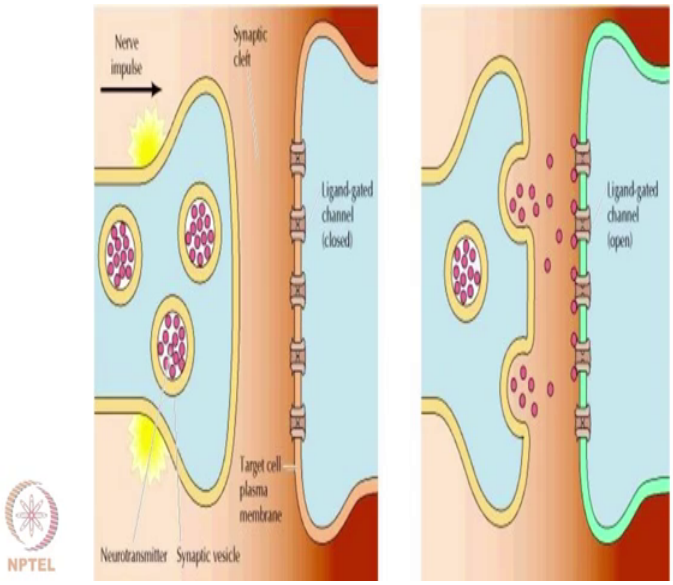

So, neurotransmitter present in the pre synaptic terminal is actually packaged in little spheres called vesicles. And these vesicles are held in place because of some protein bonds which keeps a by which the vesicles are tethered all right in place on the pre synaptic terminal.

So, when the action potential comes to the pre synaptic terminal and the locally they the membrane potential increases to high positive value. And because of that there are these voltage dependent in calcium channels which are present on a pre synaptic side which are not shown in this figure. So, so when these voltage calcium channels open calcium that is present outside.

And you know that calcium is present in high concentration outside and inside therefore, calcium rushes from outside to inside and calcium ions rush in. And then break this bonds which keep the vesicles intact in place right and when that happen vesicles start lifting towards the cell membrane and so, the y fuse with this cell membrane and release their contents; the neurotransmitter molecules it was synaptic left. And there in inside the once inside the synaptic left, the neurotransmitter molecules refuse across the short gap of the synaptic left and arrive at the post synaptic membrane and then there they bind with the receptors.

So, let us see how that happens in this more detailed picture.

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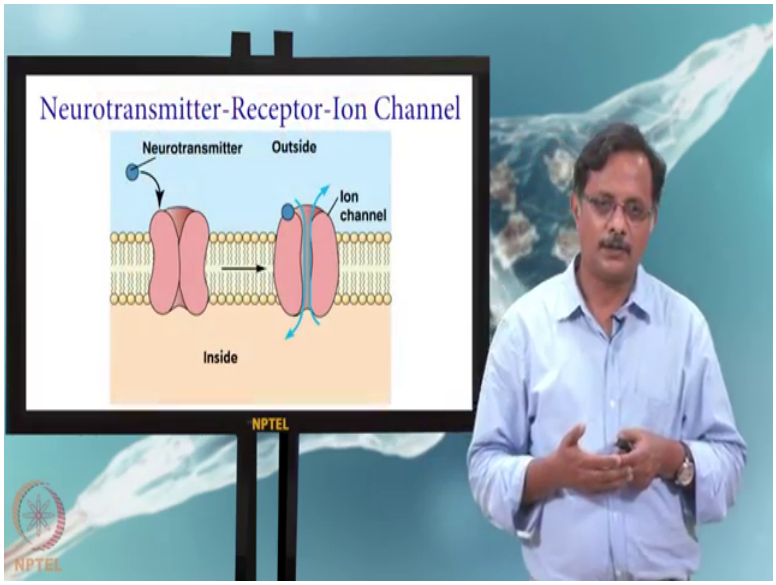

So, neurotransmitter molecule which was refused across the synaptic left is is arriving at a ion channel which is in the close state on the left side of the figure. And the neurotransmitter molecule then binds the receptor; so, in this in this case actually receptor is is kind of like a path of the ion channel itself. So, one particular ion channel ion channel is a basically a large protein with lots of parts these are called subunits.

So, the neurotransmitter molecule binds with a part of this ion channel which is a receptor itself. And the shape of the receptor in the shape of the neurotransmitter match in some sense therefore, the binding of neurotransmitter and the receptor is described as some kind of locking key mechanism.

So, when this binding takes place that event produces a certain changes in the shape of the ion channel. And because of if the channel opens and allows the passage of ions when; there is a flow of ions whether in outside the inside the outside that gives rise to a change in the membrane potential right. And that is how the chemical signal, it is released by pre synaptic terminal is connect to an electrical signal on the post synaptic side.

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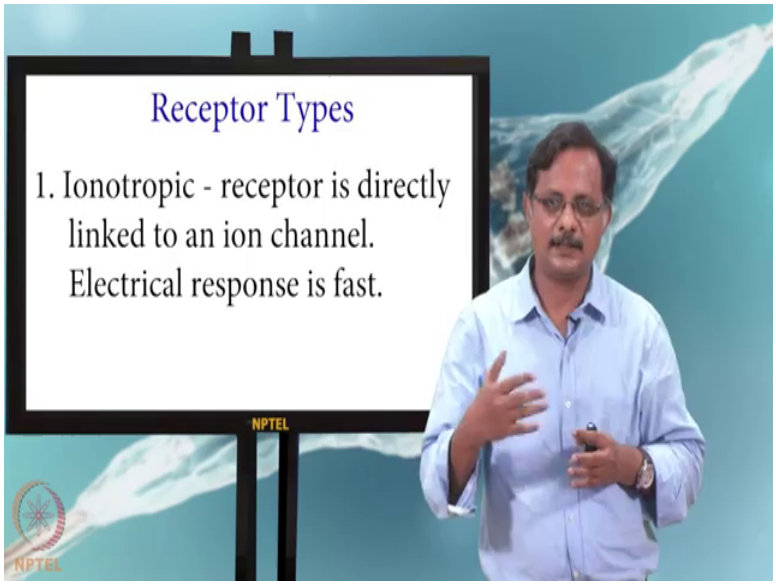

So, the receptors of two broad types they are this ionic ionotropic receptors which are where the receptor is directly linked to an ion channels; actually a part of the ion channel and responses in this kinds of receptors is fast.

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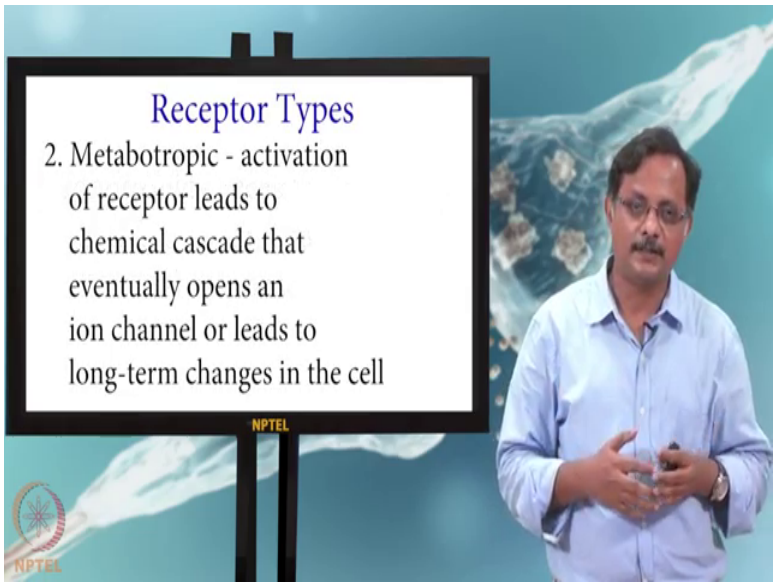

And then there are metabotropic channels where the activation of receptors leads a chemical cascades right. So, after a long cascade of signals the binding event between the neurotransmitter and the receptor triggers, a chemical cascade of signals at the end of the cascade it opens a channel and producing a flux of ions.

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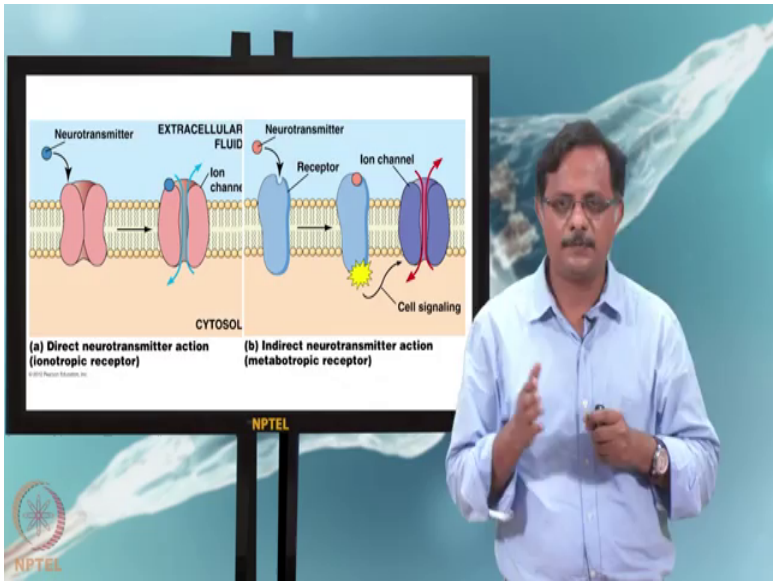

So, in this in this figure on the left side you see this direct neurotransmitter action which is a example of the ionotropic receptor on the right side you seen a example of a metabotropic receptor.

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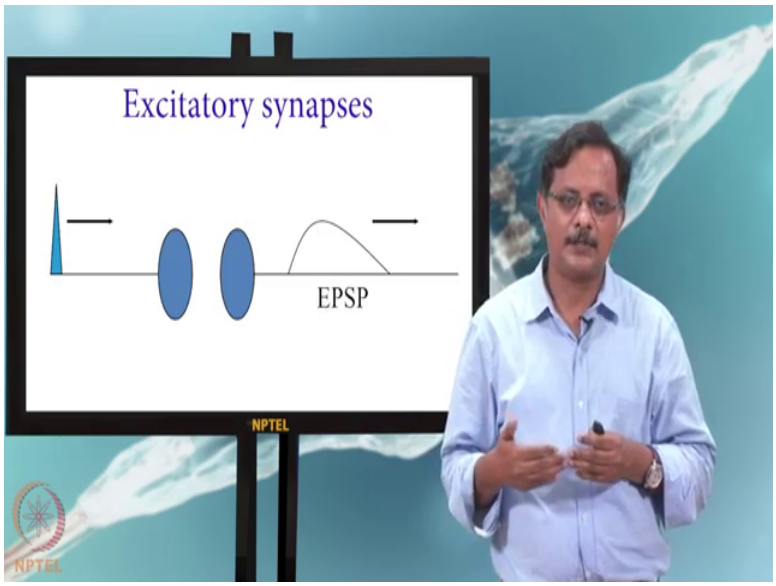

So, now, what makes a synapse excitatory or what makes a synapse inhibitory? So, you have seen in the previous segment that in excitatory synapses the PSP is the positive voltage deflection.

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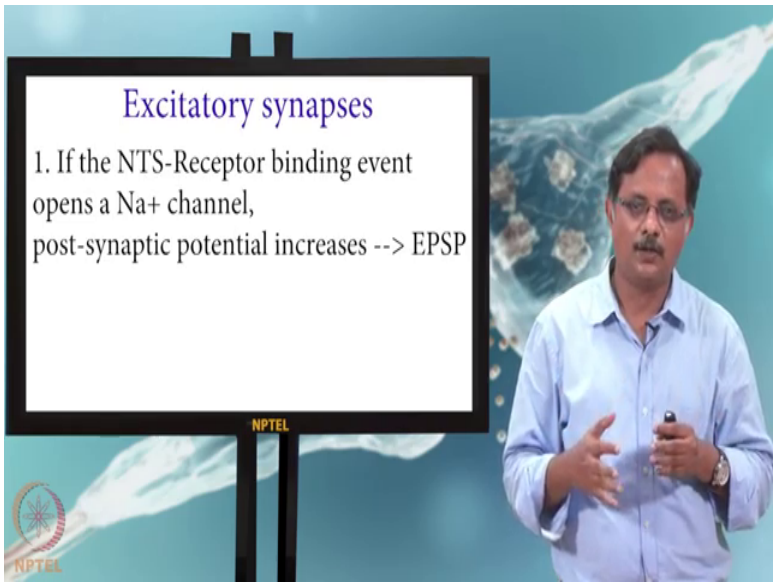

So, you get an EPSP right then that happens because the neurotransmitter receptor binding event opens a sodium channel. And therefore, sodium rushes in on the post synaptic side and thereby increasing the membrane voltage and producing EPSP.

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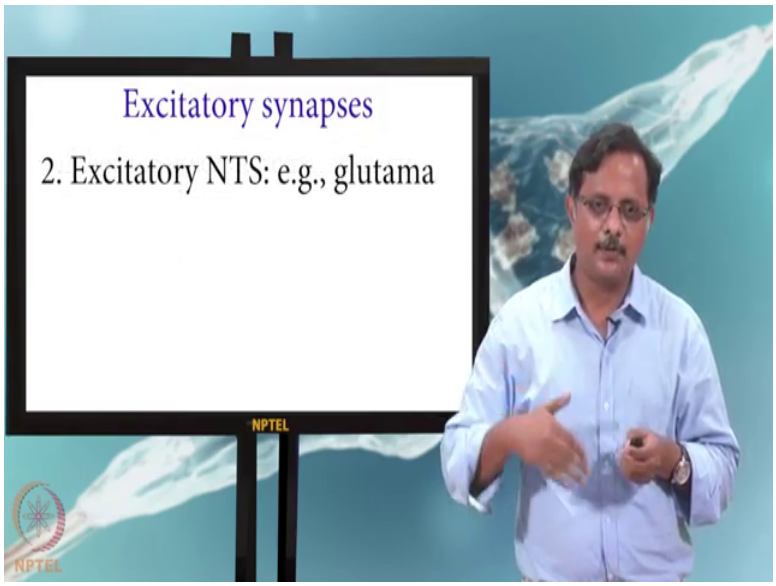

An example of excitatory neurotransmitter molecule is glutamate.

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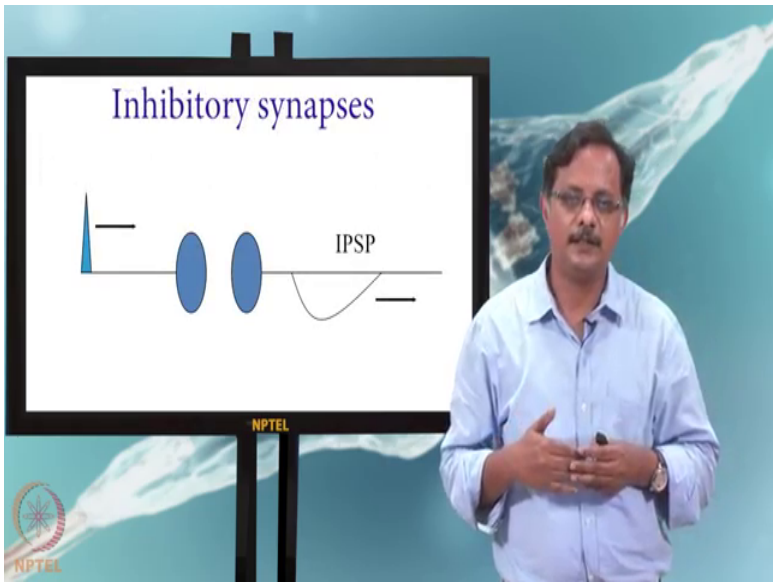

So, similarly if inhibitory synapses right when the neurotransmitter receptor binding event takes place it opens.

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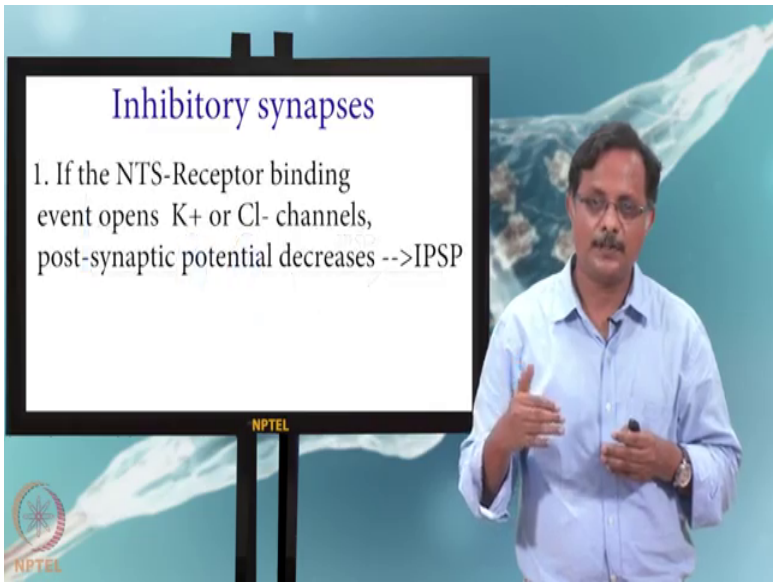

If the potassium or chloride channels on the post synaptic side; thereby decreasing the post synaptic potential and creating a an IPSP.

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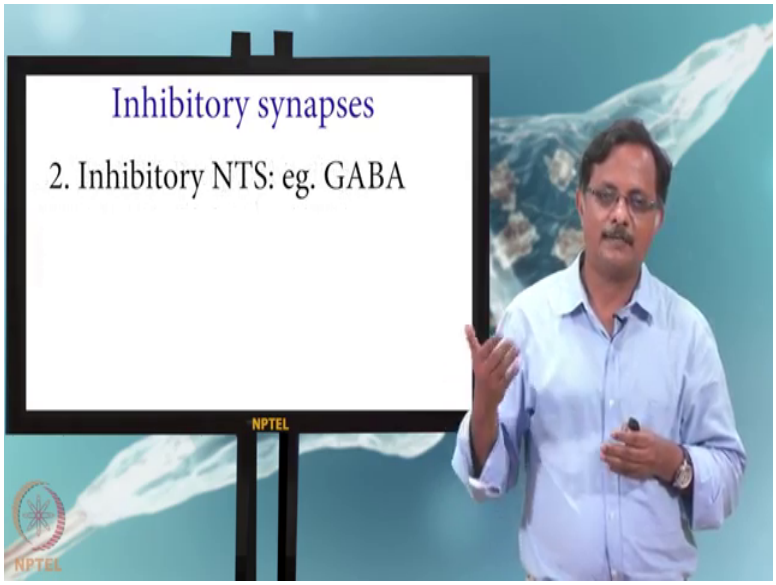

An example of inhibitory neurotransmitter is GABA.

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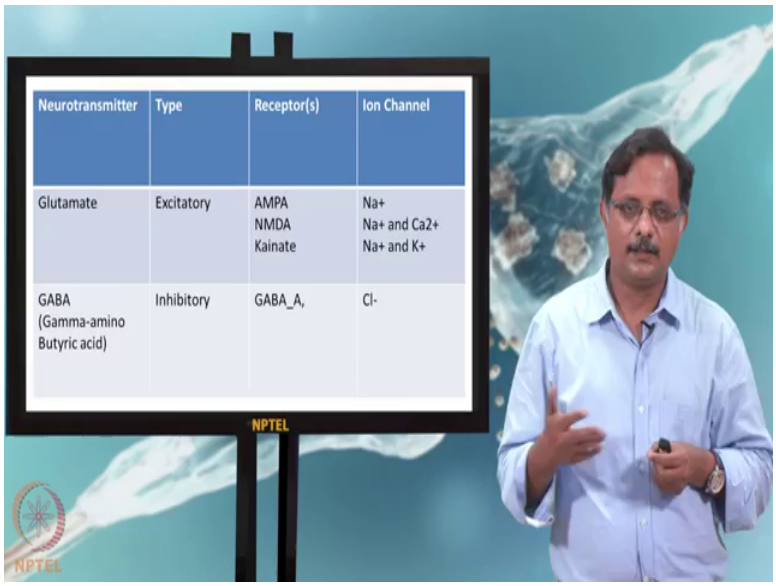

So, let us look at this to most prominent and most commonly found neurotransmitter in the brain. There is glutamate which is exactly neurotransmitter and which has three kinds of receptors receptor classes AMPA, NMPA and Kainate. And AMPA receptor when it is when the glutamate binds with AMPA receptor; it opens most sodium channels where and when it binds with the NMDA receptor, it opens channel which permits both sodium and calcium.

And when it binds with kainate receptors it open the opening of the channel a permits both sodium and potassium, and GABA has is inhibiting your neurotransmitter it has a receptor; it has a ionotropic receptor which is GABA A and when this binding event takes place between GABA and GABA A it opens a chloride channels.

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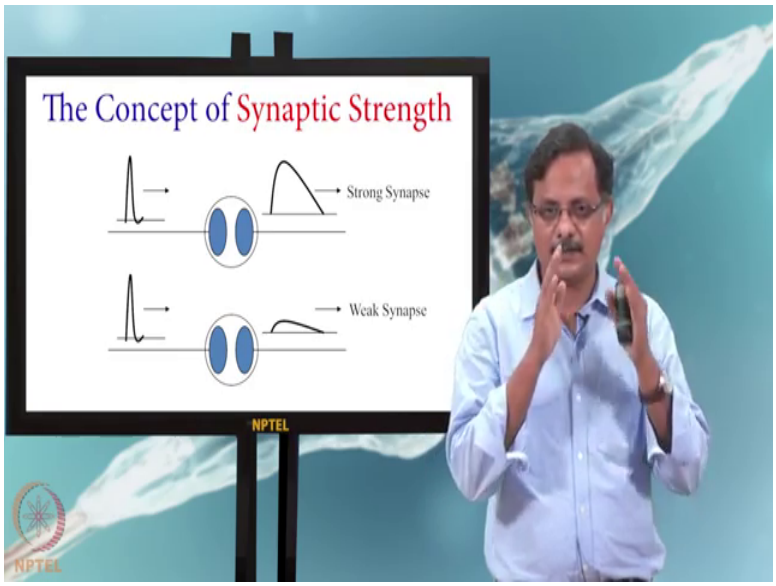

So, one more concept which you should introduce in this context is the concept of synaptic strength.

So, we have said that the two kinds of synapses excitatory inhibitory and, but we also mentioned in the last segment that the PSP is the gradient signal unlike action potential which has a fixed size and shape the PSP can have variable amplitudes. So, for a given action potential on the pre synaptic side, it produce a strong or high amplitude PSP which is a synaptic strong.

So, similarly for a given action potential on the pre synaptic side; if the PSP produces as a small amplitude then you say the synapses weak.

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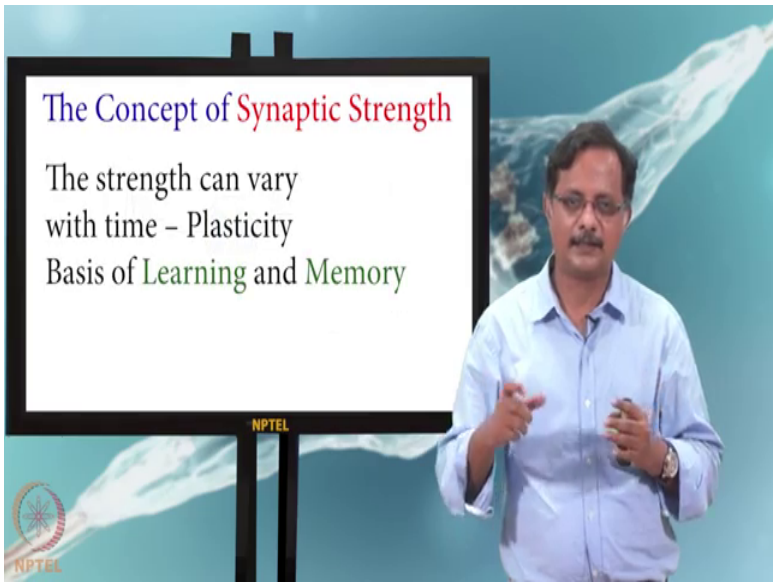

Now this denotes kind of the strength of the synapse right and this synaptic strength can also be varied with as the function of ongoing activity on the synapse. And so, this concept is called the synaptic strength and variation of the synaptic strength is called plasticity. And that is this change in synaptic strength is taught to be the basis of learning and memory and the encounter of this concept again and again in future classes.

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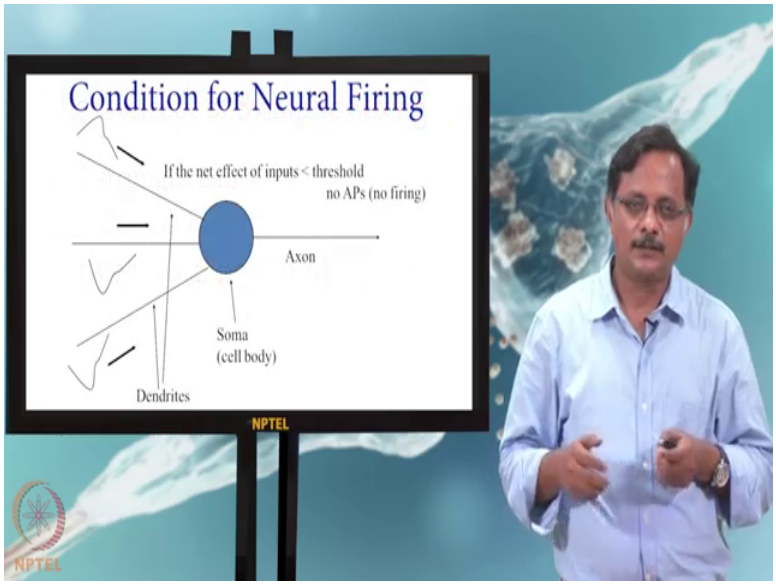

So, just to wrap up basically what we have seen so, far in this two segments of this lecture is now you have neuron the cell body and receive inputs from other neurons via

several dendrites. And in this figure the re three generating lines and one generating line is carrying a positive PSP or EPSP, the other two generate lines are carrying two IPSP's.

If all of them when the when they add up or somewhere near soma right in this case the negatives dominate therefore, the cell does not get excited. So, the it does not produce action potentials.

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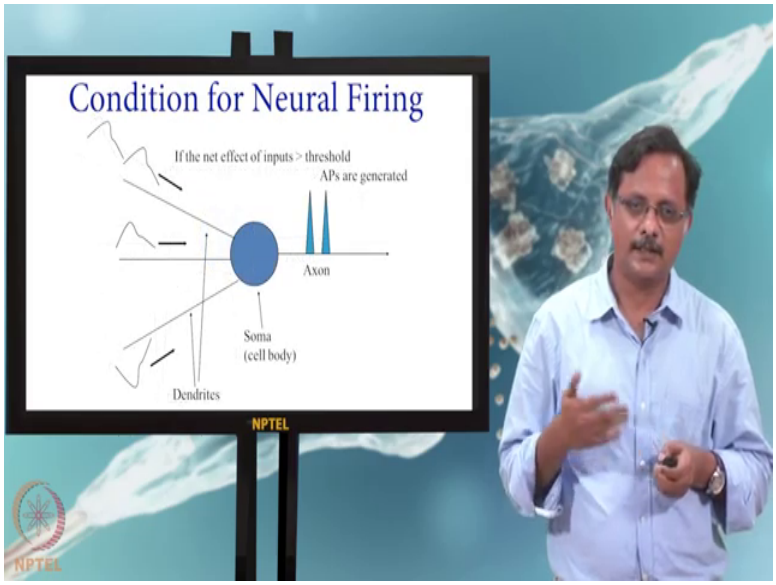

Whereas in this example the top most line the dendrite there are two EPSP waves flowing in; and a middle one there is only single EPSP we have flowing in; in the bottom one there is a single IPSP wave coming in when all of them add up in the soma right the positive dominates the negative.

So, therefore, the soma gets excited and produces action potentials which propagate down the axon.

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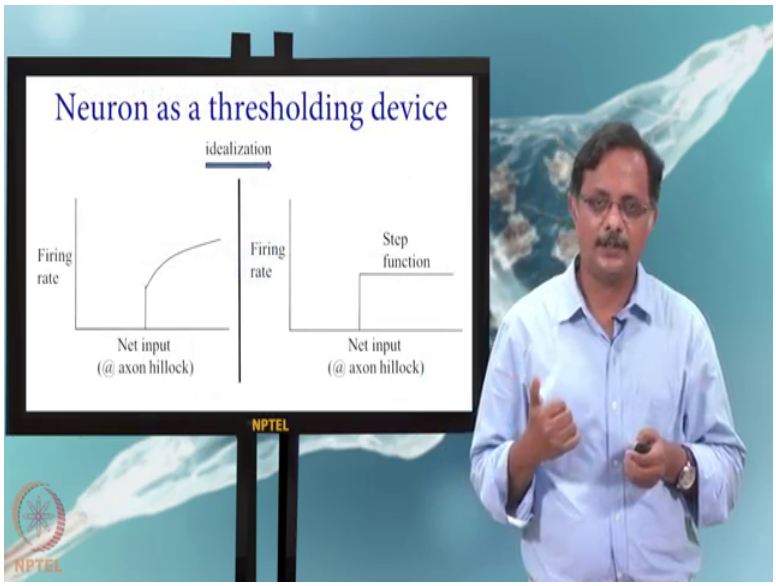

. So, with this you can think of neuron some kind of thresholding device. So, basically what neuron is doing is its adding up inputs from other neurons right. And it is taken the positive inputs and the negative inputs adding up all of them. If the net sum of all these inputs crosses a threshold value, then neuron gets excited if the net sum of all its inputs present for threshold value it does not get excited ok.

So, this is a very simplistic description of neuron I know that new neurons are lot more complicated than this. But this description is good enough to construct models and to think about what kind of communication of neurons happens in large networks. And you can also describe how different (Refer Time: 39:27) functions can be cannot be accounted for using a simple neuron model like this.

So, in the next lecture what we will do is we start with this kind of a simplified neuron model. And describe how you can construct networks large networks and with which we will try to explain lots of phenomena from psychology and neuroscience.

Thank you.