Neuroscience of Human Movement
Department of Multidisciplinary
Indian Institute of Technology, Madras

Lecture - 05
Goldman Equation

Welcome to this class on Neuroscience of Human Movement. So, in this class we will be talking about Goldman Equation.

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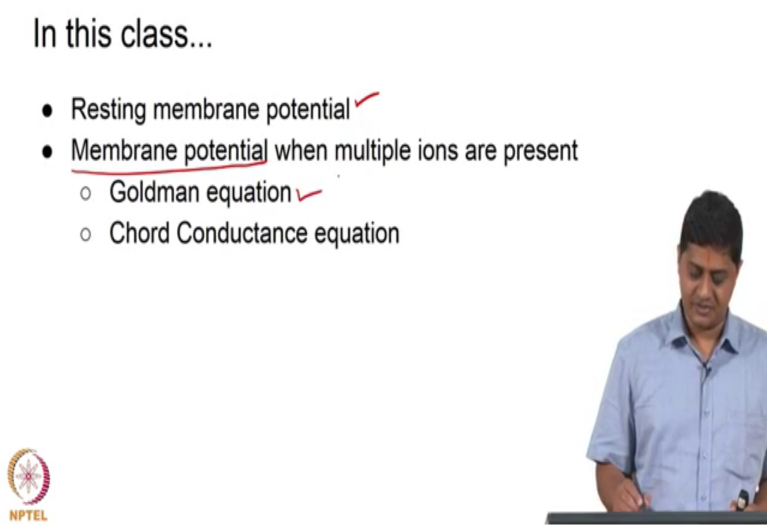

In this class...

- Resting membrane potential
- Membrane potential when multiple ions are present
  - Goldman equation
  - Chord Conductance equation

So, in today's class we will be talking about resting membrane potential, how resting membrane potential is established and maintained, and how that leads to the function of biological membrane in excitable cells, and membrane potential how that is computed. There are two ways in which it is usually done; one is Goldman's equation, the other is Chord Conductance equation.

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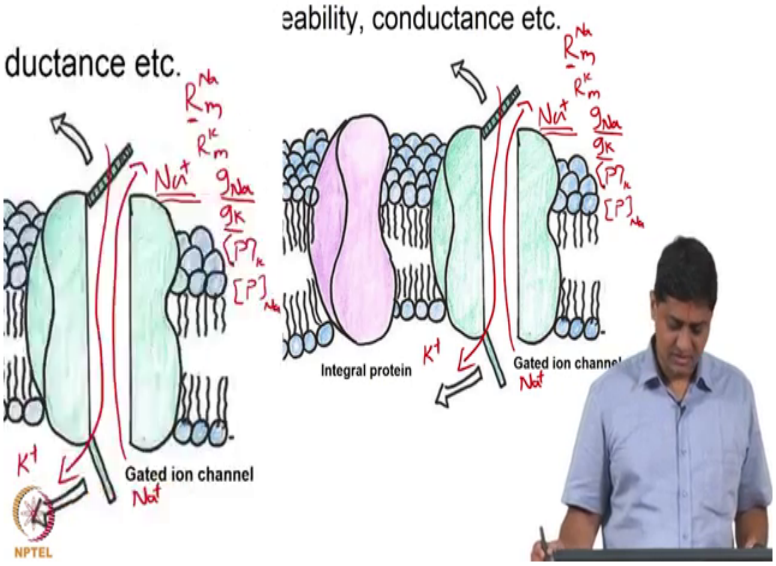

So, we have seen the biological membrane, we have seen the plasma in cell membrane. We have said that essentially this is a lipid bilayer, so there are two layers that are separated by a distance, so there is some distance. Let us say that this distance is, let us say that this is a relatively small distance. And this lipid bilayer is useful, because it has selective permeability to certain ions at certain times. So, it has channels through which it can allow transport of solutes. In this case we are interested in transport of ions, from one side of the membrane to another side of the membrane in particular. So, that is extracellular fluid and this center; that is the extracellular fluid, briefly called as a ECF and this is the intracellular fluid of ICF.

So, so there is exchange of solute in this particular case, ions from one side to the other. So, say for example, if this channel is open and let us suppose that this channel allows many ions for example. Then this channel allows transport of ions in this direction as well as in that direction. Suppose this allows sodium ions. Sodium ions are found in greater concentration outside the cell membrane when compared with the inside. So, the sodium is going to move from outside to inside, whereas potassium if it is also permeable if this channel is also permeable to potassium, then potassium will move from inside to the outside. Also note that this can be considered to be parallel plate capacitor that with some capacitance ok. I am going to call this as a membrane capacitance it.

So, at this point, this quantity is not particularly useful. In future classes we will discuss the nature of this membrane capacitors and its influence in the conduction velocity. That is something that we will discuss in future classes, but today we should also discuss one more thing, to what extent are these ions able to freely move. If say this ion is able to move less freely then it has a resistance, the membrane resistance.

It turns out that each ion can have different amounts of resistances, so we could call this as R m for sodium, similarly for potassium there is a membrane resistance etcetera. Another way of looking at that is the ability to move freely can also be defined as conductance. So, when you say sodium conductance is high, what it means is the sodium resistance or resistance of the membrane to sodium ions is less. So, another way of looking at that is as a conductance of the membrane to sodium ions or two potassium ions.

One other way of looking at that, is permeability. If this channel was more permeable to say sodium ions, then; that means, its conductances high or the resistance of the membrane to sodium is less. Same can be said about potassium, if this channel was more permeable to potassium then; that means that the potassium conductance is high and the resistance of the membrane to movement of potassium is less right. So, there are different ways of looking at that. So, we will be looking at g N a g k and also permeability to each individual ion right.

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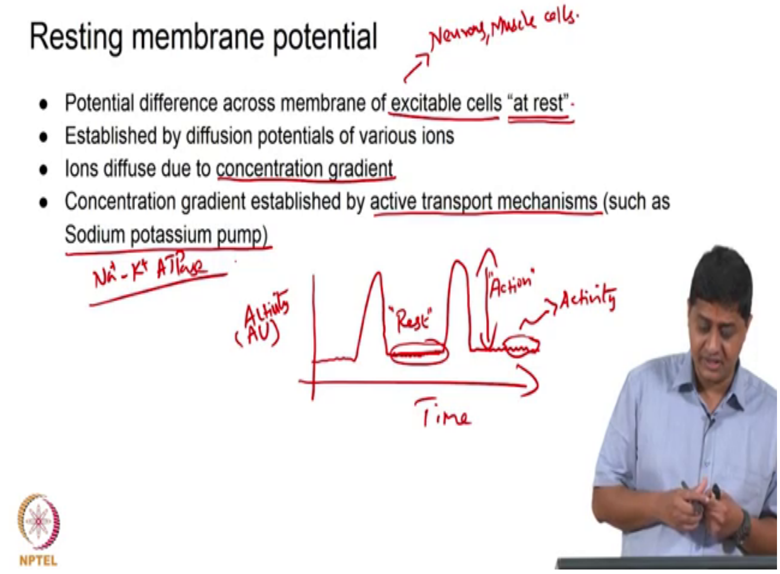

Resting membrane potential

- Potential difference across membrane of excitable cells "at rest".
- Established by diffusion potentials of various ions
- Ions diffuse due to concentration gradient
- Concentration gradient established by active transport mechanisms (such as Sodium potassium pump)

So, we defined resting membrane potential, resting membrane potential is this potential across the membrane of excitable cells at rest. So, what are these excitable cells, we have defined this earlier. These are neurons and muscle cells, are muscle fibers right, but when you say rest. What is rest? That is something that needs to be defined in general rest is the period between two bouts of action right. For example, if I am active now and between yesterday during the day and today during the day I have had a rest session right, basically a sleep can be considered to be rest session, but what is defined as rest; rest is this period between two active sessions, is it not.

So, it is not clear what this active session or active bout is that I am talking about, that is something that has to be made clear in future classes. But for example, if you consider, this is activity in some arbitrary unit say for example, and this is time. If this is baseline activity and then there is a greater amount of activity, then it reduces and then you are back in baseline activity, and then there is a, there is another bout of action and then you are back to baseline activity. There is always activity. Note there is always activity, except that amount of activity is much greater than this baseline activity. This is, this can and this period can be considered to be rest, whereas, that can be considered to be action or activity, for example.

Although there is always activity, considerable deviation from a baseline activity can be considered to be action or activity for our purpose right and how is this established? we saw earlier in the previous class that when there is selective permeability you have diffusion potentials that are generated due to movement of ions across a concentration gradient, due to the existence of a concentration gradient, when an ion moves from one side of a semi permeable membrane to another side what you have, is the development of diffusion potentials. We also defined the equilibrium potential right. So, we defined equilibrium potential for each ion separately right.

So, why do the ions diffuse? I said earlier, the ions diffuse due to concentration gradient. The question is how is the concentration gradient even established? The concentration gradient may be established by the presence of active transport mechanism we saw an example of an active transport mechanism; that is the sodium potassium pump or the N a plus K plus A T P ase, we saw this example in the previous class right.

So, its existence of the concentration gradient is the reason why there is a diffusion potential, and the concentration gradient itself is established by the sodium potassium pump which is an active process, so you have to spend energy to maintain the concentration gradient of, why would the system do such a thing? You are maintaining a gradient, if you did not maintain the gradient at the expense of energy then there would be no need for the diffusion potential to exist or any such thing.

So, it seems like there is some very important function that needs to be performed with the help of this concentration gradient, we wonder what that crucial function is, that is something that we will see in future classes right.

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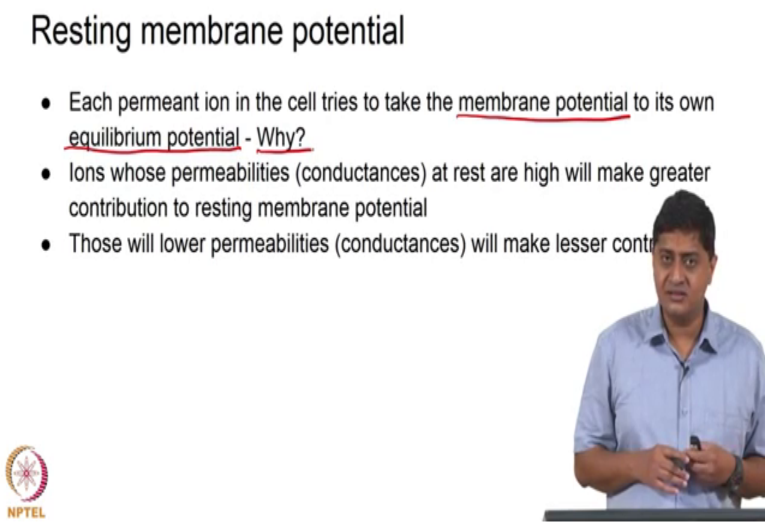

Resting membrane potential

- Each permeant ion in the cell tries to take the membrane potential to its own equilibrium potential - Why?
- Ions whose permeabilities (conductances) at rest are high will make greater contribution to resting membrane potential
- Those will lower permeabilities (conductances) will make lesser contr

So, another important point to note is that each permeant ion in the cell tries to take the membrane potential to its own equilibrium potential. Note the difference, membrane potential is the potential of the biological membrane or the potential maintained across the biological membrane between the inside and the outside for example. Whereas, the equilibrium potential is specific to an ion, for that ion that is the potential at which there will be no net movement of that ion is it not. This is also called as the Nernst potential if the biological membrane, where at the equilibrium potential of say sodium or potassium then that ion will not move, this is what we explained in the previous classes is it not.

So, why is it that the each permeant ion tries to take the membrane potential to its own equilibrium potential? Because at that point it does not have to move; there is no need for it to move, because that is the point at which the force due to the electrical gradient, exactly matches the force due to the concentration gradient for that ion, is it not, and it turns out that ions whose permeability is at rest or high will make greater contribution to resting membrane potential; that is something that we will have to justify in the future slides, we will do that, and those with lower permeability will make lesser contributions.

So, it seems like that is a net permeability for the biological membrane and different ions contribute different amounts of these permeabilities, if we could somehow come up with an equation, a relationship between that would be good and that is the Chord Conductance equation.

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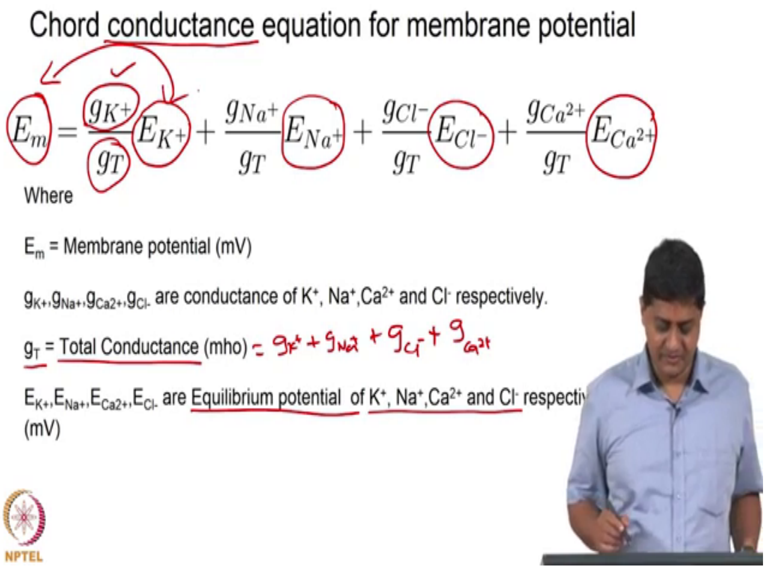

Chord conductance equation for membrane potential

$$E_m = \frac{g_{K^+}}{g_T} E_{K^+} + \frac{g_{Na^+}}{g_T} E_{Na^+} + \frac{g_{Cl^-}}{g_T} E_{Cl^-} + \frac{g_{Ca^{2+}}}{g_T} E_{Ca^{2+}}$$

Where

E_m = Membrane potential (mV)

$g_{K+}, g_{Na+}, g_{Ca2+}, g_{Cl-}$ are conductance of K^+, Na^+, Ca^{2+} and Cl^- respectively.

g_T = Total Conductance (mho) $= g_{K^+} + g_{Na^+} + g_{Cl^-} + g_{Ca^{2+}}$

$E_{K+}, E_{Na+}, E_{Ca2+}, E_{Cl-}$ are Equilibrium potential of K^+, Na^+, Ca^{2+} and Cl^- respecti
(mV)

Except that in the Chord Conductance equation we are talking about conductance and not permeability, but we said these are similar quantities, but not the same; obviously, the units are different. Here the Chord Conductance equation attempts to wait the equilibrium potential for each ion. So, here E N a E K E C l and E C a 2 plus refer to the equilibrium potential or Nernst potential of these individual ions right.

This value is waited by the contribution, relative contribution of their conductance to the total conductance. Note g T is a total conductance, what is it? That is basically the sum of g K plus g N a plus g C l plus g C a 2 plus, so there is a total conductance that the biological membrane has, how do that, how much of the conductance comes from say the potassium alone, if a lot of the conductance comes from potassium it would be reasonable to expect that E m is closer to E k, say for example,. So, we solve a problem similar to that to illustrate this principle.

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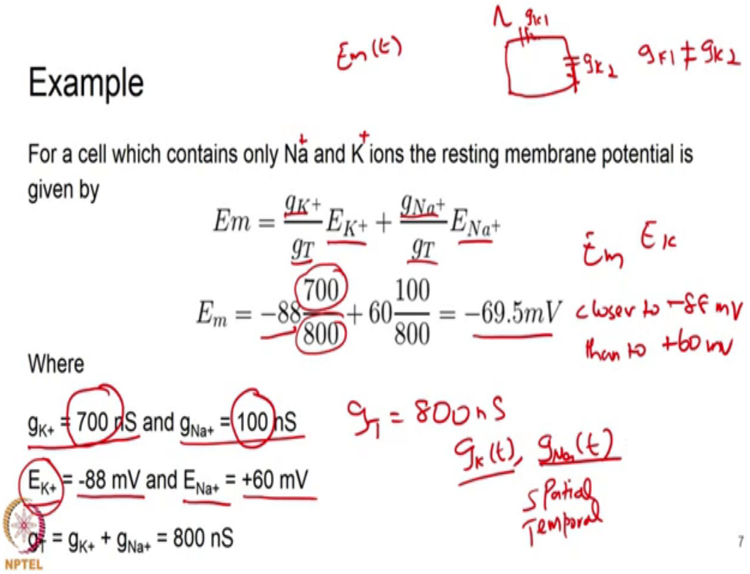

Example

For a cell which contains only Na^+ and K^+ ions the resting membrane potential is given by

$$Em = \frac{g_{K^+}}{g_T}E_{K^+} + \frac{g_{Na^+}}{g_T}E_{Na^+}$$

$$E_m = -88\frac{700}{800} + 60\frac{100}{800} = -69.5mV$$

Where

g_{K+} = 700 nS and g_{Na+} = 100 nS

E_{K+} = -88 mV and E_{Na+} = +60 mV

$g_T = g_{K+} + g_{Na+}$ = 800 nS

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Let us assume to make it simple, let us assume that a cell contains only the sodium and potassium ions, there is no other ion in that cell, and let us try to compute the resting membrane potential as functions of the equilibrium potentials for sodium and potassium and the relative conductance. Let us suppose the potassium conductance is 700 and the sodium conductance is 100. So, then g T is basically 800, is it not, 800 units, and let us suppose the Nernst potential for potassium is minus 88 millivolts, and that for sodium is plus 60 millivolts.

Now we want to know to what extent the membrane potential is influenced by the sodium conductance and potassium conductance, who is going to play a major role in this. That is easy to compute using this equation this is the Chord Conductance equation. And let us suppose I know I. Since I know all these things, I know E k, I know E N a, I know g N a, I know g K and g T is basically g K plus g N a, is it not that is 800.

Now, I could actually substitute these values. So, that is 700 by 800 multiplied by minus 88. What is minus 88? That is E k plus is it not. Now it is very easy to expect that the membrane potential E m will be close to E k, why is that, because out of 800 700 units comes from g K. So, E m is about minus 70 millivolts which is closer to minus 88 millivolts than to plus 60 millivolts. What are minus 88 and plus 60 minus 88 is the equilibrium potential of potassium and plus 60 is the equilibrium potential of sodium.

Since a lot of the conductance comes from potassium, it turns out that the membrane potential is actually closer to the potassium equilibrium potential rather than to the sodium equilibrium potential. Note actually these conductances g K and g N a are not constants, but rather are functions of time. So, essentially what you have, is g K of T and g N a of T. So, these are functions of time. Note that in a cell membrane; let us suppose this is a cell membrane, the conductance is again not a constant, so there is some conductance here and there is some conductance here. This is g K 1 and this is g K 2.

For now we are only considering a portion of the cell membrane and then analyzing this, but it is in general, in general it is expected that g K 1 and g K 2 are not the same. So; that means, there is both a spatial distribution, and a temporal distribution of these conductances. So, essentially this means that there is a distribution of the membrane potential itself, both spatially and temporarily. So, membrane potential here is going to be slightly different from the membrane potential here.

It is possible that this membrane potential is relatively high, whereas, this membrane potential is at baseline, it is possible for that to happen but far, now we will only analyze membrane potential in the relatively small area, where it is expected to be the same, so that. So, membrane potential is also a function of time essentially, because those that lead to these functions g K and g N a are also functions of time, it is expected that the E m is also function of time right and space right.

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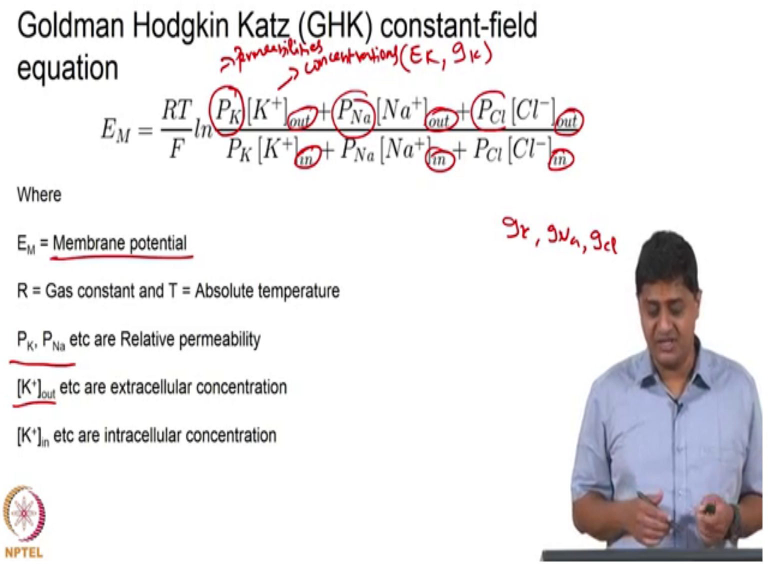

Goldman Hodgkin Katz (GHK) constant-field equation

→ permeabilities

→ concentrations (E_K, g_K)

$$E_M = \frac{RT}{F} ln \frac{P_K [K^+]_{out} + P_{Na} [Na^+]_{out} + P_{Cl} [Cl^-]_{out}}{P_K [K^+]_{in} + P_{Na} [Na^+]_{in} + P_{Cl} [Cl^-]_{in}}$$

g_K, g_{Na}, g_{Cl}

Where

E_M = Membrane potential

R = Gas constant and T = Absolute temperature

P_K, P_{Na} etc are Relative permeability

$[K^+]_{out}$ etc are extracellular concentration

$[K^+]_{in}$ etc are intracellular concentration

Another way of expressing the same thing is the Goldman Hodgkin Katz equation. Here what you have is permeabilities P K P N a P C l etcetera, which are, which can be considered equivalent to g K g N a g C l, somewhat similar to the conductances, but not the same the units are different. Suppose you have permeabilities. Here however, we are not weighing, we are not weighting the permeability by the total permeability, what we are doing rather, is something else here instead of weighting the conductance as a function of total conductance and multiplying it by the Nernst potential here, what are used are concentrations here. Concentrations and permeabilities are used instead of the equilibrium potentials and the conductances. Instead of E ks and g ks we use concentrations and permeabilities.

Suppose I want to find what the membrane potential is and I know the permeabilities of all these ions and their respective concentrations. Note there are going to be two concentrations, there is a concentration difference between the inside of the cell and the outside of the cell that is the reason we are discussing this is not. So, there are going to be two concentrations. So there is a concentration outside and the concentration inside for each of these species right, for each of this ion. There is an inside concentration and an outside concentration and the permeability, between ions is going to be different.

Suppose I substitute all these value, suppose I knew these values and I substitute I will be in a position to find the membrane potential, right.

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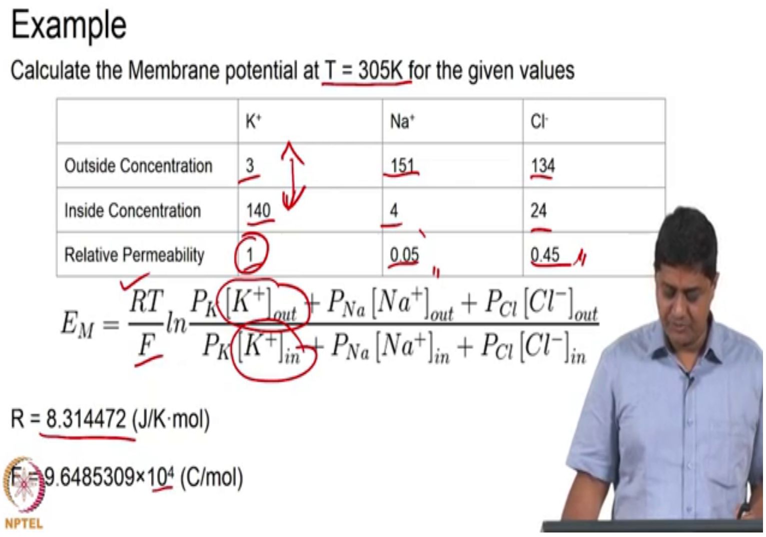

Example

Calculate the Membrane potential at T = 305K for the given values

	K+	Na+	Cl-
Outside Concentration	3	151	134
Inside Concentration	140	4	24
Relative Permeability	1	0.05	0.45

$$E_M = \frac{RT}{F} ln \frac{P_K[K^+]_{out} + P_{Na}[Na^+]_{out} + P_{Cl}[Cl^-]_{out}}{P_K[K^+]_{in} + P_{Na}[Na^+]_{in} + P_{Cl}[Cl^-]_{in}}$$

R = 8.314472 (J/K·mol)

F = 9.6485309×10^4 (C/mol)

Let us suppose I know the outside concentration and the inside concentration for these ions; this, a typical concentrations or similar to typical concentration that we saw earlier and the relative permeability is this. Note the permeability for potassium is relatively high even compared with that for sodium and chloride, is not. So, you would expect that the E k and E m are closer to each other and it is, but here we are not substituting E k, but we are only talking about concentration gradients right, because this is K plus outside and inside.

We substitute all these values and we know what is R, R is the gas constant that is the value and F is faradays constant and that is the value, and I know the temperature, say the temperature are considered is 3 naught 5 Kelvin. Say for example, then I could compute this and substitute these values and compute this, I could compute this as approximately minus 59 millivolts right.

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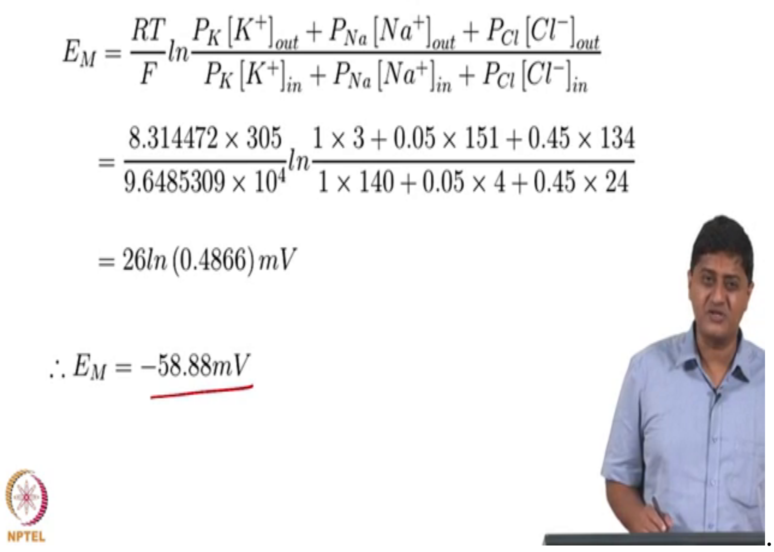

$$E_M = \frac{RT}{F} ln \frac{P_K[K^+]_{out} + P_{Na}[Na^+]_{out} + P_{Cl}[Cl^-]_{out}}{P_K[K^+]_{in} + P_{Na}[Na^+]_{in} + P_{Cl}[Cl^-]_{in}}$$

$$= \frac{8.314472 \times 305}{9.6485309 \times 10^4} ln \frac{1 \times 3 + 0.05 \times 151 + 0.45 \times 134}{1 \times 140 + 0.05 \times 4 + 0.45 \times 24}$$

$$= 26ln(0.4866)\,mV$$

$$\therefore E_M = \underline{-58.88mV}$$

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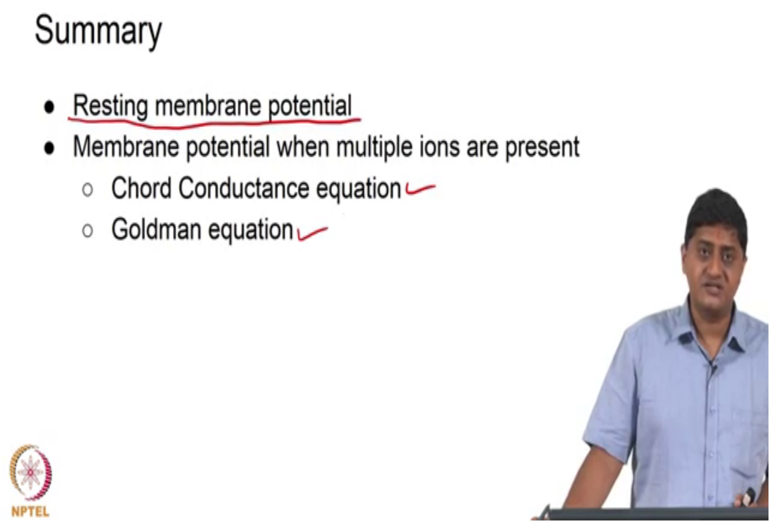

Summary

- Resting membrane potential
- Membrane potential when multiple ions are present
  - Chord Conductance equation ✓
  - Goldman equation ✓

So, essentially what we have learnt is a nature of resting membrane potential and how that is maintained and right, and how to compute this resting membrane potential or membrane potential. There are two ways of doing this we saw: Chord Conductance equation and Goldman's equation.

So, with this we come to the end of this class.

Thank you very much.