Computational Neuroscience

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Week – 02

Lecture - 11

Lecture 11 : Point and compartmental models of neurons

Welcome. So we have been going over basically the introduction that is required to go over this course. So the first part had to do with structures of neurons and the second part had to do with the basics of excitable membranes and what neuronal activity is and what we will be doing with it going forward. So as discussed in the last lecture, we will be first trying to see how we can model the phenomena of action potential production. So now you are familiar with the ideas of ion channels being present in membranes of neurons particularly voltage gated ion channels and that the membrane acts like a capacitor. So essentially we will be trying to make an electrical model of the neuron and in making the model, we will make a variety of assumptions and we will have more complicated or we can have more complicated models by including a lot of complexities and we can have very simplistic models by making a number of assumptions.

And so all this depends on the question that we are going to attempt to answer with this model or with those models and we have to accordingly make our assumption or not make assumptions depending on the questions we are trying to address. So we will go over a few of those and in general neural models if we think of single neuron spiking models, they can be basically of two kinds, one that we call a point model and the other that is a compartmental model. So let us briefly look into the structure of neurons as we have done before. Let us say we have the cell soma and then we let us say we have an axon that goes and projects and makes a synapse onto some other neurons and let us say we have multiple dendrites.

And there are branches and there are multiple synapses on those branches that are getting inputs from many other neurons. So by now you should be familiar with these ideas and so we have been saying that the most important aspect of the neuron is its membrane potential V or V_m or ΔV. We may be using these interchangeably just make sure that what we are using at a current moment just remember that we may be using any of them and this is equal to the $V_{in} - V_{out}$ that is inside the neuron and outside the neuron. So the question obviously is, is one V sufficient to describe the neuron? So is it that the entire neurons, so if I were to measure the $V_{in} - V_{out}$ physically at this location that is $V_{in} - V_{out}$ here versus, so this is the dendrite which is also has an internal solution and it is all connected here. So there is a $V_{in} - V_{out}$ here as well.

So actually the none of these $V_{in} - V_{out}s$ are equal. So in order to model this, if we want to look at how inputs from this synapse, this synapse and this synapse and so on get integrated or how they interact and cause changes in the membrane potential in the soma, then we cannot obviously assume that there is only one $V_{in} - V_{out}$ that is the membrane potential V_m depends on the position of the measurement or position along the neurons body. Let us say if we have 3D coordinate systems somehow X, Y and Z and in there the neuron is present, then each sort of patch of membrane around which we are measuring the $V_{in} - V_{out}$, so this is the inside, this is the outside has a particular location in X, Y and Z. So that is going to be the actual value of voltage and as X, Y and Z changes along the body of the neuron or along the structure of the neuron, we will have different voltages and in fact these different voltages allow the synaptic inputs to travel. If the voltage were exactly the same, there would be no reason for any current to flow around the right towards the soma.

So, obviously then if we really want to understand how currents from the synapses get integrated, how they can interact, then we cannot go with a single V. We will have to go with something like V(X, Y, Z) or in fact if we were to model it I mean on a computer that is to simulate a neuron model, we will have to go into a compartmental model that is we will be discretizing space along the neurons structure that is we will have different positions. Let us say if we are looking at one branch here of the dendrite, let us say this particular branch, we will be breaking this up into small chunks which let us say now let us say we will assume this somehow this axis is X, we can without loss of generality we can say that and these are all equal lengths delta X. So, the delta X is going to be determined by basically the resolution of delta V that we are allowed or I mean the kind of error that we are allowed in the delta V. So, we will have a ΔV or V_m a particular at this location as let us say V_i along that axis this is ΔV_{i+1}, this is ΔV_{i-1} and so on.

And when there is a branch accordingly we have to set up the different branches. So, here the assumption is that the this patch of membrane or this cylinder with I mean cylinder with a hollow inside which has the intracellular solution and the outside has extracellular solution, this entire membrane patch is isopotential that is there is no drop or change in voltage along this surface. So, depending on the problem we can get sufficiently small delta X's or even sufficiently large delta X's that will allow us to address the question that we want to answer. So, here we are breaking up the neuron into multiple compartments so that we can accommodate the changes in the membrane potential in the entire neuron itself. And so these are modeled or simulated with a compartmental models like I am just briefly described here.

So, obviously on the other end the most simple ones in terms of this delta V it is a point model where the entire neuron is isopotential is assumed to be isopotential and is a point model. And so one delta V or V_m is sufficient to describe the behavior that we are trying to understand. And so in fact, all the models most of the models that we will be talking about in this course are point models. And we will also discuss a little bit about the compartmental models as in when they are needed and so on. So, just to make sure we are on the same page that we are talking of the entire neuron as if there is a single voltage that can explain it, explain its entire neurons membrane potential.

And so there we will not be talking about how input synapses currents from different synapses are travelling along dendrites and there is an effect in the soma. We will be talking of everything coming on to that particular point that is all the inputs are coming at that and influencing only that voltage. So, with this brief idea let us just take a step into the direction of the modeling as we have discussed earlier our the membrane of a neuron is made up of lipid bilayer. So, as you may recollect the round structures are hydrophilic and the tails are hydrophobic and this is the essentially the inside of the membrane. So, we are drawing simply a patch of the neuron and we will represent the entire neuron as a single voltage as we have said.

So, now we know that the membrane can be represented by a capacitor let us say it is capacitance C_m . So, here we will not be discussing about the exact units of the capacitance or whatever electrical elements that will be involved in your reading materials there will be a discussion about what kind of units are used in these kind of modelings. So, let us say that we are representing the membrane with a capacitance. So, that is this is a C_m. So, now, we are drawing the equivalent circuit for it and let us say that there is some room for current flow.

If it were only a capacitor then and then there must be an AC current in order to have any kind of response and so, DC voltage would not change anything in this circuit if it is just a capacitor. So, there must be changes in voltage to have a current flow as you know from elementary electrical sciences. So, let us say that there are some channels which we will call G_leak and there is let us say some battery that stops the flow of the ions that are going through that leak which we will name E_{leak} and let us say there is an external current injection I_external going in and so, this is the outside and this is the inside of the neuron. So, why we are drawing these in parallel because the the the membrane the current that is going across the membrane has a path within the membrane itself. Let us say you have learned about ion channels we have not gone into ion channels as yet we are calling this G_leak which may represent a leaky channels that is that allows some baseline flow of ions and so, that is going across the membrane and the the the entire membrane is around it.

So, essentially there are two paths for the current in parallel one that is clubbed together as G_{leak} and the other that is the capacitor. So, they must be in parallel and this $I_{external}$ let us say is in our control for now that is we are we can patch on to the neuron and we can inject current in there like we have discussed in our patch clamp recordings. And so, this $I_{external}$ in the real scenario is going to be just if you give it a thought for a minute you will realize that that it is going to be the current injected by the synapses. And so, that is being the synaptic current in this particular model is being replaced by this I_external which let us say by patching we are controlling it. So, and so, here in this case we are assuming that there are no other conductances in the membrane this is the simplest kind of point model that we can have and this is essentially what we call the leaky integrate and fire model.

So, why we call it the leaky integrate and fire model is that. So, let us think of in this circuit this is circuit that most of you are familiar with if not there is a basic background in our reading material about RC circuits. And so, let us say this is this is the capacitor when and this current here is the I capacitor the current here is the I_leak going through the G_{leak}. So, first thing to understand here is what is the resting membrane potential of this neuron. So, that means, if this is V_{in} and this is V_{out} at these two nodes then this difference is our membrane potential V_m or ΔV.

So, if you think of this circuit when will there be so, we mean rest means there is as we have discussed previously there is no net current flow across the membrane. No net current flow across the membrane would happen when this $V_{in} - V_{out}$ is going to match this E_{leak} here. If the V is equal to E_L then there will be no current no net current flowing across the membrane in this model. So, essentially our V_{rest} if you let this system start from anywhere and let it sit for a while eventually the membrane potential will go to V_{rest} which is nothing, but that E_{leak} which is sort of the potential at which the leaky channels are not allowing any current to flow through them. That is whatever ions are going through they are not allowed to flow if we have the voltage at that particular value.

So, if now to in order to model this we need to be able to describe how the voltage changes with changes in the $I_{external}$ or current inputs. So, remember we are always trying to do this that there are synaptic inputs coming in on to the neuron and the neuron is then based on those inputs if it crosses a threshold produces an action potential and if it does not cross a threshold then it the membrane potential keeps going and until it crosses a threshold there would be no action potentials. So, essentially we want to know how the V is changing over time given a current input. That is if we could represent all the synaptic inputs of the neuron by $I_{external}$ then we want to be able to solve for or we must be able to simulate what the voltage is going to be over that time period given a starting voltage and at a particular time. So, we will say that the neuron is at rest let us say and so initially our V is at V_{rest}.

So, this is our initial condition at t equals to 0 and let us say we inject a current some I. So, initially the current is 0 and we inject a current some I_0 let us say that is constant for a period of time let us say T and then it is brought back down to 0. So, this is current axis and this is the time axis. So, we are essentially injecting a current pulse. So, now we want to understand now we want to be able to see what the voltage does that is the ΔV does over this duration of time when the current is injected.

So, the equations we have to write down basically the equations that govern this system that is the we essentially have from the Kirchhoff's current law if we apply that at the node where the $I_{external}$ is coming in this particular node then we have that the currents must sum to 0 that is the $I_{external}$ is equal to the $I_{capacitor}$ plus the I_{leak}. Essentially what we have is $I_{capacitor}$ is equal to $I_{external} - I_{leak}$. So, now if we write out what the $I_{capacitor}$ is what we have is it is essentially C dV/dt. So, the how the voltage is changing across time the slope of that at that particular time point is equal to whatever this $I_{external}$ is as a function of time this is in our control and minus I_{Leak} which is essentially going to be this$G_L (V - E_L)$. So, this differential equation essentially describes how the voltage is going to change as a function of time if we are provided an initial condition and a profile of this $I_{external}$ over time.

In this case we have let us say at 0 times 0 if we say that this is time 0 our current jumps to I_0 our voltage was at V_rest at that time point. So, our differential equation here will change to C dV/dt equals $I_0 - G_L(V - E_L)$ we have to replace this by I_0 and apply the initial condition that V equals to E_L at t equals to 0 and solve this equation. So, you must be familiar with solving of this linear simple ordinary differential equations and we can then see that essentially the capacitor is going to charge and go to a saturation value if at all within that time T and then is going to discharge when the current is gone. Depending on the duration T it may hold the voltage for a long time at that value and then drop or otherwise it can increase half way up or some way up depending on if the current is starting to drop here then the voltage would rise not all the way, but some of the way and then drop to the V_{rest} or E_L . So, then where is the spiking how do we do that? So, we obviously need a threshold voltage and let us say that we have a fixed voltage V_T that is the threshold voltage.

So, here we are assuming that there is some kind of a voltage that is the threshold which allows us to know when a spike would occur when the spike would occur based on the voltage that we are simulating. So, in this integrated and fire model the way the modeling is done that if the voltage continuously the additional conditions that we have here. So, if we say let us say $C\, dV/dt = I_{external} - G_L(V - E_L)$ we have this additional condition that when V reaches V equal to V_T we say that at that time point t a spike has occurred. So, we do not really need any more than knowing when the spike has occurred. So, because spikes are all or none and so as soon as we know and there is a threshold.

So, as soon as we know that the voltage has jumped above threshold or greater than equal to threshold at the very that very point there is going to be an action potential. So, essentially we can note this t down and that is a number of t's will come along time depending on the current injected and those are going to be these $t_i s$ are going to be the spike times. So, ok. So, we are saying that let us say somehow the voltage has integrated up to V_T and there is an action potential. So, what do we do next? So, at the point of the action potential at the time when there is that action potential happens we set V back to V is set to V_{reset} which usually is the E_{leak} or the resting membrane potential.

It can be varied depending on the kind of model that we are trying to do. So, this whole process can be easily simulated and so then what is the big thing that we are talking about I mean it is a simple RC circuit and we are saying that there is a spike occurring at this time point as soon as the current goes beyond threshold and given any kind of $I_{external}$ over time if we know the shape of the current over time this is time we can easily simulate this differential equation numerically and know what the voltage is and whenever the voltage crosses the threshold the V_T there is a spike and we are done. Well obviously, we are missing quite a few things and yet I would say that this integrator and fire model is very useful in spite of the fact that we are missing quite a few things. Well for the first thing that we are missing here as you may already realize and we did mention it earlier that we are assuming there are no ion channels and obviously, we know that there are voltage gated ion channels and we will see that it is the ion channels and their properties that cause the action potential. We can model the entire shape of the action potential as opposed to saying that the voltage has crossed the threshold that means there is an action potential.

We will also see that there is a true threshold V_T we can prove that there is going to be a true threshold V_T for generally for these kind of neurons. We will also show that it is going to be an all or none event the action potential is going to be an all or none event. So, to do that we have to take the help of some more mathematics which has to do with non-linear dynamics and particularly phase plane analysis and we will gradually move into how to model the particular action potentials that is using the Hodgkin Huxley model which was developed in the middle of the last century and we will see that if we incorporate the sodium ions and sodium channels voltage gated and potassium channels then that along with what we just saw as a leaky integrate and fire model then we can indeed describe the behavior of the action potential and show all the kind of properties that we just talked about without which we would not be able to prove that there is a true threshold and so on. So, there are so even the integrate and fire model the leaky integrate and fire model can be made a little more complicated without going into the Hodgkin Huxley with by addition of few simple channel terms that can incorporate the most often observed behaviors. So, for example, as you can imagine in this RC circuit that we had.

So, this is the capacitor and this is the G_{leak} and this is the E_{leak} and the $I_{external}$. If we have a constant current injection like so that we had described I_0 given how the behavior is going to be what we will see is that there is a integrated the capacitor will charge that is the integration part as soon as it reaches this is let us say $V_{threshold}$ we say there is a action potential we take it back to V_L and then it will charge again and we say there is an action potential and then it will come back and then it will charge again there is an action potential and so what we are going to see here is periodic firing obviously, because there is no difference in terms of the model in terms of the circuit at this time point or at this time point or at this time point and it is entirely deterministic and so it will keep on doing behaving in the same way and reaching threshold exactly at the same after the same duration and we will consider a spike occurring. So, actually in neurons when you patch on them in many neurons when you do this kind of current injection we do not see a periodic firing like this in most neurons what we usually see is something called spike rate adaptation and that can be easily modeled with an extension of this integrate and fire model and that is there for you to replicate from a textbook that you are following and you will be modeling that as an assignment along with the integrate and fire model and we will now gradually in the next lectures go on to describe the actual phenomena of action potentials using the voltage gated sodium channels and potassium channels on top of this integrate and fire or leaky integrate and fire model And so we in the next class we start off with the Hodgkin-Huxley equations and describe the real dynamics of a neuron in terms of production of action potentials. Thank you.