Computational Neuroscience

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Week – 02

Lecture - 10

Lecture 10 : Single Neuron Acitivity

Hello, welcome to our last lecture in the second module. So, we have been discussing about current injections in in two neurons through synapses and how they actually can then generate action potentials or change the membrane potential and so on. So, now putting all these things into more broader perspective, we will slightly discuss about what is going on at a systems level and how we are going to try and understand the system in the second part of the course. That is when we will be recording as we have been talking about for the for measuring extracellular activity or through calcium imaging indirect measures of activity . We gain that information and then what we try to do is try to understand computationally what aspect of stimuli or what aspect of behavior or what aspect of maybe decision making or some other higher order function is being is being controlled by the neuronal activity or the what kind of activity is connected to the particular behavior that we are observing. So, in general the kind of experiments that we will be talking about is either an electrophysiology with stimulus being played.

For example, here what we are showing is an auditory physiology set up where here is a speaker which plays sounds and here we have a mouse which is the experimental subject here. Here we have a 16 channel electrode array that is inside that is being put inside the brain and the animal is anesthetized here and from these these electrodes the signal is captured and this is an example of spiking along one of those electrodes. And let us say that we have some baseline when there is no perturbation being done by the experimental experimenter and then there is this green block of event which may be a sound playing which may be if it were an awake animal some kind of task the animal is doing and we have the period of spiking activity corresponding to that. It does not mean that the event that the spiking only in that exact same time window must correspond to it.

The spiking later on may also be influenced by the event that is preceding it. So that keeping these in mind what we will be show what we will be looking at that if we get this action potentials or the timings of those spikes then based on based on that what can we conclude about the the control the the the changes that are being done in this green block which as we said can be a stimulus which can be an auditory in this example which can be light and sound multisensory which can be olfactory or as we as we know there are cases where animals are trained to perform a task and we record along with the task being performed and we can try to understand based on the activity corresponding to that task period or beyond that to try and understand what kind of changes are occurring or how that kind of task is being achieved. And additionally on this we can also do some activity manipulation and then do the recording. So, for example, here we also have an optical fiber which is being connected into the neuron into the brain to shine light in there where now we have neurons that are expressing light activated ion channels that allow us to control their activity and or maybe a particular type of neurons activity and look at and then in on the electrode we are recording activity of other neurons and then we try to understand the role of those particular neurons in in the particular encoding that we are looking at. So, be it stimulus, be it task and so on.

So, here the example is for an animal that is anesthetized it can also be awake and behaving or rather awake and we can this in this case the animal is head fixed and is sitting there quietly and there is an electrode implanted onto the brain and the same recordings are being performed. Similarly, there are experiments that people do in let us say in the visual system where you have visual stimuli playing and the animal may be performing a task based on what it is seeing. And so here the idea is that the from those single neuron activities we try to reconstruct, go back and try to say what was going on here based on these neuronal activities. So, there are two sides of this that we will talk about. One is the forward problem and the other is the backward problem that we were talking about.

That is we record the activity and from that we try to infer what the stimulus was or what the task was or so on that this is also known as decoding. And there is also the forward problem that is we given this green box whatever that is it can be a stimulus and or a task as we have mentioned. We are recording this activity and we now try to see how we can understand how the from the green box we go to this activity. That is we try to model the system that is this is the coding part that is how that the things going on in this green box can be can be transformed into these single neuron activities or single neuron spike. So, both these are equally important for example, when we try to infer the decoding this is for example, very useful in brain computer interfaces where we want to look at the activity of neurons in the brain and try to infer that say for a paralytic patient we are maybe we can record from its intact the persons intact motor cortex and the we know that the person is trying to move an arm and so based on the spiking we want to learn what the person is trying to do and then accordingly we infer that and make a robotic arm do that.

And similarly the forward problem is that that there we want to model it that is so that when the when there is a change in the green box we can predict what the output is going to be. So that we do not have to do these kind of experiments anymore so that we understand the system. So, they they also will have a equal amount of applications. So, all all this will come in the second part of the course which we will be talking about in which we will be talking about this mainly the encoding coding and decoding part of it in terms of stimulus encoding primarily. So, based on what we have learnt so far so in this first 2 weeks where we have introduced you to the ideas that on which we will be building on is that we have we are we will be recording from neurons let us say a single neuron and we have talked about synapses.

So, a single neuron can have as we have discussed 1 synaptic input on there can have tens of thousands of synaptic inputs on there. And by recording we essentially we mean recording its action potentials or series of action potentials extracellularly or as we have discussed earlier using patch clamp we also know what is going on in the membrane potential before and after the action potential. So, this is let us say V m and this is extracellular recordings. So, here in when we talk of this activity of the single neuron it is entirely based on what inputs it is getting that is let us say there are 3 inputs here one is excitatory input 1 another is an inhibitory input here and another is an excitatory input E 2. So, let us say this excitatory ones are yellow and the inhibitory one is red and we are recording here.

So, based on the neurons from which these inputs are coming that is their action potential get transmitted along the axon to this terminal and as we have studied in the synaptic transmission in the previous lecture there is a change in the membrane potential inside an EPSP if it is excitatory. So, this is depicted here let us say. Then as it goes on let us say there are two E1 and E2 together there are 2 spikes close by in time on E1 on the on this axon as well as this axon and it is sufficient to make the neuron cross threshold and there is an action potential. Then as it go on you have may be an input on the inhibitory neuron then from the inhibitory neuron so on. And so here it is an inhibitory input and an excitatory input which sum together to this and here is 2 excitatory inputs along with an inhibitory input which does not allow it to cross threshold without spiking.

Now, this very picture that you have with 3 synapses think of it in terms of 10, 20, 100, 500 synapses variety of timings of these synaptic events that is spikes in the presynaptic side or the previous neuron and on top of that the location of these synapses that is also equally important which is not depicted in this figure as well. So, some of the synapses would be stronger more influence on the soma and some of the synapses are weaker by themselves. Again, based on the distance from the soma which we will be modeling the EPSP has to travel to produce a change in the membrane potential in the soma in the neuron which goes behind the final membrane potential that goes to produce an action potential or not produce an action potential. So, there can be cases where there are interactions between nearby synapses that is can be synergistic that is there are non-linear effects between them and there is amplification of them or they can simply kill each other out or even by shunting inhibition a whole dendritic branch may even be simply shunted out. So, that is how complicated it is and it is almost a humongous task if you have to model this entire thing for every neuron that is extremely difficult.

So, in a sense what we will do later on is try to see this how we can simplify it into a simpler problem like a systems modeling problem where we represent the neuron by or even the entire pathway by a black box or and think of it as a black box and try to estimate a model based on few parameters that tries to explain the entire behavior from the stimulus to the response and that is essentially what we will try to do in the second part of the course after we understand the spiking. So, in this case the phenomena that we are seeing is devoid of any changes over time at the synapses. So, there are cases where the synapses the strength of the synapses if you will is changing over time like short term depression and long term depression or short term plasticity or long term plasticity that is what we will be considering in the third part of the course that will show us how the computation of a single neuron can change. So, with all these ideas introduced to you the brief outline of going forward is essentially first we will try to model the spiking activity that is how action potentials are caused. Now, once we understand how action potentials are caused they are all or none behavior then we will try to understand and study how we analyze a series of action potentials produced by a neuron in response to a stimulus or during a behavior and so on.

So, that part will be the encoding and decoding part and following that we will be looking at plasticity where over time the system will change such that for an input A if we are getting an output B or response B spike train later on the input A is producing a different output B' and that helps the organism in a particular way in some way. So, those ideas of plasticity and how we model that all those things will come up in the third part of the course. So, I hope with the first two weeks these ten lectures you have sufficient background and you are really interested to get in into these three aspects that we will be covering over the few weeks after this. Thank you.