Computational Neuroscience
Dr. Sharba Bandyopadhyay
Department of Electronics and Electrical Communication Engineering
Indian Institute of Technology Kharagpur
Week – 09
Lecture - 42

Lecture 42: Ways of modification of Synaptic Strength

Welcome. We have discussed about synaptic transmission. We mentioned how the presynaptic sides action potential produces an event in the postsynaptic side in the case of ionotropic transmission and they can be excited in nature in the postsynaptic side excitatory effects or they can have inhibitory effects. So for example in the excitatory case if the presynaptic side neurotransmitter is glutamate which is one of the neurotransmitters and the postsynaptic side has amper receptors which are themselves cation channels non specific allowing sodium to flow and also some amount of calcium then we have a depolarization in the postsynaptic side. Similarly we have talked about the presynaptic sides neurotransmitter as GABA then we can have in the postsynaptic side if we have receptors that are GABA A receptors or GABA B receptors we get a hyperpolarization in the postsynaptic side and that is because of chloride current that goes into the neuron in this case it is cations mainly sodium and some amount of calcium flowing into the neuron. So these effects can be modified over time in a number of ways and so the components that are involved in the synapse as you see are the presynaptic side the elements that are involved and also the postsynaptic sides the elements that are involved all of these together or each of them or one of them or a combination of them can change in order to change the strength of the synapse.

So in the presynaptic side which has vesicles with the neurotransmitters so if we recall the presynaptic sides terminal we have vesicles that contains neurotransmitters in it. So these vesicles after dumping the neurotransmitter in there the unused neurotransmitter gets picked up back up by the through endocytosis by the presynaptic side and they are taken back to the endosomes which then again get fill up vesicles with neurotransmitter and that comes in. So the amount of neurotransmitter available in the presynaptic side is finite and depending on how much activity is going on vesicles full of neurotransmitter may or may not be available in sufficient amount. So that itself this itself can produce a change in the synaptic transmission or synaptic strength.

So for the process that happens this re-uptake of the neurotransmitter and then being repackaged back into vesicles requires a much longer time than it requires

for the vesicles to go and be bound to the membrane and release the neurotransmitter into the synaptic cleft. So this process is much faster and this process is much slower and hence due to this imbalance if we have a lot of activity coming in large amount of activity that is spiking it may be depending on what kind of synapse that the neurotransmitter available to be released is not I mean is not sufficient amount and hence the amount of neurotransmitter in the synaptic cleft is less compared to an earlier spike we get we can get smaller sized EPSPs. So these the amount of neurotransmitters in vesicles that are present postsynaptically that can itself modify the synaptic strength. Similarly in the presynaptic side as you remember when the action potential reaches the presynaptic terminal there are voltage gated calcium channels that open up and allow calcium to come in. So this calcium concentration in the presynaptic side if there is a larger basal calcium concentration or build up of calcium inside the terminal or even outside calcium concentration exchange then the presynaptic sides effect on the synaptic current on the postsynaptic side can be altered.

So both the calcium as well as the neurotransmitter both can influence synaptic transmission. So these are on the presynaptic side. Similarly the proteins that are involved in holding the vesicle at the membrane and those that are involved in a calcium dependent mechanism to help the vesicle release the neurotransmitter those proteins the availability of them or whether they are being synthesized in a large enough amount or not these also may influence the strength of the synaptic transmission in the presynaptic side. Similarly on the postsynaptic side there are a number of ways in which the synaptic strength can be modified. So in the postsynaptic side if you recall we have if we draw this spine with the neck there are receptors on the postsynaptic side.

So the amount of receptors or the concentration of receptors that are present in the postsynaptic side that itself can be a way to modify the synaptic strength. So if there are less number of receptors available like receptors being internalized with certain mechanisms which we will discuss later then the synaptic strength will change because the amount of current due to the receptors is going to reduce or if the number of receptors is increased then there is going to be an increase in current because you have more receptors involved to produce or allow the current injection to happen. And so these receptors can themselves be a form of changing or modifying the synaptic strength. Similarly indirectly it is also the surface area present which allows the number of receptors to be more or less depending on how much area is present on the surface of the spine that indirectly is again that is how much receptors can be present that also influences the strength of the synapse. In fact we will see that the spine size is a very good marker or very good measure of

what the synaptic strength is going to be.

So these spines can be very narrow and filipodia like when they are forming and then gradually can increase in size and become stubby which makes them actually act as stronger synapses. Similarly in the postsynaptic side there can be other ion channels that are indirectly involved in the postsynaptic side's current. For example along with the AMPA receptors there are other ion channels like the receptor NMDA which remain blocked by ions called that are magnesium ions and only when the postsynaptic side has a high enough depolarization this magnesium ion gets blocked out from the NMDA receptor pore which is an ion channel which then allows current to flow in. So these the voltage on the postsynaptic side itself is now modifying the synaptic strength by allowing the new kind of ion channels to allow more current to come in. So the presence of NMDA ion channels plus depolarization can modify the synaptic strength.

Similarly probably the most important factor in deciding synaptic strength is the concentration of calcium in the postsynaptic side and this calcium concentration can go both ways in modifying the synaptic strength. It may allow go to change in increase the strength of synapses or decrease the strength of synapses depending on its concentration and what molecules it activates downstream. So essentially it is through calcium that the main longer term modifications that take place which actually involve synthesis of new proteins in the synapses to make them more strong. For example more neurotransmitter receptors are produced synthesized and brought into the in the postsynaptic side allowing more allowing stronger current. There are ways in which more cytoskeleton proteins cytoskeletal proteins are synthesized which causes changes in the size of the spine.

Then there are other postsynaptic proteins that hold the synapse together that is like postsynaptic density 95, psd95 and so on. There are number of scaffolding proteins that are involved in giving the synapse form or a structure those proteins can also be up regulated or synthesized more and increase in synaptic strength. Similarly stopping of those processes and ability to internalize more of the receptors through other proteins that can also be happening and reduction in synaptic strength can be achieved. So we see that the changes in synaptic strength or modifications in synaptic strength can happen both presynaptically and postsynaptically. So pre and post and we also sort of eluded to the fact that there may be different time scales at which these changes can happen.

For example the neurotransmitter concentration available to be released that is acting at the scale of events or spikes occurring in a series of action potential. So it is within a scale of few seconds or even hundreds of milliseconds that such changes can take place. Similarly in the postsynaptic side also the NMDA kind

of current can actually be a very fast way if you get a small depolarization or a sufficient depolarization in the postsynaptic side to knock out the magnesium ion from the pore of the NMDA channels. Then we get a fast change in the amount of current flowing into the postsynaptic side and increases the synaptic strength. But that same way the NMDA allows a lot of calcium to come in and that calcium flow then can modulate things in a much longer time scale through protein synthesis and modify these synaptic strengths.

Similarly there may be more new synapses forming based on the more spines forming and there may be synaptic modification of synaptic strengths. That is indirectly with more and more synapses the connection between two neurons may be made stronger or more new connections with other neurons can also be forming which is also a form of plasticity and that kind of plasticity is more prevalent in during development where you get new synapses or even you prune synapses that is you reduce the number of synapses that are not useful and modify the connection strengths. So with these ideas of modification of synaptic strengths and sort of the time scales possible we will continue on to our in our next lecture about how these synaptic changes occur in the sense of what are the kind of changes that occur and how we can model them in terms of different time scales of plasticity. Thank you.