Neurobiology

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Lecture 2.9: GHK equation for membrane potential

Hi everyone, welcome to Neurobiology. In the last couple of videos, we have been looking at the concept of equilibrium potential of an ion and we have seen that each ion tries to pull the membrane potential towards its equilibrium potential. We also developed the equivalent circuit for a piece of membrane by including the conductance and the equilibrium potentials of different ions. So in this video, we will use that formulation to come up with a formula that can tell us what will be the final membrane potential when we have these different ions present in a cell and they are trying to pull the membrane potential in different directions. So let's see what that final expression comes out to be. So we want to understand membrane potential in presence of different ions and for simplicity, let's assume that only two types of ions are present potassium and sodium and these two are indeed the two most important ions in determining the membrane potential values.

One more piece of information that we have is that in the resting state of a neuron, typically more potassium channels are open than sodium channels. So if we first consider the case where only potassium channels are open and all the sodium channels are closed. In that case, what would be the value of membrane potential? Well, since sodium ions cannot move because their channels are closed, so they will not have any influence on membrane potential and therefore potassium ions will have full control in determining the membrane potential and the membrane potential will become the same as the equilibrium potential of potassium ions. Now in this state, if some sodium channels are opened, then what would happen? So let us try to understand that in a bit more detail.

So here is a graphical representation of the same thing. This is a piece of membrane. This is outside, this is inside, the inside is more negative than outside and in the membrane we have various channels embedded. So in the beginning only the potassium channels are open and the potassium ions can flow through these channels and these potassium ions will flow in a way so that the membrane potential can reach towards the air equilibrium potential which is around -75 millivolts. So the blue lines here show the chemical gradient which in the case of potassium ions is from inside to outside because inside has more potassium concentration, outside has lesser concentrations.

So this chemical gradient is from inside to outside and these orange lines show the electrical gradient which is from outside to inside because inside is more negative and potassium ions are positively charged. So they would like to move inside according to the electrical gradient and at this point when the membrane potential becomes the same as the equilibrium potential of potassium ions these two driving forces are opposite in direction and equal in magnitude and therefore there is no net driving force on potassium ions at this point. So the net driving force on potassium is zero and therefore the net current through potassium ions will also be zero. So there will be no net flow of potassium ions when this value of membrane potential is reached. So this is the default state when only potassium ions are open.

Now in this state when the membrane potential was -75 millivolts let's say a few sodium channels are opened. So this is a sodium channel and sodium ions as we know are more abundant outside and so the chemical gradient or the concentration gradient will be in the direction of outside to inside because there is higher concentration outside and lower concentration inside. So this blue arrow is pointing inwards and the electrical gradient is also in the same direction because inside is negative, -75 millivolts. So these positively charged sodium ions will be trying to move from outside to inside. So both the gradients chemical and electrical are in the same direction and therefore there is a lot of driving force on sodium ions from outside to inside and now that the channel is open and there is a driving force so the sodium ions will move in this direction.

So we have a net sodium current that is in the inward direction from outside to inside. Now the length of this arrow is shown slightly smaller than the driving force just to make the point that although there is a large driving force and sodium ions the current through sodium may not be very large because only few channels are opened. So the current depends both on the driving force as well as the number of channels that are present. So as the sodium ions continue to move they will make the membrane less negative or more positive and therefore the electrical gradient for sodium ions will reduce over time. While the chemical gradient we can assume that it does not change much because the number of ions that are present outside and inside these numbers are quite large so the movement of a few ions does not change the gradients very quickly.

So overall the two driving forces are still in the same direction but the magnitude would be slightly reduced now compared to the beginning and therefore the current of sodium will also reduce relative to the beginning. Now as the electrical gradient for sodium has changed because the membrane potential has become more positive so similarly the electrical gradient for potassium ions will also change because membrane potential is a common value for the whole neuron. The electrical gradient for potassium ions is also now reduced while the chemical gradient for potassium remains unchanged and therefore now there will be a net driving force on potassium ions towards outside which will be the difference of these two driving forces. So there is some small driving force on potassium ions towards outside but because the number of potassium channels is large there will be a relatively large current through the potassium channels towards outside. So the sodium ions are moving in trying to make the membrane more positive and these potassium ions will start moving out and as the positively charged ions move out they will try to make the membrane more negative.

So both these ions are moving and trying to change the membrane potential in opposite ways. Sodium ions are trying to make it more positive and trying to take it towards their equilibrium potential which is +55 millivolts or so and potassium ions are trying to move out to make the membrane more negative towards -75 millivolts. So initially when the sodium current is higher and potassium current is lower the membrane will be becoming less negative over time but as the potassium current also increases eventually a steady state will be reached where the sodium current and the potassium currents balance out and the membrane potential would stop changing at that point and that point will be somewhere in between the equilibrium potential of sodium and potassium as shown on this plot. So this is the value of membrane potential or voltage on the y-axis and this is time and in the beginning when only potassium channels were open the voltage was same as E_K and when we opened some sodium channels at that point the membrane potential started rising because sodium ions were moving in but at the same time potassium ions started moving out and eventually the membrane potential reached a saturating value. So this saturating value will be somewhere in between E_K and E_{Na}.

Let's look at this steady state in a bit more detail in the presence of the two ions. So at this steady state the voltage of the neuron voltage at rest V_r is somewhere in between -75 millivolts which is the equilibrium potential of potassium and +55 millivolts which is the equilibrium potential of sodium and because this V_r value is different from -75 potassium ions will move and they will try to still reach -75 which is their preferred value of membrane potential and similarly sodium ions will keep on moving and they will try to reach their equilibrium potential which is +55 millivolts. So both the ions are moving even though the membrane potential is not changing because these two currents have balanced out. So the membrane potential does not change even though sodium is trying to move in and make it more positive and potassium is trying to move out and make it more negative. Although the net current is zero the individual sodium current or the individual potassium currents are not zero both currents are present it's just that these two currents are in opposite directions and they cancel out.

We can think of it as a futile exercise that these two ions are doing trying to change the membrane potential in different directions and both are canceling out. So the membrane potential would not change but over time what would change is the concentration gradients of these two ions because ultimately there is a limit on how many ions can move before the concentration gradients start to change significantly and in that case the gradients will have to be maintained by the action of sodium potassium exchange pump or other such pumps that are present in the membrane and that will consume energy. Now let's find out what the final value of the membrane potential would be between E_{Na} and E_K. So to find a formula for that value we can use this electrical representation of the neuronal membrane. As we have seen before we can represent sodium channels by the conductance or the resistance along with the battery for sodium which basically reflects the equilibrium potential for sodium.

Similarly for potassium and chloride also we can include if we want and of course there is the capacitance and the voltage of the neuron is denoted by V relative to outside. So now if V is different from the equilibrium potential for sodium then there will be current in this path and the magnitude of current will be exactly $(V - E_{Na}) \cdot g_{Na}$. So this will be the current flowing out from the neuron to the outside if V is different from E_{Na}. Similarly if V is different from E_K then the current through this path would be $(V - E_K) \cdot g_K$ and similarly here $(V - E_{Cl}) \cdot g_{Cl}$. So a steady state will be reached if the total current flowing out through the membrane is zero.

So even if there is current in individual paths if the total current flowing out through the membrane, through all these channels is zero then there will be no net change in the membrane potential. So if we apply that condition then we can write the total current flowing out should be zero so,

$$(V - E_{Na}) \cdot g_{Na} + (V - E_K) \cdot g_K + (V - E_{Cl}) \cdot g_{Cl} = 0$$

All these terms together denote the current flowing out through the membrane and that should be equal to zero and if we rearrange these terms we can get,

$$V = \frac{(E_{Na} \times g_{Na}) + (E_K \times g_K) + (E_{Cl} \times g_{Cl})}{g_{Na} + g_K + g_{Cl}}$$

So if the membrane potential is equal to this value then at that point the net current flowing out through the membrane becomes zero. So this will be the resting membrane potential for this neuron if these are the three channels that are controlling the membrane potential and if we plug in the values for the squid axon then we get values around -69 millivolts something between -65 and -70 in most neurons.

So you can see that this value is sort of an average but it is not simply the average of these three values it is not $(E_{Na} + E_K + E_{Cl})/3$ rather it is the weighted average and it is weighted by the conductance. So if conductance of potassium is higher than the this final voltage will be closer to the potassium's equilibrium potential and so on and as we know that the conductance of potassium is highest in the resting state and therefore it is not surprising that this value comes closer to the equilibrium potential for potassium. And if we want to simplify the representation of the neuronal membrane we can actually combine these three into a single type of conductance where the total conductance will be the sum of these three conductances and the battery can be replaced by this final voltage. So these three types of channels can be thought of as this single type of channel with this total conductance and this equilibrium potential and all these channels that are open in the resting state are sometimes called the leaky channels or leakage channels. So these are channels that are always open in the resting state of the membrane and later we will talk about the active channels that are not always open but open in response to certain events happening in the neuron but these channels that are always open these are called leakage channels.

So in the last slide we obtained an expression for the membrane potential in presence of different ions and this expression is basically the weighted average of the equilibrium potential of different ions but we are still missing something in that expression. So the expression tells that the final value of the membrane potential Vr the resting membrane potential is achieved when the total current coming into the cell including the current from potassium, sodium and chloride balances out. But even when that happens the individual currents are non-zero which means that the potassium ions and sodium ions and chloride ions continue to move even though the membrane potential is not changing and is remaining at the value V_r and this situation cannot continue for too long because the concentrations of these ions will start to deplete eventually. We also know that there are active transporters on the membrane such as the sodium potassium exchange pump which move the ions by consuming energy and maintain the gradients and we have not taken these pumps into account here. So in a real piece of membrane we not only have these channels but we also have the pumps and these pumps are also carrying ions so they also contribute currents and for the final value of membrane potential to be maintained the sum of not just the ionic currents through these ion channels have to be zero but all the currents taken together including the pumps should be zero then only the final value of membrane potential can be maintained.

So even though there can be individual currents through the pump whatever is the net current through all the pumps and whatever is the net current through all the ion channels those two combined will be zero. Now it is slightly difficult to incorporate the pumps in the same expression that we obtained earlier because unlike these ion channels which can be thought of as passive elements whose currents are simply dependent on the voltage difference the exchange pumps are not passive so they are consuming energy and then they are generating currents and they do it depending on the need. So the pumps may not be active all the time the amount of current flowing through the pumps will depend on the requirements. So the final expression for the membrane potential taking into account all types of channels and pumps is given by Goldman equation or also known as the Goldman-Hodgkin Katz equation and this equation says that the resting membrane potential is equal to,

$$V_m = \frac{RT}{F} \ln \frac{P_K [K^+]_o + P_{Na} [Na^+]_o + P_{Cl} [Cl^-]_i}{P_K [K^+]_i + P_{Na} [Na^+]_i + P_{Cl} [Cl^-]_o}$$

RT over F natural log and then this term where P_K is the permeability of potassium ion, and $[K+]_o$ is the outside concentration of potassium, $[K+]_i$ is the inside concentration of potassium, P_{Na} is the permeability of sodium and so on. So this is the value of membrane potential that will be finally achieved in the presence of all these ions and these permeability values basically tell how permeable the membrane is to each of these ions which takes into account both the movement of the ion through the ion channel as well as the various pumps that are present in the membrane and for most neurons for example this could axon the permeability of potassium is highest.

So if permeability of potassium is one then the permeability of sodium is only four percent of that and permeability of chloride is somewhere in between. So you can see that the ions whose permeability is larger will contribute more to these expressions. Let's look at the Goldman equation in a bit more detail. So this expression has a structure that looks similar to the Nernst equation for equilibrium potential. We have the RT over F factor then logarithm and then we have this expression which includes the concentrations of ions.

In the Nernst equation we also had the charge here which could be a positive or a negative number but that is now taken into account within this expression. So if you look carefully you will see that for potassium and sodium which are positively charged we are writing the outside concentrations in the numerator but for chloride which is negatively charged we are writing the inside concentration in the numerator and outside concentration in the denominator and let's think about what would happen if we had only one type of ion or if the membrane was permeable to only one type of ion and this actually happens in glial cells which are highly permeable to potassium but the permeabilities for sodium and chloride are almost zero. So in this case if we set P_{Na} and P_{Cl} to be zero then all these terms cancel out and become zero and what remains is just this term. So the final resting membrane potential becomes,

$$V_m = \frac{RT}{F} \ln \frac{P_K [K^+]_0}{P_K [K^+]_i}$$

P_K P_K cancels out and what we have left is basically the Nernst equation. RT over zF where z is just one now [K+] outside over [K+] inside. So what we can say is that Nernst equation is just a special case of GHK equation.

So when GHK equation is applied to just one ion then it becomes Nernst equation and this is the more general form which takes into account multiple ions.