Introductory Neuroscience & Neuro-Instrumentation
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Lecture - 7
The Resting Membrane Potential

Introductory Neuroscience and Neuro-Instrumentation, the Resting Membrane Potential.

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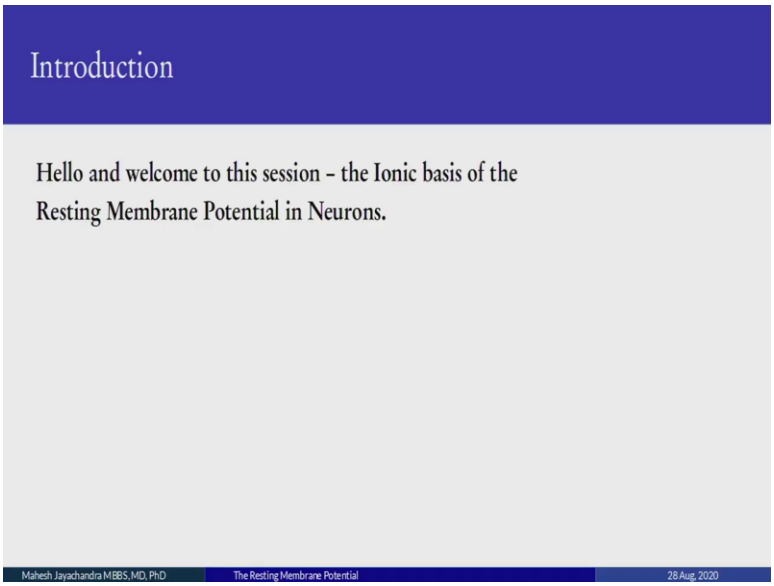

Hello and welcome to this session on the ionic basis of the resting membrane potential in neurons.

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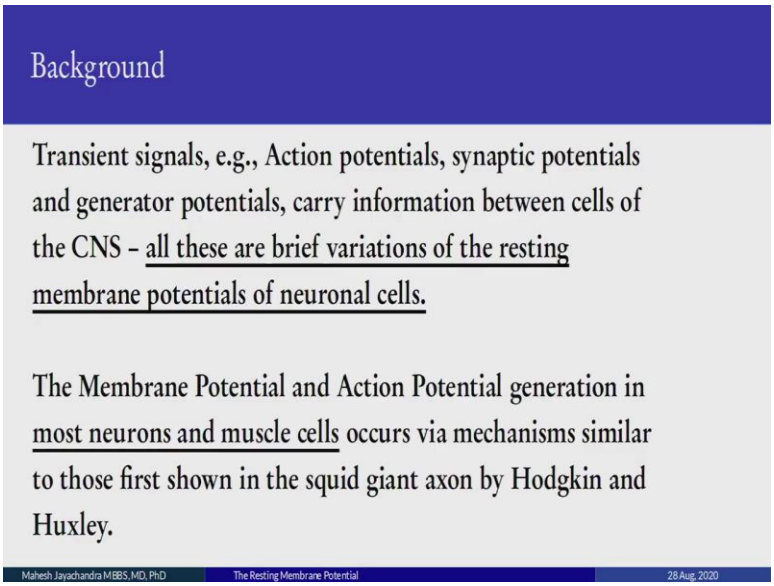

This session and the next one, the action potentials, are fundamental to understanding neurophysiology. Transient signals like action potentials, synaptic potentials, generator potentials, they carry information between cells of the central nervous system but fundamentally, all these are brief variations of the resting membrane potential of neuronal cells.

The membrane potential and action potential generation in most neurons and muscle cells it occurs via mechanisms very similar to those shown first in the squid giant axon by Hodgkin and Huxley.

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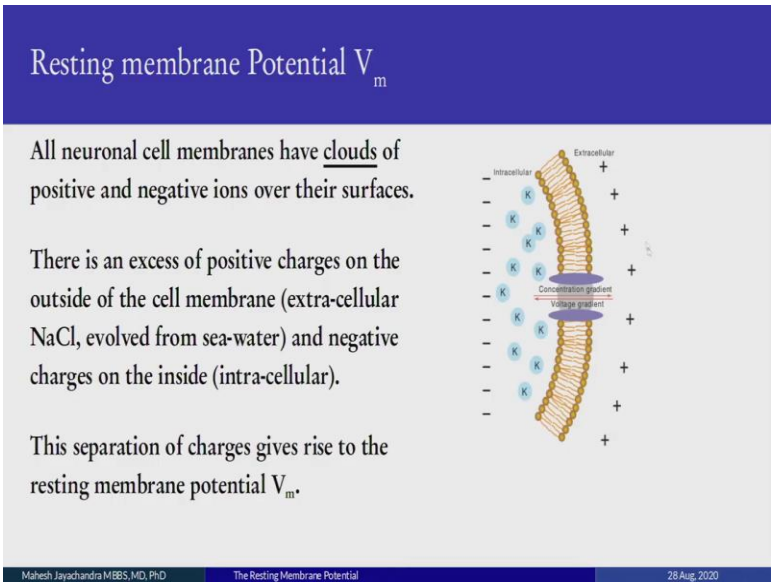

Let us consider the resting membrane potential. It is also denoted as V subscript m. In greater detail, how does it originate? All neuronal cells, in fact, all excitable cells have clouds of positive and negative ions over their surfaces.

There is an excess of positive charges on outside the cell because we all evolved from the sea, so extracellular fluid is basically sodium chloride, NaCl; and that dissociates. You have sodium ions and chloride ions and then you have negative charges inside the cell.

This separation of charges gives rise to the resting membrane potential or V subscript m. So on the right, you see a schematic you have, if you remember, the phospholipids layer and then you have an ionic channel and you have, this is inside so you have a whole bunch of potassium ions here and outside you have a bunch of positive ions.

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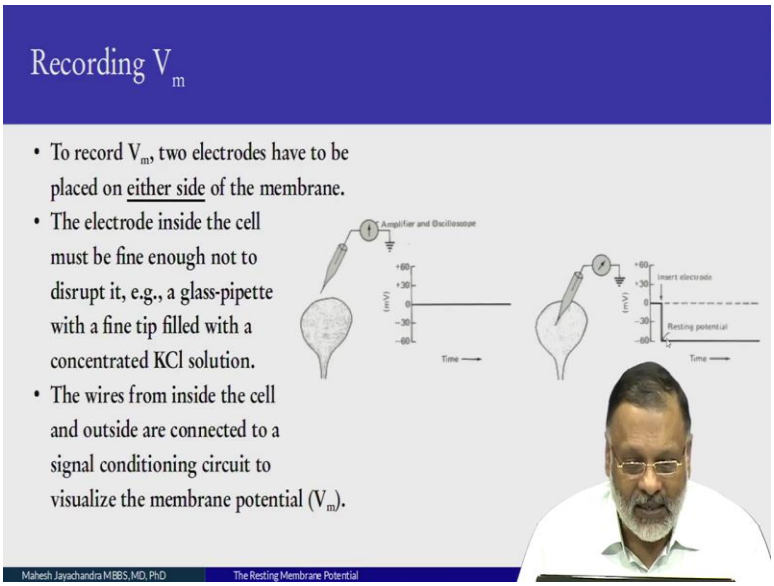

So how do we first record it? So essentially, we must place two electrodes on either side of the membrane to record the potential difference between on either side of the membrane.

So, first, the electrode must be fine enough that it does not disrupt the cell. As we mentioned earlier, you have a glass micro-electrode with a silver wire connected to the signal conditioning circuit and this is when it is outside the cell. As soon as you insert it inside the cell, your, from 0 it goes to minus 60 and that is the resting membrane potential. So that is basically, that is, it is as simple as that. You take an electrode, put it inside a cell, and see the voltage difference, so it is minus 60 from inside to outside.

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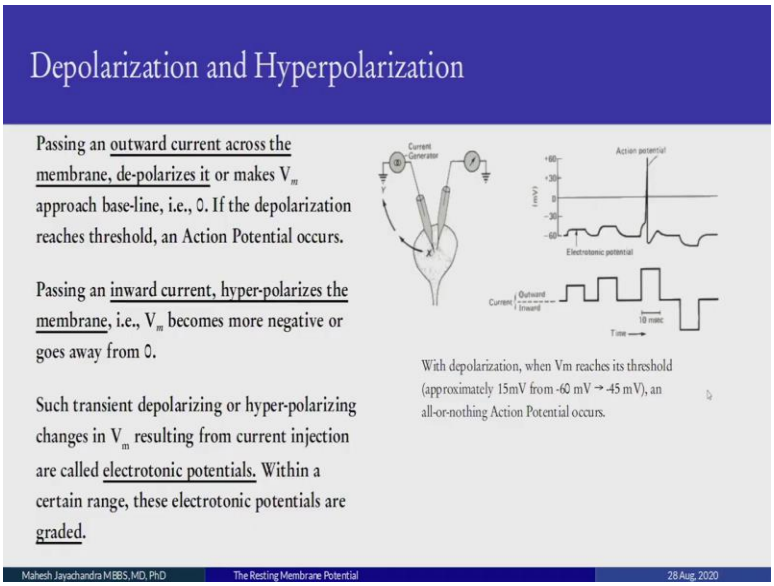

So now, depolarization and hyperpolarization. So these are terms which are used to reflect what is happening to the resting membrane potential. Suppose you pass an outward current across the membrane, you depolarize it. You are passing a current so that you are making the resting membrane potential go towards 0, you are passing a current and it goes up, from minus 60, it goes up.

Now if the depolarization potential, you keep depolarizing, you keep increasing the current, the outward current going outside, at a certain point it reaches threshold and then boom, you get an action potential. The spike, it lasts about 1 millisecond or so, and it is all or none; either you get it or you do not, you do not get half of action potential, you do not get two action, double the action potential, you just get an action potential.

And alternatively, if you pass current inward, the resting membrane potential goes down. It goes below 60 and that is called hyper-polarization. So, these transient depolarization potentials and hyper-polarizing potentials are called electrotonic potentials and within a certain range, they are graded. But once it reaches threshold, then you have the action potential. Of course, with hyper-polarizing, hyper-polarization, there is no action potential it just gets more and more hyper-polarized.

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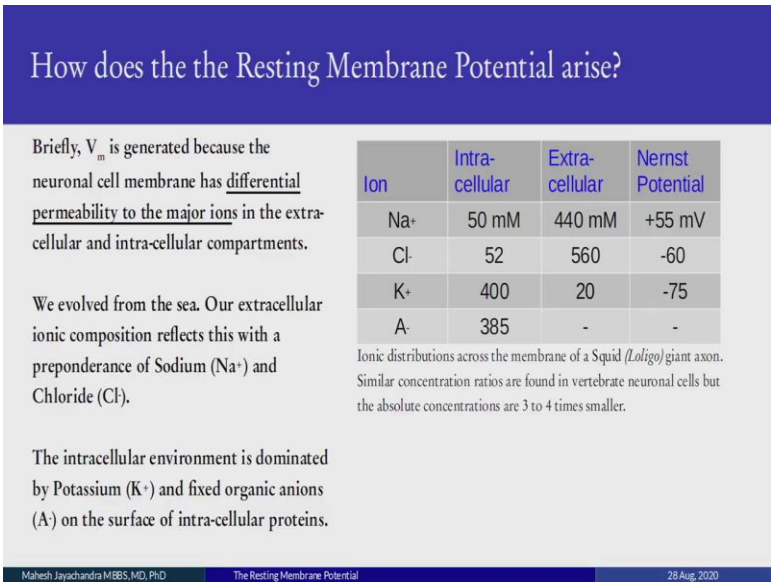

So now, the question how does it arise? And this is very interesting. One of the most fundamental things of neurophysiology can be just worked out from the concentrations, it is kind of chemistry.

So briefly, all these neuronal membranes, they are differentially permeable to major ions and they do not, they are not permeable to all ions and only certain ions. And as I mentioned earlier, we evolved from the sea, so our extracellular ionic composition reflects this with the preponderance of sodium and chloride.

The intracellular contents on the other hand is dominated by potassium and fixed anions. These are charges fixed on proteins, which are massive creatures, and they cannot move through the ionic channels, so they have to stay put and they are on the surface of these intracellular proteins.

So remember the squid, we considered it earlier. So just consider the following ion sodium, potassium; I am sorry, sodium, chloride, potassium, and the anionic charges; so these are the intracellular concentrations. So, sodium is 50 millimolar, chloride is 52, potassium, on the other hand, is 400 inside and the fixed ionic, anionic charges are 385.

Extracellularly, you have sodium and dominating with chloride 450 millimolar and 560 millimolar, there is hardly any potassium outside. In fact, the only easily available

potassium fluid is tender coconut water which has a high level of potassium, which is why it is used in therapy for rehydration.

So, with these, we can calculate something called the Nernst Potential, which gives us the equilibration potentials of these ions. Now, one thing to, we will get to the Nernst Potential in the next slide, one thing to bear in mind is in vertebrates, you have a similar relative concentration of sodium, potassium, and chloride but the absolute concentrations are 3 to 4 times smaller. So it is the relative concentrations which matter not the absolute concentrations.

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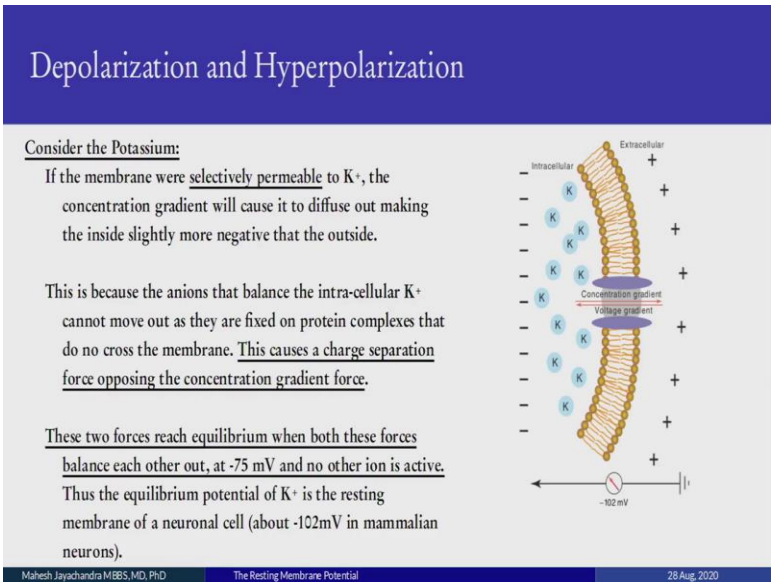

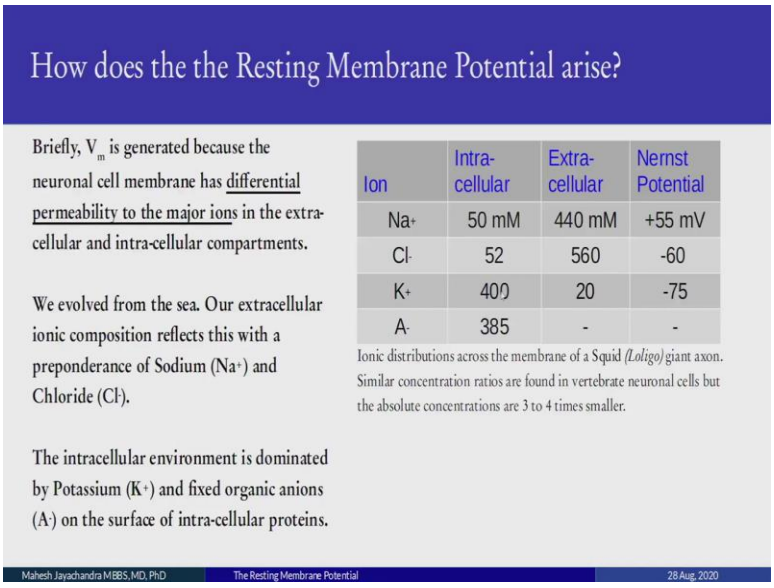

So, consider depolarization and high polarization. The cell membrane is selectively permeable to potassium. So because of that, the internal potassium will keep diffusing out because it is permeable to potassium and there is very little potassium outside compared to inside, so it will keep going out.

However, you have these intracellular anions which are on the surface of intracellular proteins, which are too big to pass through, and after a certain time, they will, there is a

charge separation, there is positive, negative and because of this charge separation, you get this gradient.

So you have this one process which pushes the potassium outside, the other process and the anions which is holding the potassium inside, so when they reach equilibrium, approximately at minus 75 millivolts and there is no other ion active, that is the equilibration potential level or the equilibration potential of potassium.

So it is the resting membrane potential and that is the resting membrane potential. And in a neuronal cell from the mammalian system, it is about minus 100 millivolts, the resting membrane potential.

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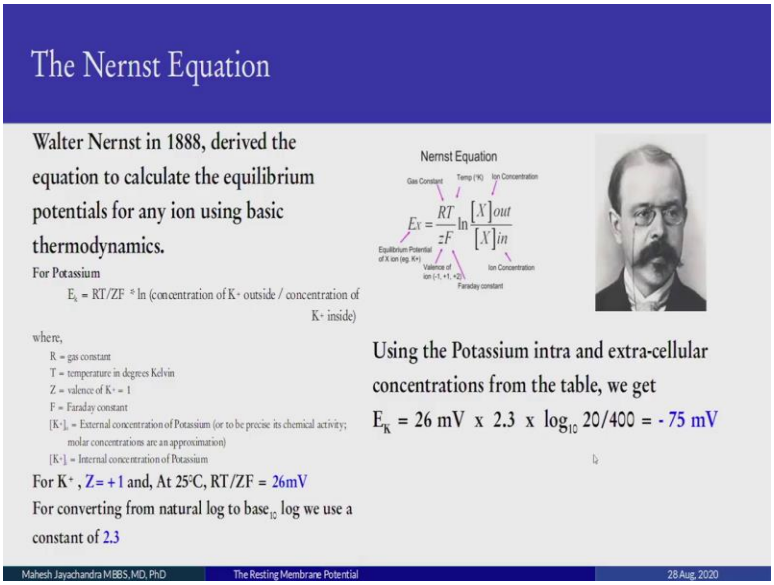

The Nernst equation. Walter Nernst in 1888 derived this equation to calculate the equilibrium potential for any ion using basic thermodynamics. So the equation is very straightforward, you can actually derive it from the Boyle's law RT/ZF.

So the equilibration potential of any ion is RT, where R is the gas constant, T is the absolute temperature, Z is the valence, and F is a faraday constant. And then, you have the natural log of that ion concentration outside over the concentration of inside.

So for potassium, its valence is 1 and at 25 degrees centigrade, RT/ZF reduces to 26 millivolts. And for converting from a natural log to $\log_{10}$, we use a constant of 2.3. So using the concentrations of the potassium in the table earlier, we can work, plug it into this equation and we get minus 75 millivolts. And we can do this for every ion which is present, chloride, sodium so on, and so forth.

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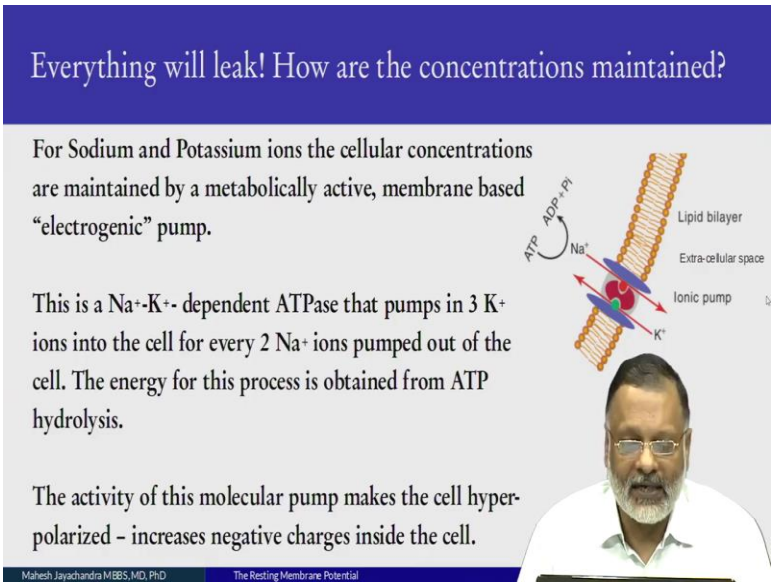

So the thing is, one question which is asked is everything will leak out, so how are these concentrations maintained? for sodium and potassium, you have a pump. It is an electrogenic pump, it is on the membrane and it is fueled by ATP.

So, it pumps in 3 potassium ions for every 2 sodium ions pumped out and ATP is converted to ADP+1 phosphate group, which provides energy to this whole system. The activity of this cell, so you are having 2 sodiums going out, 3 potassiums coming in, so obviously, the cell is going to get hyperpolarized which means the negative charges inside the cell increase.

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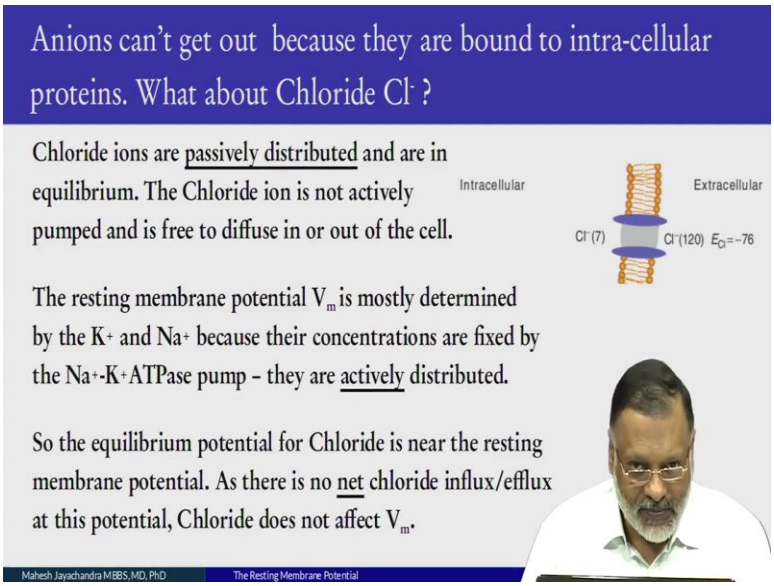

So anions cannot get out because they are bound to intracellular proteins, proteins are too big, they cannot get out. So what about chloride, what happens with chloride? So chlorides ions are passively distributed on an equilibrium. It is not actively pumped, and it can freely just go inside and outside of the cell.

So the resting membrane potential and this is a very important point is mostly determined by the sodium and potassium ion concentrations and these are fixed by the sodium-potassium ATPase pump. So they are called, they are considered actively distributed. So the equilibrium potential for chloride is near its resting membrane potential as there is no efflux or influx of chloride, chloride does not affect the resting membrane potential.

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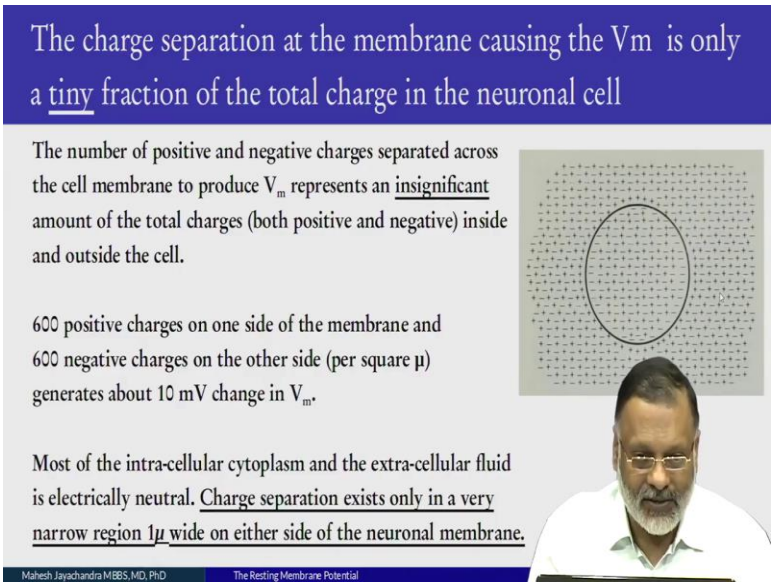

The charge separation, what happens at the cell membrane because of these different resting membrane potentials and stuff? So it is just the charge separation is very, very, very efficient. It is just a tiny fraction of the total charge in the neuronal cell. So this is the number of charges needed to cause a resting membrane potential is insignificant compared to the total number of charges inside and outside.

For example, they have calculated 600 positive charges on one side of the membrane and 600 negative charges on the other side of the membrane per square micron. It generates about 10 microvolt, millivolt change in V_m. Now, this is very, very efficient compared to if you come to the real world of electronics and stuff.

And most of the intracellular and extracellular fluid is electrically neutral. So this charge separation just exists, suppose you have a cell, it just exists on a one mu layer on either side of the membrane, the rest of it is electrically neutral.

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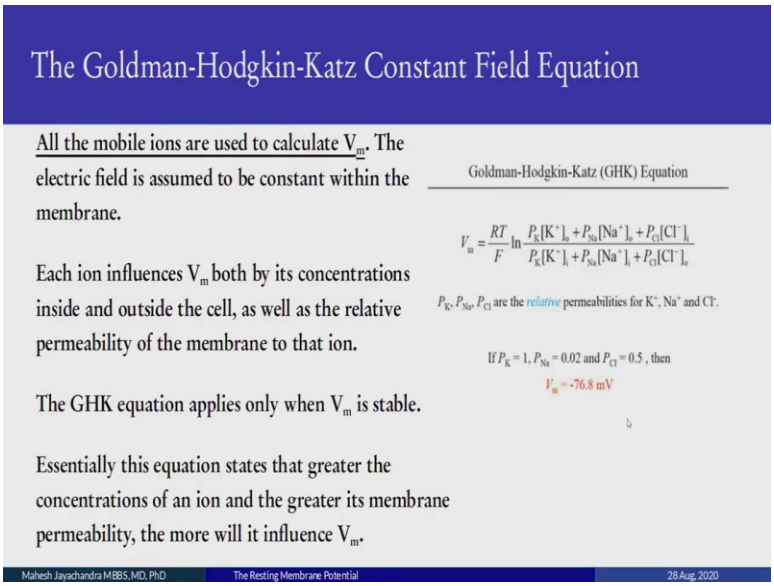

So finally, we are only talking about potassium, we talked about chloride. What happens if you put everything into the picture? So they did that and David Goldman again, Hodgkin and Katz, they developed an equation called the GHK or the Goldman-Hodgkin-Katz constant field equation.

Here all the mobile ions are used to calculate Vm and the electrical field is assumed to be constant within the membrane, hence its name the constant field equation. So each ion influences the resting membrane potential both by its concentrations inside and outside the cell as well as the relative permeability of the membrane to the ion.

Also note that the GHK equation applies only when the resting membrane potential is stable if it is swinging up and down it does not. And the bottom line is this equation states that the greater the concentration of an ion and the greater its membrane permeability, the more will it be it influence on the resting membrane potential.

So the equation in its, all its glory is on the right. So you have the resting membrane potential, you have our old friends RT/F and then you have the natural log. And now, P, K stands for permeability, so you have the permeability of potassium outside, inside; then the permeability of sodium outside, inside; the permeability of chloride outside, inside.

So PK, PA, and PCL are the relative permeabilities of potassium, sodium, and chloride. So if we can plug in these numbers where PK is assumed to be 1, NA is 0.02, and PCL is 0.5 then your V_m reduces to minus 76.8 millivolts.

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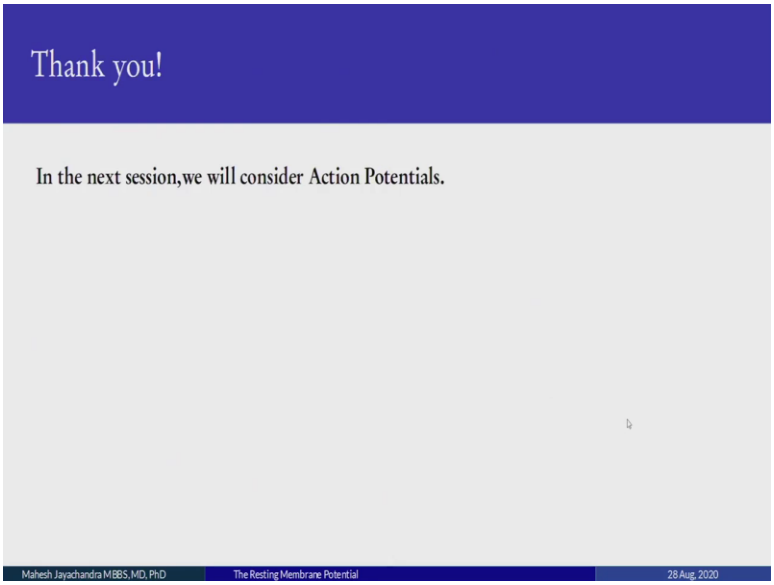

So thank you. In the next session, we will consider action potentials. However, this session will have a demo, a demo session where you will get your hands dirty playing with programs which pretty much simulate the resting membrane potential. So that will follow after this. Thank you very much.