Neurobiology

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Lecture 2.1: Origin of electrical activity in the brain

Hi everyone, welcome to the second module of Neurobiology. In the first module we looked at a basic introduction to Neurobiology. We discussed how people started thinking about the brain, what are the different tools that are used to understand the brain. We've also looked at the different types of components, the cells, neurons and glia that are part of the brain. And we have also looked at the broad organization of the human brain. What are the different parts, what are the different areas and what these areas are involved in.

One thing I should emphasize again is that it is not the case that one area is involved in one specific function. The brain is more like a network and different areas work together to generate different functionalities in the brain. Now in the last video we also saw about Penfield's experiments. How he could stimulate a certain region of the brain with electrical current and that would generate the feeling of touch in a particular area or that would cause movement of a certain area.

So these experiments clearly show that electrical activity plays an important role in the functioning of the brain. In a previous video we have also seen Luigi Galvani's experiment where he stimulated the sciatic nerve of a frog and could see the leg twitch. So that also showed that electrical activity plays an important role. So in this series of videos we will try to understand the nature of this electrical activity. How is this electricity generated in the brain.

I mean in that sense it sounds like a computer. The computer also functions on electrical components but does the brain have the same kinds of components as a computer or are these very different. So this is what we will try to understand in the in this series of videos. In the last video we saw electrical activity as measured by EEG electrodes. We can see the signal going up and down and we can see various kinds of waves but this is not actually how the electrical activity is generated inside the brain.

In fact what we measure in EEG is only an average or aggregate of the activity of a large number of neurons possibly millions or billions of neurons. If we zoom in we can actually see the activity inside each of these neurons and that's where the activity is generated. And why do the neurons need electrical activity. By now you already know that neurons have dendrites where they receive inputs and exon terminals where they give outputs but the signal travels from these dendrites to exon terminals. It has to travel this distance and it travels in the form of electrical activity.

So that's where the electrical activity comes into play. Then at the exon terminal the signal jumps to the other neuron at the synapse which can be a chemical or an electrical synapse. Then again it travels in the form of electrical activity in this neuron and so on. So electrical activity is very important for the signal to travel within the neurons and as you know many neurons the neurons come in different shapes and sizes. Some neurons are very long so the electrical activity helps in conducting the signal along the branches of these long neurons.

How does this electrical activity look like inside a neuron? Is it like the EEG waves or is it different? So let's take a look. Now I'm going to show you a trace showing the activity inside a single neuron and here it is. So this is how the electrical signal inside a neuron might look like over time and as you can see the signal shows very sharp spikes which are also known as action potentials. What we are basically measuring here is the voltage inside a neuron and you can see the signal rises and comes down to baseline then it can rise again comes down and so on. So these spikes or action potentials are very important for carrying information in the signal and we'll see how these spikes are generated and what these spikes might mean, why they are important that we'll see as we go along in the course.

So by now it is pretty clear that electrical activity is fundamental to the functioning of the brain. It's not only present at the surface that we measure through EEG, it's in fact present in every single neuron and it is fundamental to the functioning of these neurons. So let's try to now think about what might be the source of this activity inside each of these neurons. So can you pause your video and think about what might be the origin or what might be the source of this activity inside each of these neurons? Okay so the activity is actually generated by the movement of charged particles and this is true in other cases also. Inside a battery it's the movement of electrolytes that causes the generation of electricity.

Inside a metal wire in an electrical circuit it's the movement of electrons that causes electricity. So in the case of brains also it's the movement of some charged particles. Now let's try to see if we can guess which charged particles cause the generation of electricity inside the brain. Okay so now let me tell you the answer. So it's actually the movement of ions that generates electricity in the brain and these are basically sodium ions, potassium ions, chloride, calcium, various ions that are present in the nervous tissue inside the neurons or outside the neurons whose movement generates electricity in the neurons.

And now finally let's think about what causes the movement of these ions. You know these ions are not going to move just by themselves unless there is some driving force. So there has to be some driving force. So can you again pause your video and take a guess what might be the driving force on these ions. Okay so now let me tell the answers.

What is the driving force or what makes the ions move. So there are actually two driving forces. In fact, so the first one is electrical gradient and the second one is concentration gradient. And now we will see how these gradients are generated and then how they result in the electricity in the brain. Now let's take a look at the concentrations of different ions inside the neurons.

And in fact these ions are also present in other cells of our body and in pretty much the same concentration. So we can see generally what the concentrations of these ions are in typical mammalian cells. These ions can be broadly grouped into two classes depending on the amount of charge that they have. So ions that have a single charge are called monovalent ions and this includes mainly three ions sodium Na^+, potassium K^+, and chloride Cl^-. And among the ions that have the double the charge these are divalent ions which include calcium Ca^{2+}, and magnesium Mg^{2+}.

And these columns show the concentrations of these ions inside the neurons here intracellular or cytosolic concentrations. And this is the concentration of these ions outside the neurons or outside other cells. And as you can see sodium is present in the cells at a concentration of about 15 millimolar but its concentration is almost 10 times higher outside about 145 millimolar. Potassium shows the opposite trend which is it is present at a higher concentration inside and at a lower concentration of outside the cells. Chloride is similar to sodium it is present at higher concentration outside and lower concentration inside.

The divalent ions are present in much smaller concentrations and they are present at higher concentrations slightly higher concentration outside compared to inside but the overall concentrations are much lower compared to this monovalent ions that as you can see. In fact you can appreciate the common salt that we eat sodium chloride is an important like both the components sodium and chloride are important components that's where they go and they determine the electrical activity of the brain. Potassium is also present in various food products that we eat and among these three sodium and potassium are in particular important for determining the the electrical activity inside the neurons. In the last slide we looked at the concentrations of different ions inside the neurons and outside the neurons and we saw that these concentrations can be quite different and that's what gives rise to the concentration gradients that are one of the driving forces for the ions to move. But you may be wondering what prevents these ions from crossing the membrane and then balancing out the concentrations.

Well the reason that the ions cannot easily cross the membrane is because the membrane is not permeable to these ions. So to understand that let's look at the structure of the membrane in slightly more detail. So any cell including neurons has a cell membrane that separates the cytosol that is inside from the extracellular space and if we zoom into the membrane we take a small piece of the membrane and look at it from the side this is what it would look like roughly. So this is our piece of membrane this is the extracellular space and this is the intracellular space. The membrane is actually made up of a large number of lipid molecules.

Each lipid molecule has a polar head as shown by a sphere here and has hydrophobic tails which are shown by lines here. So these hydrophobic tails these are long hydrophobic molecules that are repelled by water or by other charged particles or polar molecules. So they like they tend to be towards the inside within the membrane and the polar molecules are happy interacting with water or charged molecules so they are facing the extracellular space or they are facing the intracellular space but this middle region of the membrane is hydrophobic and it avoids water or other charged molecules. But it is permeable to other non-charged or non-polar molecules for example oxygen or carbon dioxide or other small gases these can easily pass through the membrane. Some non-charged but polar molecules like water or urea can also pass through in some small quantity but large molecules or even ions which may be small but have charge cannot pass through this hydrophobic core of the membrane.

So this is what basically prevents the ions from crossing the membrane barrier and balancing out the concentrations. Okay so the membrane prevents the ions from passing and that helps in maintaining the concentration gradient. So that is good we have a concentration gradient that can act as a driving force for the movement of ions for generating electrical activity. But here is the dilemma if the membrane is preventing the ions from moving then even if we have this driving force of concentration gradient what could it will be if the ions cannot move at all if the membrane is preventing the ions from moving inside to outside or outside to inside then having this concentration gradient between outside and inside is not going to be of much use. So on one hand we do want this concentration gradient to be maintained so we want the membrane to be impermeable but at the same time we also want the ions to move in response to the concentration gradient and the way the cells have actually managed to achieve both these goals is by having certain doors or passages within the membrane that allow the movement of ions.

So even though the whole membrane is impermeable there are certain channels that allow the ions to pass through and these are called ion channels as one can expect and these also these ion channels are not always open so they can be in a closed state or an open state when they're closed the concentrations will be maintained and when they open then they can allow the ions to move through so they really function like gates. These ion channels are actually made up of proteins and because these proteins are embedded in the membrane they are also called membrane proteins and the protein structure is such that there is a passage or a pore formed inside which is not as hydrophobic as the rest of the membrane and it so it allows the ions to move through them and there are different types of ion channels as we will see so they can open or close in response to different things happening inside the cell. There are also specific ion channels for different types of ions so some channels would allow multiple ions to pass through whereas some channels would allow only one particular ion to pass through. So we now understand how the concentration gradient is made possible by the presence of a membrane. We also understand how the ion channels allow the ions to move despite having this membrane barrier but there is one more question that we need to answer and that is that how is the concentration gradient maintained over time despite the ions moving through the ion channels.

So for example the sodium ion is present in higher concentration outside and lower concentration inside. Now as sodium starts moving through the ion channels over time the concentration of sodium inside will will rise and at some point it might become equal to the sodium concentration outside and that would mean that the gradient has disappeared and eventually the sodium ions will stop moving and similarly for potassium. So if we want the the cells to function over time we have to somehow maintain these gradients despite the ions moving. How can we achieve that? So the way the cells have solved this problem is by having some pumps that basically push out these ions again to the side other side. So for example there would be a pump that would throw out the sodium ions outside and bring the potassium ions inside and here is one of such pumps.

So it's known as the sodium potassium exchange pump and what it does is basically an exchange of sodium and potassium as you can expect from the name. So here I am showing you this pump in slightly more detail. So just like the ion channels this pump is also a membrane protein. It is embedded in the cell membrane and in its default configuration it is opened it has an opening towards the inside. Now it consumes energy in the form of ATP.

So one difference between a pump and a channel is that the ion channel is moving the ions in the direction favored by the gradient. So sodium ions will move from outside to inside and because that is already energetically favored no extra energy needs to be spent to make that happen. But if we are moving sodium ions from inside to outside we are moving these ions against their concentration gradient and some energy would have to be spent in this process and this energy comes in the form of ATP which is the currency of energy in the cells. So a phosphate from the ATP group binds to this protein the pump and three sodium ions also bind to it and with the binding of this phosphate group from the ATP the configuration of this pump changes this protein configuration changes and it sort of opens up towards the outside and throws out the sodium ions. And in this configuration then it can bind to potassium ions and then it again folds inside and pushes these potassium ions inside.

So with the consumption of one ATP basically the the pump has thrown three sodium ions outside and brought two potassium ions inside and that is how it helps in maintaining both the sodium gradient as well as the potassium gradient. Now as you can see this process consumes energy. This is in fact the most energy consuming part of a neuron. About two-thirds of the energy that is consumed by a neuron is taken up by the single protein the sodium potassium exchange pump among the thousands of other proteins that are present in the cell. This one consumes a very large share of energy but it is very important if the neurons have to function over a long time.

Now this is not the only type of pump that is present there are many many other pumps that are present that moves different ions across their concentration gradient. So there is a pump for calcium ions there is a sodium calcium exchange pump and so on. So all these pumps work together to maintain the gradients. So far we have seen the basic molecules that make the generation of electrical activity possible in neurons. Thank you.