Computational Neuroscience
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Week – 10
Lecture – 47

Lecture 47 : Spike Time Dependent Plasticity

Welcome. We have been discussing long term potentiation in this week and we had covered how long term potentiation and long term depression happens that is the mechanisms behind it. And we started with the ideas of how different kinds of manipulation of the activity in the presynaptic side can lead to potentiation. So, or depression let us look back into what we had covered last that is if we have a presynaptic neuron make an action potential we make the neuron fire that action potential while we are measuring EPSPs postsynaptically we get an EPSP let us assume that it is a excitatory synapse and we do a manipulation which is either high frequency stimulation or low frequency stimulation that leads to in one case it leads to after we measure the synaptic strength again it leads to potentiation which carries on for a period of hour or more. And similarly for the low frequency stimulation if we do the same measurement again we actually get a long term depression and that is also carried on for a long period of time or similar periods of time. So, we have essentially long term potentiation and long term depression.

So, we said that this high frequency stimulation is essentially a correlational activity or even almost I mean it is like a causal activity in the sense that pre is making the post neuron fire in that case we get potentiation that is strengthening of synapses and if we have a causal like activity or de correlated activity then we get depression and this is a causal in the sense that postsynaptic neuron fires before the pre. So, it is almost like an a causal kind of phenomena if we think of a unique one directional flow of information and I mean in fact in the synapse mostly synaptic transmission as we have studied is forward directional there are of course retrograde signals that we have not discussed, but it is not really causing spikes in the presynaptic side. So, it is as though it is a causal. So, in these in these scenarios while this produces potentiation and depression remember we must have postsynaptic neurons activity also that comes into play.

Here it was it happened to be with the high frequency stimulation we have the postsynaptic neuron fire such activity that led to long term potentiation. Similarly with the presynaptic low frequency stimulation it so happened that we get depression, but what about if we control the activity on the both the neurons ourselves.

So, that is what we will consider first which is the spike timing dependent plasticity spike timing dependent plasticity. So, here we recall our same idea we have pre neuron whose axon terminal is ending on the spine of a post neuron. So, this is our pre and we will have our post here just say here and its dendrite is drawn here its axon is projecting somewhere else.

And so we are patched on to both the neurons simultaneously as in all our previous cases, but in those cases we were not making the postsynaptic neuron fire any action potential or we were not controlling the activity of the postsynaptic neuron. So, the activity that we did in the patch on to the postsynaptic side was only for measurement measurement of the synaptic strength. And then we did a high frequency stimulation presynaptically and saw the effect on the synaptic strength. So, here we explicitly control the activity in the pre and post. So, again if we do the measurement where we make the pre neuron fire an action potential and then we measure the postsynaptic strength.

And here we then the manipulation that we do is what we will call pairing that will bring about the induce the long term plasticity. So, what we will do is let us say since both are in our control we do a current clamp on the presynaptic side and also the postsynaptic side and make the neurons fire action potentials at t_{pre} and t_{post} times. So, this is the postsynaptic action potential and this is the timing of the presynaptic action potential. So, let us say that we have the pre action potential at this time point where the post action potential occurs at this time point. So, they are both on the same time scale.

So, in other words we have a gap of some delta time between the two spikes that is our t_{post} minus t_{pre} is equal to this delta time interval that is our gap in the spike timings of the two neurons that we are controlling. And we repeat this or this is what we will call pairing we paired these two action potentials at a gap of delta time multiple number of times 100 times with sufficient gaps in between each pairing. So, that there are not any effects introduced from next subsequent spikes. So, now if we again go forward and measure the postsynaptic neuron strength let us say what we get is from A prime. So, let us say this amplitude is A prime and this amplitude is A.

And if we do this long enough multiple number of times and we see that indeed we have a long term change in its synaptic strength and we have this A prime continued for a longer period of time. So, now the change the fractional change in synaptic strength of this synapse is given by A prime minus A divided by A normalized by the original synaptic strength. Let us we will call this as little delta let us say δW synaptic weight change. So, now if we take the similar idea and plot here the x axis is delta that is T_{post} minus T_{pre} and on the y axis we

plot our δW. So, that is we are now saying that we do multiple experiments and multiple number of neurons of similar pairs of neurons and do this experiment for delta that is very close to 0 maybe a millisecond or 10 milliseconds and so on and a variety of deltas.

And similarly we can get delta to be negative by explicitly making the postsynaptic neuron fire and action potential before we make the presynaptic neuron fire and action potential. By a period this delta which also can is varied across a number of values and based on this based on many such experiments if you plot the individual points for results of each experiment we generally get a curve or we generally get a scatter which is more like this. So, in other words what we are seeing is that as we in the positive delta as we go further out in delta that is the T_{post} is occurring further and further after the T_{pre} the degree of potentiation that is the degree to which the synaptic strength is increased reduces. And this if we fit a curve it is more or less like an exponential decay and depending on the neuronal type we get this limit to be around 40 milliseconds 40 to 50 milliseconds. And similarly when we look at the negative deltas the closer the presynaptic spike is to the postsynaptic spike.

So, we have the postsynaptic fire an action potential and immediately after that the presynaptic neuron fires an action potential that is close to here this provides a depression. So, here for positive delta we are getting potentiation and for negative delta here we are getting depression. And in the same manner as we go further negative values the degree of depression keeps on reducing until it does not matter anymore. So, there is a window so again if we fit a curve it is generally the same exponential kind that best fits it. And this is there we get an asymmetric sort of strengthening and weakening curves that is the depression has a larger window that is a larger length over which the interaction produces depression.

Whereas in the positive delta side the potentiation occurs with up to much lesser values of delta this is almost like 80 milliseconds or so minus 80 milliseconds or so. And of course these numbers are not very important in the sense that in the sense of the concept of spike timing dependent plasticity. But they do mean something in terms of the mechanisms that are involved and it actually would vary from synapse to synapse or different the types of neurons that are being connected between with particular synapse or it is the synaptic type also the neurotransmitter involved and so on and so forth. So this this window that we have drawn of T_{post} minus T_{pre} and how the synaptic strength is modulated by this different spike timings is what we call the spike timing dependent plasticity learning rule or STDP window. And this is the learning rule for a synapse that is Hebbian in nature.

What we mean by Hebbian in nature again if it is correlational and causal

so to speak otherwise then we get potentiation and if we have a causal activity or de-correlated activity between the pre and post side we get depression. And so this is Hebbian spike timing dependent plasticity learning rule. And so now obviously as we mentioned that there are not one kind of synapse and there is extreme specificity of the types of synapses between two neurons. And so similarly many people have studied multiple neuronal types that are connected to each other through particular types of synapses and quantified the or rather derived the learning rules explicitly controlling the spike times of the pre and post synaptic site. And there are a variety of observations that have occurred.

So they are not necessarily Hebbian they can be totally anti Hebbian in the sense that the learning rule actually is exactly the opposite of what we just saw. So T_{post} minus T_{pre} and so we are getting so this is again our δW and this again in that window we get depression now for a causal activity that is correlated activity in the post and the pre and in the opposite side we get potentiation. So as you may well appreciate this is not the only kind that is observed there are few other kinds that have already been observed and remain to be more remain to be discovered. And so this has to be more experimental basis that we derive this learning rules. So for example we have certain inhibitory synapses that have a learning rule that is of this nature where they are primarily depressive in nature.

So they are depressive in nature that is when pre and post neurons occur simultaneously in a correlated manner nearby each other positive or negative there is depression. And far out there is for a limited window there is potentiation. So this potentiation of course needs to be there otherwise with activity this synapse will completely cease to exist finally because we have no limit to the I mean it will keep on depressing itself and will basically have no activity transmission anymore. So this is another kind of synapse there are multiple other kinds where you have something like this that can lead to synaptic plasticity in with this particular kind of learning window. And there are many others that you can look up with searching for STDP learning rules and each of them have are for a specific type of synapse between two specific types of neurons in a particular region of the cortex or the brain rather.

So obviously the question then arises that if spike timing dependent plasticity is the way we have to model synapses then do we need to then know all the kinds of synaptic learning rules this kind of learning rule which is I mean really impossible almost at least with the current kind of methodologies and so on. So deriving the learning rules for all possible synaptic types then becomes difficult and so we require some other theoretical approaches to see what the learning rules can be or should be. So these require certain criteria or certain optimization principles

that will guide our sort of derivation of synaptic learning rules. And so far there has been very little work in this direction although I will refer you to work by Gal Chechik you can find it in a neural computation journal paper. The explicit reference will be there in your reading material you can take a look if those who are theoretically minded and want to take on analytical problems these what they showed is that with certain criteria or certain physical quantities that need to be optimized in that case they showed that what with maximal information transfer under certain other conditions they could clearly show that in order that if the synapse was getting modified in a particular manner based on the timing of the spikes then that would turn out to be learning rule that is like the STDP learning rule that we see for hebbian plasticity.

So this was theoretically derived using maximal information transfer from the presynaptic side to the postsynaptic side with certain other constraints. So I am not going to go into the details of this work because it is heavily mathematical and it depends on I mean not all of you may want to approach this kind of a problem but those who want they can read the paper and do it and so the question arises then based on the activity of the presynaptic side of pre and post neurons of certain types and by knowing their particular functional properties that is we know what their natural statistics of activity is in the preside and the postside or have an make an idea of how they are behaving and then we introduce the constraints of similar kinds with maximal information transfer then can we derive the or predict the plasticity rules if STDP rule can be predicted. So if we can do this prediction then we can test out in different kinds of synapses as to what the STDP rules turn out to be and basically come up with modifications of our theoretical approach if we do not match and if we do match then we go ahead with further kinds of synapses. So this is a kind of approach that remains to be taken up for further work because there is very little work that has been done in this direction and I think we had discussed this very point in our last live session where we were among multiple questions about what should we what are the primary problems to tackle in neurosciences and so on or in computational sciences I had mentioned that this is the one of the kind of problems that can be very important in terms of understanding and changing our views about computational neuroscience and if we can derive these theoretically it is going to be make a huge impact and remember this STDP we have done it based on only a single spike pre-synaptical and a single spike post-synaptical. So there are there is a lot of work now it is not to do with just one spike and correspond with one spike in pre and post.

So there is work that has been going on with bursting of spikes with a burst of spikes pre-synaptically and or some pattern of doublets or triplets of spikes

and so on. So again so this leads to a very complicated situation in terms of deriving what the actual spike timing or activity dependent plasticity rules are. So that is why I am saying that with theoretical approaches if with basic one kind of synapse and then with these theoretical approaches if we can show and predict the observed behavior in experiments and then we can go forward with many other kinds of synapses. So it is imperative that we think about the problems in this manner in a more general manner in order to further approach problems that we will be tackling or you will be tackling beyond this course if you are going into the neurosciences particularly in computational neurosciences. So with this we will be concluding this lecture on STDP and now we will in the next lectures consider how we implement STDP or long term potentiation long term depression in models of I mean in theory in models of neurons in computationally. Thank you.