Computational Neuroscience
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Lecture – 20

Lecture 20 : Analysing HHE with Phase Plane Analysis -II

Welcome. So, we have ah discussed the anode break excitation phenomena and we had one more ah thing to ah discuss ah regarding the Hodgkin-Huxley equations and explaining ah based on the phase plane analysis ah that is ah relative refractory period. So, ah if we consider ah spiking of a neuron ah then immediately following the ah spike we have a period of time that is called the refractory period. Ah the beginning part is absolute refractory and the next part is called relative refractory. So, if we ah if we consider this as the voltage axis and this as the ah time axis and let us say this is our ah V_{rest} ah at this point we have the voltage here. Now, let us say we have some current injection at this time point and ah let us say that ah it goes up it crosses threshold there is an action potential created that goes back down and then gradually ah it goes back up to our V_{rest} again.

So, the the period in this intervening period where H has gone on to ah 0 to become 0 that is the sodium channels are inactivated. Ah So, remember when the voltage goes up high here ah H time constant also reduces from the τ_m ah τ_H V curve and also the value of H at the high voltages is goes to towards 0. So, when this voltage is coming down by the time it reaches the bottom of it H is already at 0 which means that none of the sodium channels can be activated or even if the m's are open at that voltage H will not allow sodium currents to open because H is 0. So, that particular period where we have sodium ah channel ah inactivation that period is called the absolute refractory period.

So, which means that in this particular period no matter how much current we inject ah we cannot get an action potential. So, even if we inject a current here because the sodium channel cannot open ah none of the sodium channels can open almost we cannot get an action potential. But in the following period we have what we call is relative refractory and that is a period where we have actually we need a higher current than usual to produce an action potential. So, if if in this state where there was no action potential ah in green there was nothing preceding there was basically silence in this green period ah before the action potential then ah the size of the current required this is the size of the current pulse that size of this current required ah is much smaller or comparatively smaller than the size of the current that would be required in the relative refractory period to produce an action potential. So, this height here this height I and let us say this is I_0 before the spike this I needs to be much greater than I_0 to produce an action potential.

So, and this gradually goes reduces to I_0 when the neuron comes to V_{rest} and beyond I mean basically when everything ah all the getting variables come to their steady state value at V_{rest} we do not have any more relative refractory, but intervening period we require a larger current to produce spiking. So, this also ah comes in into play in some of the coding ah aspects that we will talk in the next ah part of the course. And the absolute refractory is ah very easy to understand in the sense that H is ah practically 0. So, there cannot be any spiking and ah there cannot I mean just simply simulating the Hodgkin Huxley we can see ah that H is extremely low and that region is ah what we what will be absolute refractory, but why does that we have the relative refractory period is our question. So, ah in order to explain that again we need to go into ah a Hodgkin Huxley equations and analyze it in the relative refractory period with our ah phase plane analysis.

And ah since this has to do with a threshold or a production of an action potential now with a larger current or a larger change in the membrane potential required to go beyond threshold ah we will obviously now again consider the V_M reduced system. So, if we will again consider the V_M reduced system. So, if we draw the phase plane here that is we have V on this axis and M on this axis ah we have our d ah M/dt equals 0 which is the M nullcline which is as in our previous lecture we saw is going to be the same and this is our V_{rest} here. And at V_{rest} when the there is no external current. $I_{external}$ is 0.

And m, n and h have their values at the steady state values at V_{rest} then if we draw the dV/dt equals 0 nullcline. So, this is the d M/dt equals 0 now on top of it the usual d M/dt equals 0. V-nullcline then we have this behavior as we have shown earlier where this is this particular node the lowest one which we will call R the resting node which is stable . Similarly, the next node which we will let us say mark in red is the saddle node this is simply a recollection of what we have done earlier and then again we have another node which is a stable node here at the m equals 1 value and a high voltage value around minus around plus 53 millivolts. So, in this kind of scenario we have a threshold that is determined as you know now by the stable manifold coming in from m equals 0 axis and we have if we consider this line along the resting membrane potential wherever it cuts the stable manifold the yellow line cutting the red manifold say stable manifold that is where the threshold is.

So, voltages initial voltages through current injection reaching anywhere on this yellow line before the stable manifold will go back to resting membrane potential and anything beyond it will go along this line along this the unstable manifold and go back on go up to that stable node on to the top right and will produce an action potential. Now if we consider the middle of the action potential or towards the end of the action potential we had we have h and n different from what it is at rest. So, we know that h was at let us say we have $h_{\infty}(V_R)$ I should use white we have $h_{\infty}(V_R)$ as we saw earlier is around 0.

6 or 0.59. Now what happens is if we consider that h is more or less fixed at the values it reaches towards the middle of the action potential that is when h has dropped down to about 0.1 let us say. I mean that is what we tried to explain that when we have the h values when we have the voltage reaching a very high value our h is reducing going to 0 and then it is trying to get back up and that is let us say it is starting from 0 and then going back up and let us say our h has reached around 0.1 and is staying there. Then we can plot the corresponding d V/dt nullcline or the V nullcline that is this particular d V/dt equals 0 curve or the V nullcline with the new value of H that we will see is that there is a shift upwards in the d V/dt nullcline.

So, what happens here is that this has reached here and follows that sort of same pattern. So, essentially we have the resting membrane potential or the this stable node almost at the same place whereas, the saddle node shifts and is still a saddle at a higher voltage and as the saddle node get shifted to a higher voltage it also drags along with it the stable manifold to a higher value or to higher voltage values. So, our saddle node is moving from this particular point initially to the new value because our d V/dt nullcline has shifted upwards and thus the corresponding stable manifold with the saddle node that provided the threshold that also moves to the right. And so as you can now see if we track the yellow line the threshold of the system has increased by a few tens of millivolts. In fact, what we will what if you simulate this you will see that it goes to about around minus 40 millivolts instead of the minus 56 millivolts that was there earlier.

So, that means, now we need a larger current to move the neuron from V_{rest} effectively V_{rest} or close by to go beyond the threshold and produce an action potential. So, here remember we are moving I am sorry we should be drawing this on a yellow line remember when we inject the current at V_{rest} we are moving along this yellow line and that is effectively starting the system at a different V value and that V value required is much higher to cross the threshold now. So, this is what we can say is effectively happening during the relative refractory period. So, in this period even though the V_r is at or the voltage is at rest or very close to rest the same values of V_r before the action potential do not reflect the same condition of the system remember it is only V_r. So, the previous history of the system which is the lowering of h or sodium channels being inactivated and h staying there makes the system behave in this manner and this phenomena allows us to see the relative refract allows us to explain the relative refractory period.

So, with this particular discussion we will come to the towards the close of our first section and we will discuss a few points that we have made so far is that the most important points is that action potentials are all are non-events and that is because the neurons have a threshold or rather a true threshold we have something called absolute refractory we have something called a relative refractory we have something that is called the anode break excitation which we will see later as a post inhibitory rebound phenomena that is a hyperpolarizing current is essentially an inhibitory input and this post inhibitory rebound that is basically an excitation or spiking post an inhibitory period is because of the ABE phenomena and this also plays a role in coding of let us say stimulus offs or stimulus turning off can be signaled with this post inhibitory rebound and there are many other applications or concepts that can be explained with the post inhibitory rebound phenomena and of course, we have understood in this section the Hodgkin Huxley set of equations and the Hodgkin Huxley reduced set to explain the above phenomena. So, going forward we will be requiring all these things in our understanding of coding by neurons for example, if we talk of the absolute refractory and relative refractory what this says is that there is a natural bound on the maximum possible firing rate of neurons that they will naturally saturate because of a period following an action potential that the that is some period where no action potential can happen that of obviously, bounds the the number of potential that can occur within a limited period of time. So, essentially the rate of action potential occurring is has a max bound. So, and we will see that rate of action potential is going to be measured that will be often used and that has been often used by researchers in neurosciences to understand coding performed by neurons . So, the other two that is all or none events and true threshold behavior will essentially allow us to model the spikes as in in the spike trains as a sum of events or allow it to be modeled as a point process .

So, we will be discussing these points later on. So, the size of the action potential will not matter, but they they will be simply dots or events in time and so that tells us that we can have action potential strains to be modeled as a point process . And this of course, we have already mentioned the post inhibitory rebound in terms of stimulus off periods and so on. So, since the max rate since the rate of action potentials is an important measure of response it also becomes important to model the firing rate with simpler models of neurons. So, in the Hodgkin Huxley equations we require to model the ion channels they are opening and closing and the behavior of the different kinds of gates activation and inactivation gates which requires which involves a lot of computation and it requires more involved modeling which also requires us to estimate the kind of ion channels that are present and their properties on every type of neuron.

So, if the generation of action potential process is not crucial in terms of the questions that we are understanding and if timing of the exact timing of the action potentials are not as important for the questions that we are trying to answer with our modeling. We can reduce the Hodgkin Huxley equations to much simpler point models of neurons. So, for example, if you think about the action potential process the M, H and N if we remove that from the Hodgkin Huxley equations you had we had already discussed that which is the leaky integrate and fire model. So, since the firing rate or rate of action potentials are important then we all we need is the number of action potentials that are occurring and not the entire process of action potentials. So, all we need is using this idea of a true threshold that neurons have we only require to simulate the voltage only up to the threshold point and beyond that we do not need to consider modeling the voltage waveform because that requires modeling the ion channels.

So, if we remove the ion channels in the leaky integrate and fire we only need to find we only need to define the threshold and know when an action potential occurs because they are all or none events that is sufficient. However, the exact time is not going to be correct in terms of the real neuron in the sense that because the upstroke till the threshold event is involving the m currents or the m activation gates of sodium channels we will have the voltage reaching threshold slightly later based on simply the capacitor the charging of the capacitor and the active m conductance is removed. So, but if that timing is not important just that there would be an action potential is sufficient and in these cases what we model in more detail is the $I_{external}$ going into the neuron 1. So, if we if we can get a better idea of what the input currents are on to the neuron then our probability of firing or firing rate over time can be estimated to very good degree and we can understand variety of things as we will see later on in the lectures. So, and these can be extended further beyond with more ion channels little more ion channels explaining some adaptation phenomena which is more of the relative refractory period like phenomena that is that makes action potentials go further and further apart as if we have repetitive firing.

So, these issues are covered in your textbook with using the spike rate adaptation and adaptive exponential there will be a small discussion on this in your reading materials and leaky integrated fire of course, is important and you will have exercises in modeling them also. So, from here the next stage is that as we had discussed earlier that we will now be recording activity from neurons that is strains of action potentials and there will be events occurring either stimuli or some behavior or some other phenomena where would be occurring parallely and we would from those action potentials try to understand how those action potentials encode that phenomena or that stimulus and so on. So, that will be our second part of the course. Thank you.