Computational Neuroscience

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Week – 01

Lecture - 02

Welcome. We have introduced you to the structure of neurons where we looked at the axon as the output side of neurons and the dendrites as the input side of neurons and we briefly introduced to the idea of the structure called spines that are present on dendrites which form the site of input to a neuron from a previous neuron. In this lecture we will be talking about the structure of networks of neurons and the synapses that allow these networks to happen. So we saw that Ramon y Cajal's work showed that neurons are different entities independent entities and it is the synapses that make connections between different neurons and this is where there is no continuity in terms of the inside of the previous neuron and the inside of the next neuron and that is where the whole idea of the neuron doctrine is established. That is through the synapses there is information transmission but there is no physical connection between the insides of the two neurons. There are different other kinds of synapses which are the chemical the electrical synapses unlike the chemical synapses that we are talking about which actually provide a direct connection between the inside of one neuron to the inside of another neuron and that is a special kind of synapse or those are special kinds of synapses and they are present extensively during development and are present so that there is activity that is synchronized between neurons of different types or different neurons can be made to have the same kind of activity which may be required more so during development.

But our discussions for this course will be mainly limited to the chemical synapses which are the most important synapses because of their involvement in plasticity and information processing and so on. That is the whole idea of learning is through synapses between neurons. So let us go into sort of how we came to know about these things again we refer back to work done by Ramon y Cajal and these are examples of their observations or Ramon y Cajal and some others observations showing how intricate these connections are and networks are that form within the brain. So both the examples here and here on the top two have were created by Cajal by based on observations as you can see that there are a number of fibers this is I believe from the cerebellum and there are a number of parallel fibers going in which are making connections at different stages with neurons here whose dendrites are protruding up and then their output is going through where they are making again connections with other dendrites of other neurons.

And similarly here we see that there are synapses that are formed on the neuron at multiple locations. So we had said that synapses form on what we call dendritic spines which are mushroom like mushroom body like structures on the dendrites as we said earlier. It is not necessary that synapses have to form on these dendrites but they can also form as here on the cell soma itself like we see here. So these are the axon terminals that are making connections on to the cell body with making finger like projections on to the cell body covering the entire soma and these kind of synapses can exert very heavy control on the next neuron like here. So these synapses are extremely strong as you can see that there are many many contact points.

So the idea of the strength of a synapse will be coming up later on for here you can imagine it is almost like the many points of control are adding up to the strength of the synapse. So then another the two other examples are shown here with the arrow diagram show the flow of information as well. So there are a type of neuron that are providing information coming from the top going down and put providing an input on to one type of neuron at the next stage and that axon projects on to the cell body of another neuron and that proceeds that sends the information out to the next stage and this is how again in this example also this is how the system of neurons that is the networks are organized. So how the networks are formed during development, how the networks are changing or how they are labile, how they adapt to different situations that we will take up in the last part of the course is when we discuss about synaptic plasticity. So the basic idea here is that the input so to speak of a neuron comes on to another neuron through the structure called synapses and a neuron can have as you see in these diagrams can have many different synaptic contacts from the same neuron or can have multiple inputs from many different neurons or they can also have simply one input.

So the order of magnitude of the number of synapses that can form on a single neuron varies from one to tens of thousands and so based on how these neurons are interconnected with each other through the synapses determine the function of the network and we really do not completely understand how there are general principles that guide these connections to form and although a lot of work has been undertaken to create what we call the connectome or the brain connectome where we talk about exactly how the connections are made from neuron to neuron in different regions of the brain. Those are open areas that people are working on. We do have some ideas of what is connected to what kind of neuron and so on but those are very I mean those are basically scratching the surface. There is a lot of specificity of connections that form between neurons so it is not that if this diagram says anything it is not that everything is connected to everything. So there are only specific types of neurons that connect with specific types of neurons and those are probably what need to be understood in order to fully understand structures of networks.

So with this idea let us go into a more deeper understanding of what we call the dendritic spines or the synapse from with the presynaptic terminal and the postsynaptic terminal. As you can see on the left there is an entire jungle of neurons with dendrites and axons shown here and there are multiple locations at which synapses can be forming. So if we look at one particular neuron here this is the cell soma and all the dendrites are marked here by marking a particular protein with fluorescence and those allow us to see exactly where the dendritic spines are formed. So as you can see from this image the cell soma is dark that is on the cell soma there is barely any spine although there are synapses on there but as you go out on the dendrites there are hundreds of spines making which are the sites of formation of synapses with previous neuron. So a blow up of small region allows us to see here basically what a dendrite is like so here is the dendrite going through and on top of it there is a spine like so that is this part is the spine head.

And this part is the spine neck and as you can see there are an immense number of spines that are formed so each of those are sites of synapses. So what is actually happening in the synapse what is the form of connection how is information transmitted from one to the other. So that is depicted on the right hand side here. So as we said if we consider the dendrite say this is the inside of the dendrite of a neuron and this is the neck of the spine and this is the head of the spine so this entire thing is the spine then a synapse forms on top of this like so this is the stereotypical structure so this part is the axon terminal of the previous stage. So if we have a neuron here whose axon is going and then we have a neuron here whose dendrite is here with a spine at this location if this neuron is making a synapse with it this particular region is what is drawn here.

So this side the first neuron, neuron 1 here and this is neuron 2 here its axon is going out here so this particular side on this neuron 1 side this is called the presynaptic side which is depicted here as the presynaptic side and the spine side is called the postsynaptic side here the spine is not drawn completely this is it is only showing this top part here and this is the postsynaptic side. So in between there is a gap and that is what we call the synaptic cleft. So how is information transmitted from one to the other we will be talking about it in greater detail when we discuss the synapses and model them computationally but for now we need to understand the basic idea behind the synapse and that is there is something in every synapse which is called a neurotransmitter. So this is these neurotransmitters are loaded in synaptic vesicles so what the neurotransmitters are is that they are chemicals they are molecules that act as a form of messenger from the presynaptic side to the postsynaptic side. What the neurotransmitter does its mechanism of action on the postsynaptic side that depends on the receptors of those neurotransmitters present in the postsynaptic side and those are proteins that are expressed on the postsynaptic side.

So we have these vesicles that are packed with neurotransmitters that are present at the axon terminal on the membrane at in the just outside the synaptic cleft or just adjacent to the synaptic cleft and when information needs to be transmitted from the presynaptic side to the postsynaptic side that is from in this direction it is the action potential or the membrane potential change that transfers from the soma and goes along the axon to the axon terminal and causes a membrane potential change in the presynaptic terminal that allows a process by which the neurotransmitter gets released into the synaptic cleft here as described in this diagram. And then there are these postsynaptic receptors they have sites where the neurotransmitter can go and bind and then cause changes or current injections into the postsynaptic neuron. So they are we will talk in greater detail about exactly how the action occurs or rather how the next neuron is manipulated by the presynaptic side through these neurotransmitters and their receptors we will talk in detail in later lectures. So for now what we need to understand is that this synapse is the site of connection between two neurons. It is the information that is communicated from the presynaptic side that reaches the postsynaptic side via the neurotransmitter and the neurotransmitter receptors.

The neurotransmitter being in the presynaptic terminal, the receptors being in the postsynaptic terminal and then the way in which the neurotransmitter receptors behave when the neurotransmitter binds to the neurotransmitter receptor that determines how the presynaptic neuron changes the postsynaptic neurons activity or its membrane potential. So the details of the manner in which these occur are well understood and there are multiple different players in this little synapse few micron structure with nanometers level gap between them and there are intricate details that actually control different behaviors at synapses. And how these synapses change over time will be the probably the most important part of the course in the sense that that allows us to learn how processing occurs, how learning occurs, how memory forms, how we adapt to different situations, how we make decisions, how we change at fast time scales and so on. All these things are dependent on these particular structures, heavily dependent on these particular structures called synapses. So as I was mentioning it is not necessary that the synapses have to form on spines like here like we have described here and here.

The synapses can form directly on to the dendrites. So if this is the dendritic shaft then a synapse can form like in this manner on the dendrite itself. So this is the presynaptic side and this is the dendrite of the postsynaptic side. So there is no spine here. Even the spines can be of different forms.

They can be the narrow neck and mushroom like structure. They can be thin filipodia like structure and so on. Similarly the synapses can also form directly on to the soma as we saw in the previous slide where there is, there are number of synaptic contact made by the same neuron on the soma of that neuron of another neuron. So now the most important thing that we have not discussed and just alluded to is the currency of computation or the action potential. Not just the computation but also communication between us.

As we said that information in some form is coming to the synaptic terminal or the presynaptic terminal and that is being communicated to the next stage through the synapse. That is being communicated from the presynaptic side to the postsynaptic side through these receptors via the neurotransmitters. So what is it exactly? What is it that carries this information? And these are what we call spikes or action potentials. So what is the action potential? We will discuss in great detail when we try, when we understand how this action potential occurs and for that we will be looking into the revolutionary work of Hodgkin and Huxley who also got the Nobel Prize in physiology and medicine in 1963 for their work in the late 40s, early 50s about understanding quantitatively how the membranes of neurons can produce action potentials and how it is transmitted from one neuron, from the neuron along its axon and how later on how that influences synapses and information is transmitted from the previous structure to the next structure or previous neuron to the next neuron. So what is this action potential? So if we were to measure or record somehow as described here the membrane potential of the neuron from its soma that is as we had drawn let us say this is the membrane of the neuron, we have a lipid bilayer as described here which separates the inside and outside of the neuron.

Let us say this is the inside and this is the outside. There are different ions at different concentrations on the two sides of the membrane and that creates a difference in the potential in the two sides. So if the potential inside is V in or V_i potential outside is V_o, then this difference $V_i - V_o$ which we will refer to as V membrane or the membrane potential or delta V sometimes or even sometimes just V. We will depending on the different cases we will be using all these terms and this is the basis of all the computation this membrane potential and if we were to record as depicted here the membrane potential of a neuron so that is shown here then this along the voltage axis there is a point at which the neuron stays the membrane potential stays at rest that is when there is no activity when it is simply stationary and there is no perturbations on to the neuron then the membrane potential stays constant based on the equilibrium of the different ions and that turns out to be around minus 60 to minus 70 millivolts around that it varies from neuron to neuron and in during different states also. And gradually because of this input from the previous side and its influence on the post side because of the neurotransmitter there may be changes in the membrane potential that is it can be excitatory where the membrane potential increases or which we call depolarization or it can be inhibitory where the membrane potential decreases which is what we call hyperpolarization going beyond going being the membrane potential down towards the negative side.

So in this implicitly we have already introduced two different kinds of synapses. Synapses that are excitatory that is they move the post synaptic membrane potential upwards. Synapses that are inhibitory that push the membrane potential downwards or towards the resting state. So depending on the kind of inputs coming on to the neuron as we saw there can be thousands of inputs coming on to a neuron and what influence it has on the membrane potential of the neuron that can be recorded by recording this membrane potential and as you can see the membrane potential changes and there is a point which we call a threshold potential or V_T when the membrane crosses that potential there is an event called the action potential that shoots up the membrane potential up to plus 20 milli volts or plus 40 milli volts around there. So this is a huge excursion from minus 60 to plus 40 around 100 milli volt excursion within a very short time period.

This is a millisecond or so a few milliseconds 1, 2, 3 depending on the type of neuron but it is indeed very short and very fast. This event which we will show later on is all or none that is it is either occurring or not occurring and it occurs whenever it crosses the threshold. This event is the action potential or spike and is the currency of computation and communication between neurons. So this action potential or this change in membrane potential when it travels from the soma along the axon to the axon terminal here as described then there is a process by which this neurotransmitter gets released. So that is where the connection of the communication between neurons and the computation by the previous neuron is coming in.

It is the action potential that is generated based on computation in the soma or the axon hillock as we described in the very beginning of the axon and that is communicated via the synaptic terminal to the post synaptic neuron to produce an excitation or increase in membrane potential on the next side or inhibition that is decrease in membrane potential on the next neuron through these synapses and the neurotransmitter and its receptors. So this completes the full circle. Now this membrane potential change in the post synaptic neuron whether it is excitatory or inhibitory and how other inputs are coming in over time that determines how the processing or computation done by the next neuron the post synaptic neuron is determined and if it produces a series of action potentials then those action potentials are again transmitted or communicated along that neurons action terminal to the next stage neuron and so on. So this is sort of the basic crux of how the information is flowing in the nervous system or in at least in the central nervous system which we will try to understand in terms of how these action potentials are generated quantitatively. We will also understand how the series of action potentials produced by a neuron actually carry information about the external world or the mental state or what have you and in the last part of the course we will be talking about how these synaptic structures are modulated or rather how synaptic plasticity occurs based on the activity of the presynaptic side and the post synaptic side in a self organizing manner that is totally activity dependent and self engaging that is based on the activity the synapse itself modulates or changes itself and the system learns.

So with this we come to the end of the structure of networks of neurons and networks of neurons and synapses lecture and we will carry on in the next lecture with information flow in the nervous system. Thank you.