

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



Lecture - 03
Membrane Physiology - Part 2

Good morning. Welcome to this class on Neuroscience of Human Movement. This is part 2 of our discussion on Membrane Physiology.

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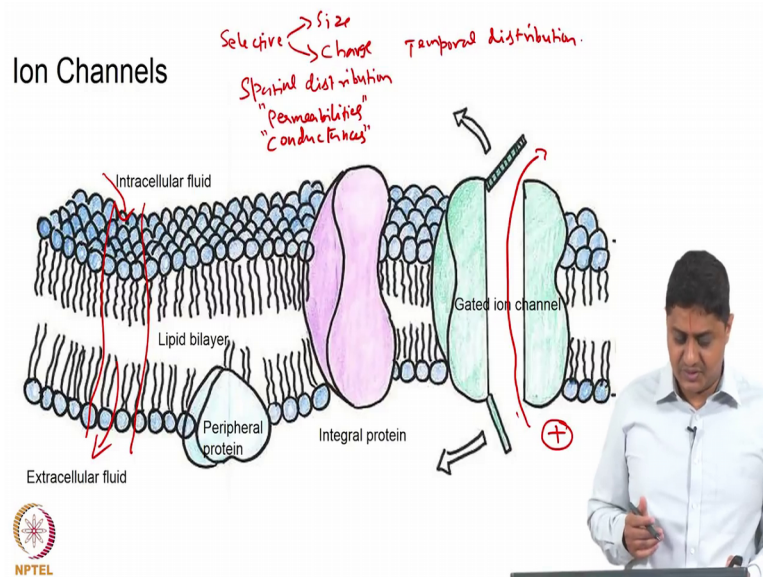
In this class...

- Ion Channels
 - Voltage gated
 - Ligand gated
- Diffusion potential
- Equilibrium potential



So, in this class we will be talking about Ion channels, different types of ion channels, right give a couple examples of this ion channels; Voltage Gated ion channel and Ligand Gated or Chemically Gated ion channel and we will be talking about diffusion potential and we will be at least defining the equilibrium potential function.

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So, we discussed the case of plasma membrane in the previous class. Suppose substance or an ion has to be transported from say one side of the cell say from the outside of the cell. Let us say this is a cation and this has to be transported from outside of the cell to inside of the cell. Suppose this has to happen, there must be channel, there must be a protein that must allow this transport to happen. Note that these channels may be selective. So, in general these channels are selective and this selectivity may be due to size or maybe due to type of charge. Some channels may allow only cations, some channels only may allow sodium, but not potassium, some channels may allow cations, but not anions etcetera.

So, also note that these channels are distributed along the length of the plasma membrane. So, that means that there is spatial distribution of these channels. Also if this channel is open, the probability that this ion is going to get transported say in this direction or suppose there is a different channel here and a different ion gets transported in that direction say for example, the probability that this channel is open governs to a large extent whether that ion will get transported or not. So, this probability is usually represented in terms of permeabilities or to use a phrase, to use a term from physics and electrical engineering conductances.

So, if a channel allows, if the probability that the channel is open is very high, then the channel has high permeability for an ion or high conductance for transport of that ion.



Also, note that this probability is a function of time. It may be open at certain times, but not be open at other times. So, that means, there is also a temporal distribution of the opening and closing of these channels. So, there is both a spatial distribution and a temporal distribution and that affects permeabilities and note not all channels allow all types of ions to pass through. So, there is also selectivity in terms of which ion passes through. So, what you have is a relatively complicated situation where different channels allow different types of ions and they are open at different times depending on different conditions. So, how do we study this and studying this could somehow inform us about the function of the cell membrane itself, right.

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Ion Channels

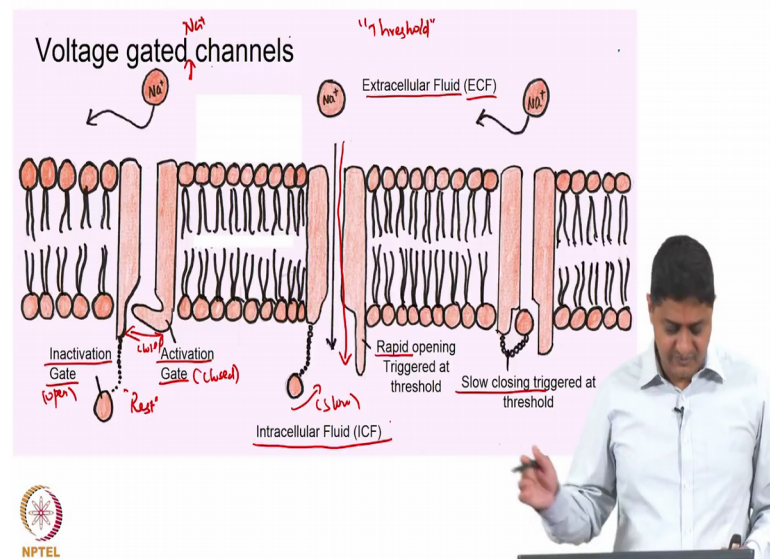
Ion channels:

- May be selective - charge or size → *selectivity*
- May open at different times *temporal*
- Distributed along cell membrane *Spatial*



So, as I said ion channels may be selective, they may be have to be based on charge or size, they may open at different times, they are distributed along the cell membrane. This is the spatial distribution part, this is the temporal distribution part and this is the selectivity part, right.

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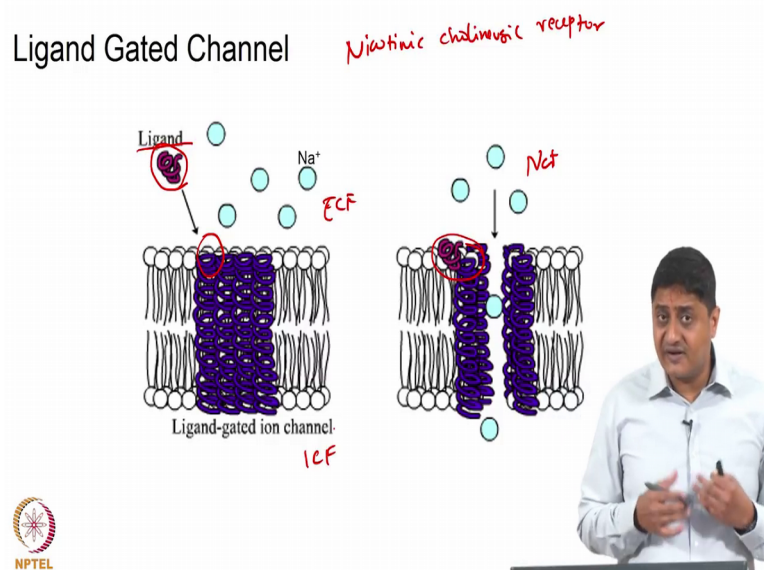
So, an example of channels is the Voltage gated sodium channel. Here is the case of the Voltage gated sodium channel. So, this is opened or closed, this is controlled by the potential difference across the membrane when the potential difference reaches a particular point also called as a threshold. When a threshold is reached, this channel undergoes conformational change or this channel undergoes a change in the structure in such a way that it allows or disallows the ions to be transported.

So, let us take the case of sodium getting transported in this Voltage gated sodium channel, ok. This is a Voltage gated sodium channel. So, Voltage gated sodium channel in this case as soon as the threshold potential is reached, what happens is that command to two gates. So, this channel has two gates; one is called as an activation gate and another is called as an inactivation gate. Both of these gates are given command to change from their current position. Please note what the current position is. The current position is at rest, the activation gate is closed and the inactivation gate is open. This is the rest state and when threshold is reached, both of them are given command to change from their current state. That means, the activation gate must open and the inactivation gate must close, but these two are timed differently. These two processes are the closing of the inactivation gate and opening of the activation gate are timed processes. They happen at different time lengths. It turns out that opening of the activation gate is a rapid process and closing of the inactivation gate is a relatively slow process, right. Both of them are triggered simultaneously, but one is a fast process and the other is a slow process. So,

this will effectively result in a small amount of time at during which the channel is open and during this time a lot of sodium can enter inside the cell from the excess, a little fluid, right.

So, on top is the extracellular fluid; in the bottom is the intracellular fluid. During the brief time during which the inactivation gate is closing and the activation gate has already opened, during that brief time gap, lot of sodium enters inside and this is a crucial event which we will discuss in future classes, right.

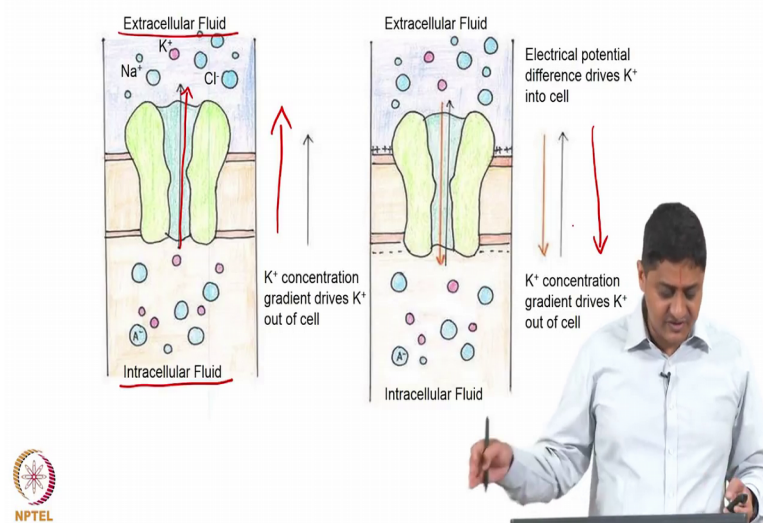
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The other example is the Transmembrane protein or the channel called the Ligand gated channel. So, this involves a particular chemical binding to a particular binding site like here. So, once this chemical binds to its binding site, this channel opens and allows transport of sodium for example, right. The classic example is the case of the nicotinic cholinergic receptors in the neuromuscular junction which we will discuss in great detail in future class, ok. So, this means when this ions are transported from one side say this is sodium and this is getting transported from the extracellular fluid to the intracellular fluid say for example. When this happens, it creates charge separation what effect does this have is of importance for us in discussion. So, let us see what would happen.

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Membrane Potential



Here we have taken the case of a potassium channel. Suppose there is a potassium channel that is open and when it is open, note potassium is present in great quantity inside the cell when compared with outside the cell, right. So, as potassium travels in that direction, so when the channel is open, potassium is going to slowly go out from inside of the cell as it is traveling from inside of the cell to outside the cell it takes one positive charge from inside to outside also. So, basically the concentration gradient is in that direction, but as the amount of potassium builds up on the outside, the potential difference prevents the build-up of more potassium outside the cell. Basically the electrical potential gradient is in that direction. That is why these two are in different colors, right. This is the electrical gradient and that is the concentration gradient so in two different colors, right. So, these two are against each other. That means there must be a point at which some sort of equilibrium must be achieved. What is that point that is of interest for us and we will discuss that in future class, ok.

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Equilibrium potential

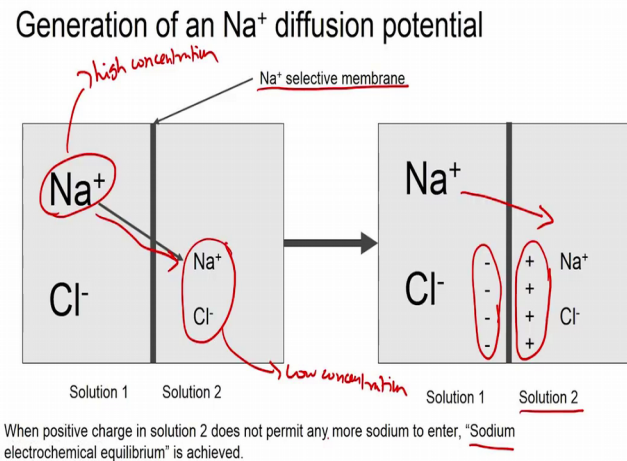
- If a cation "diffuses" down a concentration gradient, a potential difference is developed
- This potential difference starts resisting further diffusion of cations in the same direction
- At some point, the potential difference does not allow any more cations to enter in the same direction - diffusion completely stops!
- This is "Electrochemical equilibrium" and the potential is the "Equilibrium potential" of that cation.

"Nernst"



So, if a cation diffuses down a concentration gradient, a potential difference is developed as I said in the previous slides and this potential difference start resisting further diffusion of cations in the same direction. So, that means as the amount of cations built in one in one side of the cell, that means that more and more cations cannot go or the ease with which the cation can move in the same direction is reduced, right. At some point the potential difference does not allow any more cation to enter in the same direction. So, basically what happens is the diffusion completely stops or the transport completely stops, although there may be concentration gradient. The concentration gradient may be present, but the electrical gradient will not allow any more cations to enter, right. So, what is achieved at this state is an electrochemical equilibrium and the potential at which it is achieved is called as equilibrium potential of that cation, are also called as Nernst potential of that cation, right. So, we will discuss that in the next class, ok.

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Let us consider the case of the sodium and discuss how diffusion potential is generated in the case of. So, let us consider the situation where there is a hypothetical membrane that separates two chambers of sodium chloride. In one chamber, you have a relatively high concentration of sodium chloride and in the other chamber, you have a relatively low concentration, and the membrane is selective only to sodium, but not chloride. So, that means what happens is that only sodium will get transported from the region of higher concentration to the lower concentration, but not chloride. What this will do is that it will create more positive charges on the right side of the chamber or in solution 2 and that means, effectively making the left side a little less positive or a little more negative. So, it creates a charge separation. At some point, the amount of positivity in the right side of the chamber does not allow any more sodium to diffuse through regardless of what the concentration gradient is. The gradient might still be in this direction or the concentration gradient might still be in this direction, but potential difference will not allow any more transport of sodium. At this point, sodium electrochemical equilibrium is achieved. The point at which that happens is Nernst potential of sodium.

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Generation of an Cl^- diffusion potential

Cl⁻ selective membrane

Solution 1 Solution 2

Cl⁻ Na⁺ Na⁺

Na⁺ Cl⁻ Na⁺ Cl⁻

Solution 1 Solution 2

When negative charge in solution 2 does not permit any more Chloride to enter, "Chloride electrochemical equilibrium" is achieved.

NPTEL

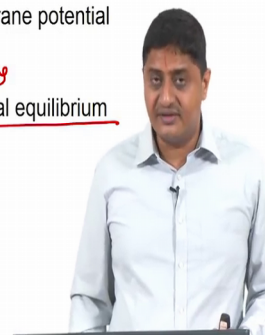
Likewise for chloride, suppose I had a chloride selective membrane, the opposite will happen. The right side will have a buildup of negative charges and the left side will have buildup of positive charges effectively creating charge separation one more time chloride will get transported, but after some time, chloride transport will be prevented effectively stopping any more chloride transport. The point at which this happens is the chloride electrochemical equilibrium, right.

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Summary

- Ion channels - selective (Charge or Size)
- Ion channels distributed along cell membrane *essential*
- Depending on status of gate, channels may be more permeable (have high conductance) to specific ions or less permeable (have low conductance)
- Opening & closure of gate may be due to membrane potential ("Voltage gated") or chemicals ("Ligand gated")
- Diffusion potential - caused due to diffusion *of ions*
- Equilibrium potential - potential at electrochemical equilibrium

Nernst



So, in summary what we have seen is that ion channels may be selective in charge size and they are distributed along the cell membrane. There is a spatial distribution and they may be open at, open or close at different times. So, they may be more permeable or have high conductance to specific ions or may be less permeable or have low conductance to different set of ions and the opening and closing of these channels may be due to membrane potential or voltage gated or maybe chemically gated maybe for example, maybe Ligand gated and the potential that is caused due to diffusion of ions is called as diffusion potential. And, the potential at which the electrochemical equilibrium is achieved is called as a equilibrium potential or Nernst potential. We will discuss Nernst potential in the next class.

Thank you very much for your attention.