Computational Neuroscience
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Week – 11
Lecture – 55

Lecture 55 : Developmental Cicuits

Welcome. So, we have been discussing how plastic plasticity is implemented and explain and is used to explain variety of phenomena. And we have so far looked at short term plasticity, bit of long term plasticity in terms of adaptation and also in terms of attention. And so now, we will talk about implementation of long term plasticity to explain some developmental phenomena in terms of how circuitry develops in the cortex over development over the periods of development. So, in in this case if you recall our cortex is a layered structure with layer 1, layer 2 3, layer 4, layer 5 and layer 6. And of this our layer 4 is the thalamo recipient layer.

So, thalamus which takes information from more subcortical stages from fine originally from the periphery finally, via the thalamus the input comes and makes a synapses the on neurons in layer 4. And then processing in the cortex starts there and it carries forward in terms of going to layer 2 3 or other regions wherever it is required. So, but the circuitry is not like this this thalamus to layer 4 connection which is the probably the beginning of the cortical processing. It is not like this when the brain is developing it is quite different.

So, and there are stages through which this happens and initially what happens is that there is a layer of neurons called subplate neurons and these are present transiently. So, the the the layer 1 2 6 is not there at that time there is cortical plate that comes out from there later on, but what is present is only the subplate layer of neurons first. And it is the thalamic axons actually come and make a synapses on to the subplate neurons, SP neurons. And the then actually when the other neurons are other layers are developing neurons actually propagate through that the subplate region and there are collaterals of axons from the thalamus or that make connections with layer 4 neurons. So, this is a layer 4 input neuron, the layer 4 subplate neuron and there are connections between the subplate neuron and the layer 4 neuron.

So, we have then gradually with development what happens is that these 2 die away and the subplate layers as I said was transient that also goes away. And what we get is this final circuitry in the adult. And the subplate is present in a very short

I mean not short I mean in a very specific period of time during development and it also happens to coincide with some of the critical period plasticity that is observed in the sensory systems. That is manipulations of the environment in which the animal is growing causes profound changes in the circuitry and behavior that last for the life lifelong, but the same kind of environmental changes after the critical period do not induce such permanent changes. So, so it is thought that that the subplate neurons can play a role in this kind of critical period plasticity.

So, if we now go back step by step it is the the most interesting part is later on this is the subplate neuron and let us say we have a thalamic neuron. So, initially it is like this then there is a second part that let us mark it with this blue. And then finally, from here it becomes what we have discussed that is the thalamus which is layer 4 the thalamus directly to the layer 4. So, how how is this kind of thing achieved from the initial stages and then it goes on to the case where the subplate neurons output dies away and the thalamus to subplate neuron input also goes away because the subplate is not there anymore. So, and how is the blue synapse in the top getting strengthened.

So, if you think about it let us say the thalamus is providing spike train inputs on to the subplate neuron. Let us say or I mean there is evidence that supports it that the that this synapse thalamus to subplate synapse let us call it T S synapse T S this synapse T S is strong that is it this synapse can make the subplate neuron fire action potentials. So, whenever there is a spike in the thalamus because of the synapse T S almost all the time the subplate neuron is also producing action potentials. Now the blue synapse the synapse let us call this the synapse T 4 that is weak. So, it is not being able to drive the layer 4 neuron initially.

So, because the thalamus to subplate synapse is strong the subplate neuron is firing action potentials and if the subplate to layer 4 synapse is strong it will make the layer 4 synapse fire action potentials. So, if this is let us call this the synapse subplate layer 4 S 4 . So, what is happening is with a synaptic delay layer 4 neuron is producing action potentials. So, essentially what is happening that the thalamic action potential is causing the layer 4 neuron to fire via the subplate. So, thalamic action potential is causing the layer 4 neuron to fire action potentials via the subplate.

So, this is the layer 4 the this is the subplate thalamus I am sorry this is the subplate and this is the layer 4 neuron. So, with gradual synaptic delays the layer 4 neuron is firing action potentials after the thalamic input. And remember when there is a thalamic spike there is a spike along this sine terminals along this particular line. So, that is an action potential in this path is also an action potential in this path they are collaterals. However, this synapse is unable to drive the layer

4 neuron, but if you now see the thalamic spike which is now let us consider this particular synapse that is extremely weak that is our thalamus to layer 4 synapse.

So, what is happening here that presynaptically the thalamus is firing action potentials and postsynaptically layer 4 just a little later is firing action potentials not due to this particular spike not due to the spike in that is in the presynaptic terminal from the thalamus to layer 4, but due to a spike that is being caused through the subplate neuron from the thalamus to subplate to layer 4. So however, with this scenario there is a pairing STDP type pairing in that particular ST 4 synapse. It is as if that the input from the thalamus is causing the spike in layer 4 through that synapse, but it is actually not through that synapse it is something else is driving the postsynaptic neuron indirectly and it is as if that it is a causal phenomena from input from the thalamic synapse to the layer 4 synapse. And so because of that this correlated activity in the layer 4 and the thalamus to layer 4 synapse you get strengthening of the ST 4 synapse and as the ST 4 synapse strengthens and strengthens what happens is that the layer 4 is now being driven gradually being driven directly by the thalamic input. So, if we go here what is happening is we are getting long term potentiation initially at this thalamus to layer 4 neuron synapse because of the pairing that is being caused by the same thalamic input via the subplate.

This is being potentiated LTP in this one. So, now what is happening as the thalamic synapse on layer 4 gets stronger the thalamus itself is capable of firing making the layer 4 neuron fire action potentials. So, now if we have a thalamus action potential here in these cases this particular time points. The layer 4 neuron is firing action potentials at one synapse delay only. So, this is basically synaptic delay here this is the synaptic delay here and so on.

So, but now what is happening to the spike that is coming through the subplate neuron based on the same thalamic input. Now, that is now becoming a causal it will depend on the exact delays that you implement in here, but you can it is it is becoming a causal in the sense that the layer 4 neuron is now firing action potentials before the subplate output to the layer 4 neuron because thalamus is now directly driving layer 4. So, there is one synapse delay now that is coming in between the subplate input and the thalamic input to layer 4. So, that way what happens is there is long term depression in this particular synapse and this is gradually this will gradually die away. So, since the subplate output is getting going to die away what happens is basically since the output activity is gone the subplate is not playing a role anymore and that pathway is abolished and in fact the subplate neurons go through apoptosis there is another idea that they get integrated in some other form in neurons in layer 5 and 6.

However, the ultimate objective of removing and driving the the layer 4 through the subplate where this part of the circuitry now goes away and the LTP in the this synapse finally, causes the thalamo cortical circuitry to form. So, this has been an idea that is present that subplate neurons are involved in developing the thalamo cortical circuitry and this can be actually easily modeled with leaky integrate and fire neurons leaky integrate and fire neurons in of subplate and layer 4 and with spike timing dependent plasticity at the synapses actually only the two synapses on layer 4 is sufficient to show that. So now, the question is what is the implication of this? So, there are phenomena that can be shown to happen during development that are dependent on the subplate that is if the subplate is removed then ocular dominance columns do not develop and so that with monocular deprivation what is expected that is not seen and these can be actually replicated with the same ideas in a model where you incorporate long term potentiation and long term or long term depression with spike timing dependent plasticity in the synapses during development. So there are many many many examples of models where the long term potentiation long term depression or spike timing dependent plasticity can come and play a role in explaining phenomena and in the modeling of these phenomena. So continuing with the idea of the subplate and this long term potentiation and depression there are cases where you can you actually have let us say another developmental I mean developmental plasticity that has been observed is the expansion of tonotopic area of a particular tone frequency.

So, in this particular case as we have discussed let us say this is this area is representative of the primary auditory cortex and there is tonotopy which what we mean by that is that there is an ordered arrangement of neurons selective to low frequencies on one end and high frequencies on the other end and there is a gradual change in the selectivity of the different frequencies across the surface of the primary auditory cortex or A 1. And during critical period if one particular frequency is presented repeatedly in mice or rats these experiments and also other species it has been shown that there is an expansion so originally if this frequency f naught has a representation region that is within that within those two vertical bars within that band let us say neurons in this region in normally developing animals represent 7 kilohertz frequency that neurons in this region respond strongly or are most sensitive to 7 kilohertz. And now during critical period if the animal is exposed to 7 kilohertz continuously for those four days with repeated gaps then this area is expanded that is the number of neurons now responding to the 7 kilohertz increases in terms of the area covered by those neurons in the cortical region. And so this expansion in the in the number of neurons in over the tonotopic axis can is a development on phenomena so in the sense that if you present this 7

kilohertz the same protocol to an animal that has passed the critical period and then you look at its tonotopy then this kind of change does not happen. So obviously in the there are there is machinery or things in the critical period that are not present later on and that allow this to happen during only that developmental period.

And so similarly just like the previous example in this case also we can do a modeling with the sub plate neurons. So in the other case we are looking at a single neuron output in layer 4 and in this case we will look at multiple neurons in layer 4 as the output neurons. And let us say you have sub plate neurons here so this is the sub plate layer this is the layer 4 layer and let us say these are the different frequency channels this is representing the different frequency channels. So let us say low frequency to high frequency and repeating the same circuitry we have this let us say is the thalamus we have low frequencies to high frequencies on the two ends and inputs from here come and project on to the sub plate neurons and then a weak input goes on to the layer 4 neurons and there is a strong input from the sub plate neuron to the layer 4 neuron and this kind of thing is present across the frequencies but additionally if we now keep convergence and divergence so what I mean by that is that now we will go into a more abstract way of representing it this is the thalamus layer this is the sub plate layer that is this is the layer 4 layer if the thalamus now projects to sub plate from multiple frequencies multiple regions of the frequency axis and the same is projecting to layer 4 neurons but weaker synapses and the sub plate layer this here is also projecting with some profile in terms of convergence on to one neuron in layer 4 if you have a network developed in this manner with this particular profile of inputs from thalamus to layer 4 that is weak then first of all with normal activity of thalamus you can show that the layer 4 will develop a sort of a tuning that is layer 4 will develop a tonotopic axis which is very obviously expected based on the arrangement of the inputs and our previous example where we have the thalamic input to layer 4 getting stronger based on the indirect spiking of layer 4 through the sub plate now in this same model you can now do the exposure to a one particular frequency during development when the sub plate neuron is present and that again because of that over exposure to that particular frequency and the divergence and convergence of inputs throughout the three layers it you can actually easily show the expansion of the tonotopic expansion of the particular frequency in the tonotopic axis in that that comes about in layer 4 so if you have one particular frequency you will find that the neurons in layer 4 in a wider range of neurons become more selective to the exposed frequency which is this f naught so these are these are examples of how you can incorporate long-term plasticity is like STDP as we saw in explaining a variety of phenomena the explicit exercise of doing the model I leave it up to

you and it is not totally feasible to do the modeling in this course itself by I mean showing you the modeling I am only taking you through the idea and if you are interested then you can do it yourself now that you know that how you implement the leaky integrate and fire model all these these these you have basically two types of neurons sub plate neuron and layer 4 neuron and you have you can have a multiple number of them obviously and you know how to incorporate a synapse and you can also incorporate the spike timing dependent plasticity in these cases or if you want to use a rate based model you can use a rate based model which has problems associated with it but you can now actually embark on this path of taking up projects where you explain phenomena or plasticity phenomena with these kind of models in using leaky integrate and fire neurons and spike timing dependent plasticity. So with this we come to the end of our module on plasticity in implementation of plasticity and explaining variety of phenomena in the different cases and so we will go on to our next week for discussions on theoretical aspects of plasticity and some ideas of optimal coding and I think some research problems current topics that we can I mean that will be useful for you. Thank you.