Computational Neuroscience

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Week – 02

Lecture - 06

Lecture 06 : Membrane Potential and All or None Spike

Welcome to week 2 of our computational neuroscience course. So over the past few lectures we have ah gone through the introduction that is sort of more of the biological introduction about the course that is we have discussed the structure of neurons, what is an action potential the structures present in the brain the broad structures there, how we record activity from neurons and what we mean by activity is basically the membrane potential of neurons. So in this weeks lecture we will be talking about the excitable membranes and neural activity in more detail with mathematical treatment of membrane potential and what spikes are and so on. And we will go into the details of how action potentials are created, how current injection is happening in a neuron and so on to in order to understand the dynamics behind the creation of action potentials and also we will understand how synapses act and how action potentials are communicated across from one neuron to another and all this will be done with, with a quantitative understanding. So what we have been discussing so far is that we have introduced the idea of the action potential and we said that it is the membrane potential of the neuron that is the membrane potential if, if we have a neuron then the V in or the potential inside the neuron minus V out that is the potential outside the neuron that is what we will call as V and/or the V membrane or ΔV as you may recollect. And this ΔV is what is, what contains anything to do with computation by these neurons.

And we had said that Hodgkin-Huxley showed how these this ΔV can produce has signatures of the currency of computation which is spikes or action potentials nearly in the middle of the last century. And these events or action potentials are also called spikes and these are the ones that are also communicated across synapses when based on the release of neurotransmitters and uptake of neurotransmitters on the postsynaptic neuron by the postsynaptic neurotransmitter receptors. So we have a particular thing here that says record and we have understood how we record the different activities the different ways in which we can record activity from neurons and it is ultimately this membrane potential that we are recording that becomes the most important. So, let us delve into how this membrane potential is actually created in the neuron and how this changes with time.

So, if you recollect from your high school chemistry. If we have a semi-permeable membrane let us say in an with an aqueous medium and this semi-permeable membrane is separating the aqueous medium on the two sides. Let us say we have ion particular type of ion I ah on one side and the same ion ah on the other side, but on the right hand side let us say it has a concentration of C_2 and on the left hand side it has a concentration of C_1. Now ah since this is a semi permeable membrane that is ah there the ion can flow across the membrane and ah depending on the amount or the concentration of the ion on the two sides ah there will be a flow of ion from the higher concentration to the lower concentration side. However, as there will be a difference in the amount of ions on the two sides there will also be a potential that it will be developing on the two sides.

So if we say that if as as the ion moves from one side to another side it is the chemical potential that when it is counter balanced by the electrical potential at that time this ion I becomes ah comes at equilibrium and let us say that this equilibrium is reached when the potential on the left hand side is V_1 and the potential on the right hand side is V_2. So if we let the ions sit in this aqueous medium ah and let us say if the concentration C_1 and C_2 is maintained that is it is large enough ultimately when the potential difference V_1 or V_2 minus V_1 is equal to a particular V equilibrium or we will call V reversal potential or V_{rev} or V_{eq} for that particular ion that this ion there will be no net current flow across the membrane. So if if we think of it in this way that the the total electrochemical potential on the left hand side if we write it as μ_0 ion "i" or rather μ_{i0} + RT log C_i + ZFV_i. So for the ion "I" on the on on one particular side if we say the side is 1 here then this particular we set it by the super fix 1. This is the electrochemical potential on the side 1 that is on the left hand side and this has further terms if we allow the free energy to I mean if we allow the potential to have include the pressure and temperature and other forms of way in which this free energy can change from on the left hand side.

Similarly on the right hand side we have μ_{i0}on the side 2 it is also going to be the same because this is the molar free energy and that is essentially in this case the potential of the ion at unit concentration and 0 potential that is if we have the concentration of the ion "i" to be unity in this in this frame work with the proper units and similarly if the potential is 0 then the overall potential in the ion is this μ_0 and that is not going to be unchanged on the two sides and it will be additionally the electrochemical potential on the right hand side will have the term RT logC_2 + ZFV_2 plus the other terms which we will assume to be constant on the two sides that is terms due to pressure temperature and so on and they will not come into the picture. So when the two sides the ions are at equilibrium these this electrochemical potential must balance each other out. So in that sense if we write that down that means this if we equate the left hand side electrochemical potential to the right hand side electrochemical potential and this μ_0 is going to cancel out and so we are essentially left with RT log C_i let us drop the suffix "i" and return to this particular form of writing the concentration that is C_1 we are assuming that it is only ion "i" here and plus ZFV_1 again we are dropping the suffix "i" and replacing the V_{1i} by V_1 and this will be equal to RT log C_2 + ZFV_2. So now if we relate the if we take the move the ZFV to the other side we will have $V_2 - V_1 = RT \log log\,(C_1/C_2)$ and this if we have a particular concentration of an ion as C_1 on one side and C_2 on the other side then this equation on the right hand side of the equation provides us the difference in the potential on the two sides that is the V_2 minus V_1 that is the difference in potential in between in the two sides at which the ion will be at equilibrium and so there will be no net current flow across the membrane. So this essentially is what we will call for an ion as the equilibrium potential V_{eq} or V_e or also the V_{rev} or the reversal potential of the ion.

This is basically a sort of a marker to tell us how ions will flow across a membrane if there is a path available for ions to flow then what amount of current will flow across the membrane or in which direction that ion will flow will be determined by the actual membrane potential actual potential difference and the reversal potential for that particular ion. So for neurons as we had mentioned earlier the key players in terms of the ions are sodium, potassium, chloride and calcium of which we will see that the with the sodium and potassium ions only a lot can be explained. So how is the membrane potential what is the membrane potential for neurons so it will depend on this C_1 and C_2 or C concentration outside and inside of each of the ions and finally if we have the ions all the ions at rest that will determine what the potential membrane potential of the neuron is going to be. So the concentrations present in the neuron inside the neuron for sodium, potassium, chloride and calcium are approximately the values given here that is 20 millimolar for sodium inside and 120 millimolar for sodium outside. Similarly potassium the amount of the concentration of potassium is extremely high in the outs in the inside of the neuron and it is low outside the neuron.

So sodium and potassium have the exact opposite nature of their chemical gradient that is if the concentration where the driving factor then potassium would be flowing out of the neuron because of the high concentration inside and sodium will be flowing into the neuron because of the high concentration of sodium outside. And similarly chloride has the similar nature as sodium that is the chloride concentration is low inside the neuron and very high outside the neuron and calcium too is extremely small in terms of its concentration inside the neuron and outside the neuron. So if we now use our idea of V2 minus V1 is our V equilibrium or V reversal then this will be determined by (RT/ZF) log(C_1/C_2) or C_{out}/C_{in} in and this is my V_{in} - V_{out} that is our the way we will be defining membrane potential. So when the membrane potential will be this V_e for that particular ion let us say sodium then the sodium will not flow across the membrane that is it will be at equilibrium. So given the Z is unity for sodium, potassium we will replace the Z by +1 for calcium it is +2 that is the amount of charge there and for chloride obviously it is -1.

So accordingly this Z will be plugged in R and basically RT/F at 25 degree centigrade is known and that is around 59 millivolts if we take this as log 10 and so that allows us to calculate what the V equilibrium is for sodium potassium chloride and calcium. So what we see is if we calculate then the approximate values of the equilibrium potential of these key ions are plus 45 minus 90 minus 75 and plus 120. So what does this actually mean that it is plus 45 minus 90 minus 75 plus 120. As we have been saying if the membrane potential that is this V in minus V out is equal to plus 45 millivolts then sodium cannot flow across the membrane or rather the net flow of sodium will be 0 across the membrane that is the amount of sodium going out and 90 coming in will remain equal. Similarly for potassium if the membrane potential is minus then it will then potassium will not flow similarly for chloride and calcium.

Another way to think about these numbers is that if we have the potential of the membrane at a particular value V or V membrane or ΔV then it is the equilibrium potential of that ion that will determine which way the ion will flow. In other words if a path is available for the particular ion in question let us say we are considering sodium ions and let us say sodium at a particular voltage V if there is a possibility of sodium to flow across the membrane then the sodium ions will flow in a direction such that the voltage V is pulled towards this plus 45 millivolts. So let us take a step back we have said that earlier there is a resting membrane potential and so that means that at equilibrium that is when the neuron is left undisturbed the membrane potential stays around minus 60 millivolts this can vary from neuron to neuron and based on state but it is approximately around this value so between minus 50 to minus 70 sometimes even lower. So we are saying that this is at rest so if there are paths available in the membrane for sodium to flow at rest sodium will flow across the membrane in such a way that this minus 60 millivolt is pulled towards plus 45 millivolts that is sodium's reversal potential but we are saying that it is at rest so there in comes a contradiction so that is there is no sodium flowing at that time or at least it is at rest in the sense that the net ion flow across the membrane is zero. So that means that the sum total of all the currents that is if we have the total current as I sodium that is the amount of sodium flowing I potassium that is the amount of potassium flowing across or the net amount of potassium current across the membrane and I chloride and I calcium and all the other ions this net current across the membrane would be zero at minus 60 millivolts.

So even though at rest which is the membrane potential is minus 60 and it is not equal to the equilibrium potential of any of these ions here we are still at rest because first thing is that it is actually the net current flow is zero. Further it is also determined we had implicitly been saying this that if there is a path available for that particular ion across the membrane. So that we will later on see is determined by the ion channels and the probability of those ion channels being open at a particular voltage and we will discuss that in great detail later. And so the current the sodium current flowing at minus 60 millivolt is not simply determined just by this plus 45 millivolt and its difference from minus 60 but also the conductance present in the membrane which will allow the sodium to flow or not flow even. So if at minus 60 millivolts the path for all the sodium for all the paths for sodium to flow inside or outside of the neuron is zero that is there is no path available then this I_{Na} also would be zero.

In fact what we will see is that there is a very very small conductance for sodium at this resting membrane potential. Similarly for potassium also it is actually a very small conductance available at minus 60 millivolt for potassium and hence at rest the minus 60 millivolt membrane potential is not pulled towards minus 90 millivolt by the potassium ions. Similarly the chloride ions and the calcium ions all have very low membrane potentials I am sorry very low membrane conductances at this potential and it turns out that the voltage is voltage adjust itself such that this net current flow turns out to be zero and that is what we mean by the resting membrane potential. So the concepts that we have here is that we have a particular reversal potential or equilibrium potential for each ion and this equilibrium potential or reversal potential guides us to think of the way the ion that particular ion will flow when the membrane potential is different from that equilibrium potential. So when the membrane potential is different from that equilibrium potential the ion will flow in such a way that the membrane potential will go from the particular value to the equilibrium potential.

So and at rest it is minus 60 millivolts and so that happens because the net current is zero at that point and that current is determined by the amount of conductance available for the different ions at play at that particular potential. So it is we will go into more detail about this process in later lectures when we go on but here the main point is to understand how the membrane potential is created and how it changes depending on the membrane potential itself or how the conductance is changed and so on. So just to tell us we have been saying that the membrane potential is pulled towards equilibrium or equilibrium potential. So let us say the membrane potential is minus 40 millivolts and at that time there is sufficient sodium conductance available let us say. So that means the direction in which the sodium ions will flow is that such that the minus 40 millivolt is made to go towards plus 45 millivolts and that means the sodium being positively charged it means that sodium will go into the neuron from outside to inside that is positive charge will go in and that will create the potential or that will cause the potential to go higher towards the equilibrium potential of sodium.

Similarly if let us say the membrane potential is minus 40 millivolt and let us say a substantial amount of conductance for potassium is present and so the potassium equilibrium potential being minus 90 millivolt the potassium will flow in such a direction such that this minus 40 millivolt is pulled towards minus 90 millivolt. So again as potassium is positively charged it will flow from inside to outside of the neuron in such a scenario so that the membrane potential or the potential inside is gradually lowered compared to the outside that is the positive charge is going out of the neuron. And chloride similarly will actually try to flow in in the same scenario because of its negative charge it will do the positive charge the same thing as sodium. So with this in the background we will next in our lectures try to understand how these ion channels or the conductances that we were talking about work in the membrane and provide parts to the different ions and how all these ions and how all these together create finally create action potentials depending on the current injection into the neurons through synapses or artificially when we are experimenting as we saw in patch clamp recordings and so on. So we will start off with the rest of the ideas of membrane potential in and excitable membranes in the next lecture. Thank you.