**Computational Neuroscience**
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**Lecture - 41**

Lecture 41: Plasticity - Synaptic Transmission and Synaptic Strength

Welcome. So, we ended our last discussion sort of with the motivation for studying plasticity or synaptic plasticity per se. So we saw how based on the requirement of an animal in the case that we discussed it was a ferret, how the receptive fields of neurons in the auditory cortex change based on the requirement. And depending on the kind of task the changes could be drastically opposite and would imply separate mechanisms in terms of the plasticity that is occurring. What we mean by plasticity we have alluded to this term earlier also is the change in synaptic strengths. And so in order to understand about synaptic plasticity which gives the brain probably the most powerful tool and helps the brain to adapt.

So we will have to learn about the synapses. So we know in from our initial lectures that synapses are where two neurons connect with each other. And typically if we have a presynaptic neuron whose axon projects to the postsynaptic neuron on dendritic spine or even on the dendrite or on the soma. And the study of the way this synaptic transmission happens is important in order to understand how this synaptic modifications take place.

And we are referring to chemical synapses here that is synapses that use neurotransmitters to basically transfer information from the presynaptic side to the postsynaptic side. And there are also synapses that are called electrical synapses which are not quite the same I mean which do not function in the same way as chemical synapses there it is a direct connection. So in our discussion about synaptic plasticity we will limit ourselves to the chemical synapses. So what is it like let us delve into it. So as a cartoon let us say this is the neuron whose cell body is there which this is the axon of the neuron which is projecting out.

Let us say these are dendrites and we have the axon terminal here and this is let us say an exaggerated dendritic spine on the dendrite of a postsynaptic neuron. So this is dendrite and we have the cell body and this has an axon which again has axon terminal communicating to another neuron. So we need to understand what exactly happens in these synapses in order to understand how changes take place in synapses. So if you recall from our earlier lectures essentially for that purpose in modeling of neurons we take the synapse as a source where there is a current

injection. So how does that current injection take place? So here let us enlarge the whole idea of the synapse that we have circled there.

Let us say this is the dendritic spine which is a mushroom like structure with a narrow neck and that comes off the dendrite. So in this presynaptic side there are vesicles that are coated with a particular protein clathrin and these vesicles contain what we know as neurotransmitters that is specific to that synapse. And these vesicles can be sitting right at the membrane at the presynaptic side containing the neurotransmitter molecules inside them. Now remember that we said that it is the action potential based on which neurons compute and it is the currency of communication between neurons and so when this particular neuron the presynaptic neuron produces an action potential this action potential gradually I mean travels along the axon what we mean by that is that the membrane potential at the different points on the axon is changing and depolarizing and then repolarizing just like the action potential and finally the action potential reaches the presynaptic terminal here and so this the membrane potential here at the presynaptic terminal is depolarized because of the action potential that has occurred and this depolarization causes voltage gated calcium channels so there are what we call VGCCs or voltage gated calcium channels that open just like our sodium channels that we had talked about and potassium channels that we have talked about that are voltage gated because of this depolarization these voltage gated channels open and calcium flows in so calcium ions flow in because of this depolarization why does it flow in if you remember that this is when it is depolarized it is about plus 40 millivolts or around there and the $E_{calcium}$ or the equilibrium potential for calcium is about plus 140 millivolts so when there is a path available for calcium the membrane potential will be pulled towards $E_{CA}$ and that is how the calcium ions would flow and so basically that means to make the inside even more positive calcium ions go into the presynaptic side into the terminal and then there is a well understood elaborate calcium dependent mechanism based on a number of proteins that are involved that these vesicles ultimately dump their neurotransmitter into the gap which is called the synaptic cleft. So these neurotransmitters then are taken up by neurotransmitter receptors on the postsynaptic side so let us say the neurotransmitter is released from the preside and they are go and bind to neurotransmitter receptor and these receptors can be of two types one in which they are themselves ion channels and in another case they are not ion channels but just G mainly G protein coupled receptors.

So what we mean by that is that these are transmembrane proteins that are connected to couple of other proteins that are inside the membrane and there is a binding site for the neurotransmitters so that when the neurotransmitter binds

due to the conformational change there is activation on release of a molecule in the inside of the smile or in the postsynaptic side which then through multiple second messengers that is it then goes and activates more different molecules and then each of those can activate further many molecules and so there is a cascade of operation I mean cascade that happens and finally there is activation of some molecule that goes and turns on or turns off or opens or closes an ion channel. So what we are seeing is in this second case there is an indirect opening of or indirect opening or closing of ion channels. It is indirectly affecting ion channels. So these are two different kinds of synaptic transmission. So one case that is very fast because the receptor itself is an ion channel and it is essentially a ligand gated ion channel in the sense that instead of voltage gating it is the concentration of the neurotransmitter in the synaptic cleft that determines the probability of opening of these receptors or these ion channels that are receptors and so more the neurotransmitter more of these receptors are open and that allows ions to flow into the postsynaptic side or out of the postsynaptic side and these are called ionotropic this is ionotropic transmission ionotropic that is directly by ion channels and in the other case this is called metabotropic transmission and this is slow generally smaller in size and longer lasting.

So this opening of ion channel that leads to ion flow into the postsynaptic side is basically the current injection into the postsynaptic neuron. So this ion channel finally causes the current injection which can be positive or negative depending on the ion channel or depending on the receptor and the neurotransmitter. So now the question is what are the kind of effects that can happen? So if we recall our circuit model or point model of the neuron we have this capacitor then if we talk of the Hodgkin-Huxley type of neuron so there will be a number of branches for each ion channel type as you are aware of and then $G_{leak}$ and $E_{leak}$ and there are batteries corresponding to the equilibrium potential of the specific ions that are involved and here we had this $I_{external}$. So this $I_{external}$ is the current that reaches the soma from such current injections at the synapses. So if we draw the spine here like this there is some current injection here and that causes that basically travels up to the soma of the neuron and so there are there can be tens of thousands of synapses that are spatially at different locations which interact with each other also over in the same dendritic branch and all of these effects as you have learnt earlier finally reaches the soma which depending on whether it crosses the neuron crosses the threshold there is an action potential which goes forward.

So now the question is that if we are learning something so if you recall our case of the ferret where we had a passive listening ferret and then behavior or actively listening ferret the two situations where the work that we spoke about the

recordings were being done from the same neuron under the two conditions with the same stimuli that is the noise like stimuli followed by tone which has to be detected in one case the animal has to detect the tone that is the active case and in the other case the animal is not performing any behavior not does not need to detect anything or perform any behavior. So inputs are same in one case we saw that the receptive field changes for the same neuron so that change is what we call that is reflected in the receptive field is the plasticity happening because the same stimulus is now producing a different kind of spike different set of spikes due to the same stimulus. So that change I mean and that change is not stochastic kind of change it is a significant change and on average that effect is seen. So that means that the although the inputs reaching the soma or the synapses are the same there are changes that have happened due to the active behavior phase and that usually happens or rather other than some top down input coming and modulating synapses that can that usually happens with the change in synaptic strength and what do we mean by synaptic strength it is basically a measure of how much current injection is happening at the synapse and these kind of changes can happen at multiple time scale. So this example that we talked about is a very rapid kind of change and during development there are changes that take a long period of time when a baby learns to speak it takes a I mean months to years based on which the baby learns to speak and that also involves plasticity any motor skill that we acquire involves plasticity all sorts of adaptation involves such changes in synaptic strength.

So what is the synaptic strength that is measure of the current injection or the amount of depolarization that is achieved by a presynaptic spike. So how do we measure it we recall our previous cartoon where we have a presynaptic neurons axon terminal and then the postsynaptic neuron spine on the dendrite and we have the postsynaptic neuron soma and if we can manage to patch on to two connected neurons neurons that are connected by a synapse. So let us say the green one is pre and our red one is post. So we have clamped on I mean we have patched on to the two neurons and now basically either we can go to current clamp or voltage clamp and make the presynaptic neuron fire action potentials or the postsynaptic neuron fire action potentials or we will see the effect of an action potential in the presynaptic neuron on the postsynaptic side. So what is done is using current clamp on the presynaptic side so using a current clamp on the presynaptic side we make the presynaptic neuron fire an action potential at a particular time and this action potential is based on a current injection in the current clamp and at the same time with the current clamp we measure what the voltage change happens in the postsynaptic side.

So in the postsynaptic side we are measuring the voltage change let us say this is the rest and during this point there is an action potential in a slight delay we see a jump in the membrane potential and that stays like this. So the green and the red curves are not to scale or in the same scale here when we have an action potential this is obviously range of 100 millivolts and this is in the range of few millivolts to tens of millivolts. So order of 1 millivolt and that is order of 100 millivolt. So what is essentially happening here since the voltage change is depolarizing due to the presynaptic spike so this is depolarizing that means the synapse is an or the current injection is excited in nature this is an excited transmission. So and this potential this kind of the event like thing is called the excitatory postsynaptic potential EPSP and let us say if the synapse is inhibitory and we do the same experiment for example if it is neurotransmitter is GABA where the presynaptic neuron is GABAergic that is the neurotransmitter produced is gamma amino butyric acid.

So the GABA receptors are essentially chloride channels GABA A and GABA B and so when the GABA neurotransmitter is released and the ligand gated chloride channel which is the GABA receptor it opens it allows chloride to go into the neuron based on its direction of flow for its equilibrium potential is negative 90 millivolts. So in that case the current that we the voltage change that we see is hyperpolarizing or it is in the negative direction and this we call the inhibitory postsynaptic potential. So excitatory and inhibitory and this is the postsynaptic potential that is we are measuring the voltage change or potential change at with a spike in the presynaptic side what is happening due to the spike after synaptic transmission on the postsynaptic side. So this measurement on the postsynaptic side can also be done within voltage clamp or keeping the voltage at rest and in that case what we would measure are currents and so let us say this is zero current at rest when the membrane potential is held at rest and if we have a spike in the presynaptic side at this particular time point as before then with a slight delay we would we can see a current injection of this form and this downward current negative going current is the convention used for inward currents that is into the neuron and hence it is excitatory in nature because there are positive ions going into the neuron and this is what we will call the excitatory postsynaptic current. So EPSC and EPSP and so similarly in the for the GABA case we will have an inhibitory postsynaptic current or IPSC which is outward in nature or positive going current.

This is the inhibitory postsynaptic current and so they have a specific type of shape which is usually a gamma function like or sometimes even modeled with a exponential decay and we will be looking into those aspects later on in our lectures on synapses and synaptic plasticity. So the measure of synaptic strength is either

the size of these EPSPs and EPSCs so this size here the amplitude or this size here or any of these the size of the event due to spike in the presynaptic side in the current or in the voltage can be used as a measure of the strength of the synapse. So larger the strength of the synapse that means the stronger or the larger amount of current injection that would happen or the larger amount of depolarization or hyperpolarization would happen in the postsynaptic side. So this is generally what is used as the strength of a synapse that we can determine experimentally. Another measure of strength of a synapse is the charge transfer in the postsynaptic side and that is essentially the integral of the EPSC integral of the postsynaptic current that is area under the curve.

So since this is a current and that is basically our charge. So with these kind of measures our synaptic strength is characterized and this is again remember we are talking of the stereotypical synapses that and majority of our computational models will be based on such synapses. There are there can be other forms which you must keep in mind other I mean since especially let us say it is metatropic the current would not look like that neither would the postsynaptic potentials look like the gamma function or alpha function and or exponential decay. They would be of different kinds and but for our models we will in this course we will be talking about these kind of events due to a presynaptic spike. So now in these cases what we will be doing is that we will be looking into how these synapses or the synaptic strengths get modified over time and we will be discussing such modifications in our next lecture where we will talk of how synaptic modification takes place. Thank you.