Transport Phenomena in Biological Systems

Prof. G. K. Suraishkumar
Department of Biotechnology Bhupat and Jyoti Mehta School of Biosciences Building
Indian Institute of Technology - Madras

Lecture - 58
Mobility of Ions Across a Membrane

Welcome back, we are looking at a situation where there is a simultaneous concentration gradient and electrical potential gradient, we had derived the Nernst equation yesterday as well as we saw the Nernst Planck equation. Essentially we looked at the condition of electro diffusive equilibrium when there is no net movement of an ion under the influence under the combined influence of an electrical field as well as a concentration gradient.

An electrical potential gradient as well as a concentration gradient that is what we had seen in the previous class let us continue further. In this class we are going to look at mobility of ions across a membrane. You know this highly relevant, extremely relevant for the biological engineers and of course, in the human body, as we will see.

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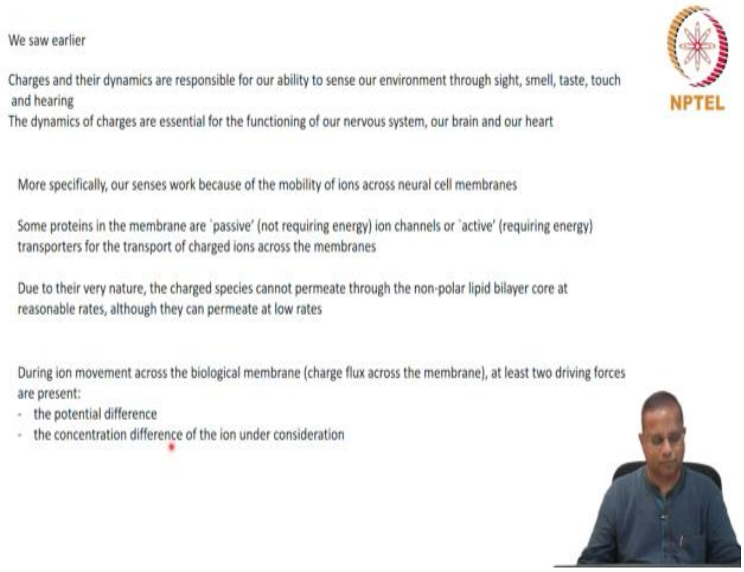

We saw earlier

Charges and their dynamics are responsible for our ability to sense our environment through sight, smell, taste, touch and hearing
The dynamics of charges are essential for the functioning of our nervous system, our brain and our heart

More specifically, our senses work because of the mobility of ions across neural cell membranes

Some proteins in the membrane are 'passive' (not requiring energy) ion channels or 'active' (requiring energy) transporters for the transport of charged ions across the membranes

Due to their very nature, the charged species cannot permeate through the non-polar lipid bilayer core at reasonable rates, although they can permeate at low rates

During ion movement across the biological membrane (charge flux across the membrane), at least two driving forces are present:
- the potential difference
- the concentration difference of the ion under consideration

We saw earlier charges and their dynamics, or at least we stated earlier charges and their dynamics are responsible for our ability to sense our environment, through sight, smell, taste, touch, hearing, the 5 senses and so on so forth. We said that all these 5 senses work by the charges and their dynamics. The dynamics of charges are essential for the functioning of our nervous system, our brain, our heart, this is also we saw the same sentences.

More specifically, our senses work because of the mobility of ions across neural cell membranes, neurons, neural cells, neurons, they are large cells and our senses work because of the mobility of ions across the neural cell membranes. Some proteins in the membrane are passive they do not require energy for transport such as ion channels or active, which require energy such as transporters for the transport of charged ions across the membrane.

In other words, there are 2 ways by which ions can get across the membrane. Apart from regular diffusion, the rates of ion diffusion through a lipid bilayer membrane are very, very slow, especially charged and there is a hydrophilic head a hydrophobic core and a charged particle moving through such an environment is very difficult from the point of view of the nature of molecules involved.

And therefore, the permeability of ions across a lipid bilayer membrane is very, very small, so low that we can usually, can neglect it unless you are considering very long times and so on. So, in the absence of reasonable diffusion reasonable transport rates of the ions across the liquid by layer of the membrane, it is through the proteins that the ions can get in and out of the cell.

There are 2 ways by which that happens one is passive way through the ion channels and an active way through the transporters. Passive means it does not require energy to transport an ion from one side to the other. Active it requires energy it requires the breakdown of ATP to provide the energy for transport of ions across that protein both are involved. Due to the very nature the charged species cannot permeate through the non-polar lipid bilayer core at reasonable rates.

Although they can permeate at low rates, very low rates, this is what we discuss in detail just now, during ion movement across the biological membrane, and the charge flux across a membrane, recall charge flux across membrane sorry, mass flux across a membrane many chapters ago. At least 2 driving forces are present man driving force we already seen here we are bringing in another driving force.

These 2 driving forces are the potential difference if there is a difference in charges across a distance in this case a membrane there is going to be an electrical potential gradient. There is a potential difference across a distance. There is a potential gradient and the concentration difference of the ion under concentration both these are going to contribute.

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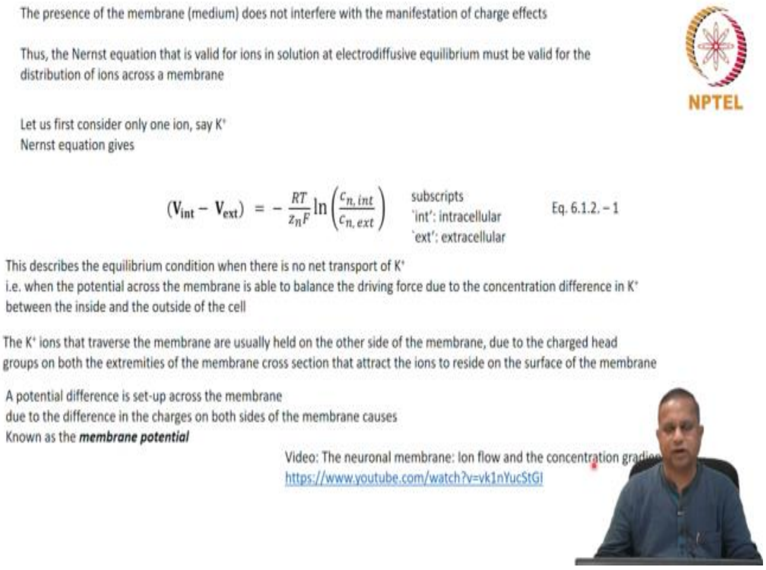

The presence of the membrane (medium) does not interfere with the manifestation of charge effects

Thus, the Nernst equation that is valid for ions in solution at electrodiffusive equilibrium must be valid for the distribution of ions across a membrane

Let us first consider only one ion, say K^+
Nernst equation gives

$$(\mathbf{V}_{\text{int}} - \mathbf{V}_{\text{ext}}) = -\frac{RT}{z_n F}\ln\left(\frac{c_{n,int}}{c_{n,ext}}\right) \quad \text{Eq. 6.1.2.-1}$$

subscripts
'int': intracellular
'ext': extracellular

This describes the equilibrium condition when there is no net transport of K^+
i.e. when the potential across the membrane is able to balance the driving force due to the concentration difference in K^+ between the inside and the outside of the cell

The K^+ ions that traverse the membrane are usually held on the other side of the membrane, due to the charged head groups on both the extremities of the membrane cross section that attract the ions to reside on the surface of the membrane

A potential difference is set-up across the membrane
due to the difference in the charges on both sides of the membrane causes
Known as the ***membrane potential***

Video: The neuronal membrane: Ion flow and the concentration gradie
https://www.youtube.com/watch?v=vk1nYucStGI

The presence of the membrane, it is essentially a medium does not interfere with the manifestation of charge effects this we already know, it is a field effect. So when as long as it does not effectively shield the field and so on and so forth, it is not going to play a role in the manifestation of the charge effects the presence of the medium in this case, a membrane. Thus, the Nernst equation that is valid for ions in solution.

And electro diffusive equilibrium must be valid for the distribution of ions across the membrane nothing prevents it, think about it. You have a medium, liquid medium, let us say, in which we derived the Nernst equation. Here we are going to replace the liquid medium with the membrane that is it. Let us consider only 1 ion say potassium first. Let us develop our understanding with 1 ion.

And then we can extend that to the relevant ions there are not many by the way, the Nernst equation gives and just direct application of the Nernst equation the potential in the intracellular space minus the potential in the extracellular space is nothing but $(V_{in}-V_{ext}) = -(RT/z_nF)\ln(c_{n,int}/c_{n,ext})$. ln is the natural log, $c_{n,int}$ is the concentration in the intracellular space and $c_{n,ext}$ is the concentration in the extracellular space this is what the Nernst equation tells us intracellular extracellular of course.

$$(\mathbf{V}_{\text{int}} - \mathbf{V}_{\text{ext}}) = -\frac{RT}{z_n F}\ln\left(\frac{c_{n,\text{int}}}{c_{n,\text{ext}}}\right) \qquad (6.1.2\text{-}1)$$

This number is 6.1.2 - 1 let me again repeat that this numbering may not be continuous in these lectures, but these numbers are referred to the numbers of equations in the textbook and to provide you with easy reference to textbook material. I am using the same numbers here that I suppose would be helpful. This we said is validate electro diffusive equilibrium. And therefore, this equation describes the equilibrium condition when there is no net transport of potassium ions.

That is, when the potential across the membrane is able to balance the driving force due to the concentration difference between concentration difference in potassium between the inside and outside of the cell. So see there are 2 things 1 is there is a difference in potential across the membrane, 2 there is a difference in concentration of potassium across the membrane. Both are going to try out, opposite ways the same way, whatever it is.

And when there is no net transport of potassium ions, it means these 2 are balanced out, the sum of those equals 0 that is what we have seen I am just reemphasizing that, the potassium ions that traverse the membrane are usually held on the other side of the membrane, they do not go into solution due to the charge head groups on both extremities of the membrane. Membrane cross section that attract ions to reside on the surface of the membrane it is just for some detail.

We are not going to get too much into this particular aspect of it being on the surface and then going into the extracellular space and so on so forth. But you need to at least know that this exists. And show a potential difference is set up across the membrane due to the difference in the charges on both sides of the membrane this is known as the membrane potential.

The potential that is created due to the charge difference of as a membrane is called the membrane potential. Video, the neuronal membrane ion flow and concentration gradient this nicely explains whatever I said here, this will be a nice reinforcement for the understanding of this principle.

(Video Starts: 09:07)

These 2 chambers represent the inside and outside of a biological cell a phospholipid membrane separates the 2 chambers both chambers contain a potassium salt dissolved in water as potassium ions and anions. The salt is 20 times more dilute on the outside of the cell than the inside, creating a steep concentration gradient, but no ions move down the concentration gradient.

Because the phospholipid bilayer is impermeable to these charged hydrophilic atoms. And despite the difference in salt concentration, the ratio of potassium ions to anions on each side of the membrane equals 1 and the membrane potential is equal to 0 millivolts. The solutions are electrically neutral so no charge accumulates on the inside or outside of the membrane. Now let us insert a potassium channel into the phospholipid bilayer.

This channel allows potassium ions to diffuse down the steep concentration gradient the corresponding anion does not fit through the potassium channel and is left behind. As a result of potassium movement, the ratio of potassium ions to anions becomes different inside and outside the cell, causing the inside of the membrane to develop a net negative charge. At first, diffusion is the dominant force moving the potassium ions across the membrane.

But as the inside fluid becomes more negative, the negative electrical force pulls the positively charged potassium ions back through the potassium channel into the cell. Eventually, the electrical force pulling potassium ions into the cell exactly counterbalances the force of diffusion pushing them out. This is the equilibrium potential, where electrical and diffusion forces are equal and opposite, and there is no net movement of potassium ions through the channel. Despite the concentration gradient, the charge difference between the 2 sides is the equilibrium potential and for potassium, this is approximately negative 80 millivolts.

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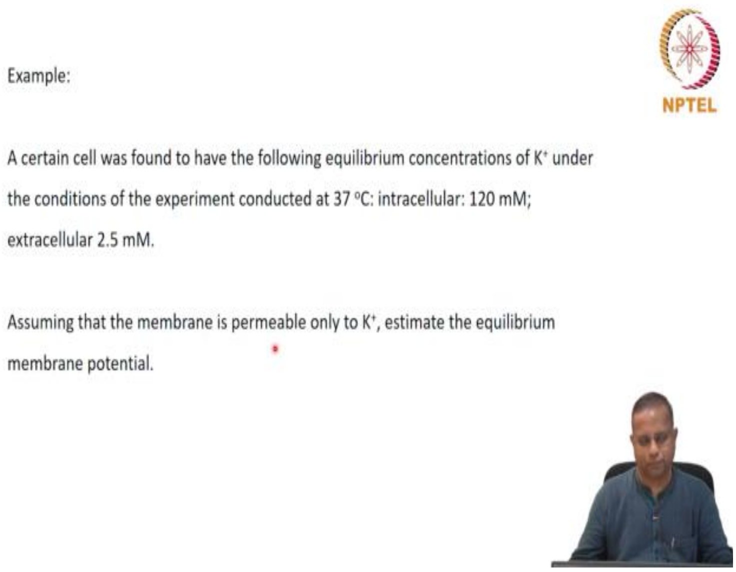

Example:

A certain cell was found to have the following equilibrium concentrations of K^+ under the conditions of the experiment conducted at 37 °C: intracellular: 120 mM; extracellular 2.5 mM.

Assuming that the membrane is permeable only to K^+, estimate the equilibrium membrane potential.

Let us workout an example we will take this case, I have given you some information because it is new and then I am coming up with an example just a variation of the theme. A certain cell was found to have the following equilibrium concentrations of potassium under the conditions of the experiment conducted at 37°C. The intracellular concentration was 120mM. The extracellular concentration was 2.5 mM is very standard for neural cells the human body. So these could be taken as thumb rule values, there will be variations of course, but around this you will have where you have an idea that in the absence of any other data, you could assume these, assuming that the membrane is permeable only to potassium, estimate the equilibrium membrane potential this is the problem.

Pause the video for a few minutes and think about the problem. And then we will take a look at the solution, pause please. Hopefully you have a better mental picture of the situation here. A certain cell was found to have the following equilibrium concentrations of potassium under the conditions of the experiment intracellular concentration extracellular concentration given you are asked to find the equilibrium membrane potential assuming that the membrane is permeable only to potassium.

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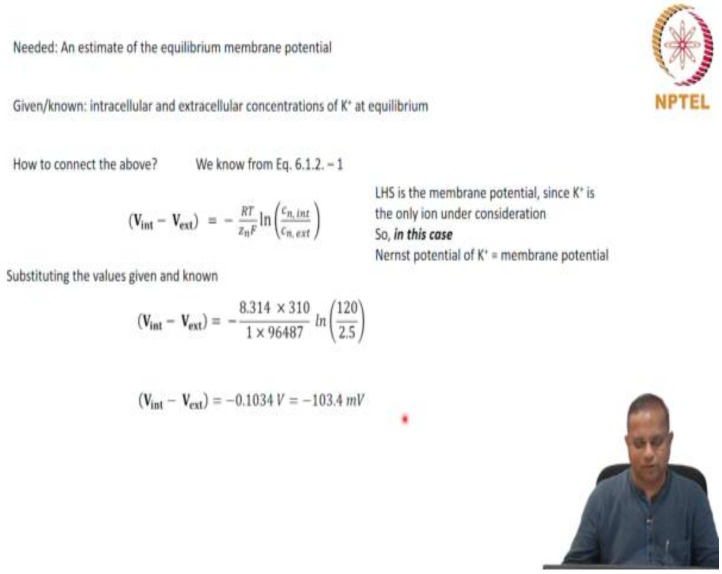

Needed: An estimate of the equilibrium membrane potential

Given/known: intracellular and extracellular concentrations of K^+ at equilibrium

How to connect the above? We know from Eq. 6.1.2. – 1

$$(\mathbf{V}_{\text{int}} - \mathbf{V}_{\text{ext}}) = -\frac{RT}{z_n F}\ln\left(\frac{c_{n,int}}{c_{n,ext}}\right)$$

LHS is the membrane potential, since K^+ is the only ion under consideration

So, ***in this case***

Nernst potential of K^+ = membrane potential

Substituting the values given and known

$$(\mathbf{V}_{\text{int}} - \mathbf{V}_{\text{ext}}) = -\frac{8.314 \times 310}{1 \times 96487}\, ln\left(\frac{120}{2.5}\right)$$

$$(\mathbf{V}_{\text{int}} - \mathbf{V}_{\text{ext}}) = -0.1034\, V = -103.4\, mV$$

So, what is needed is an estimate of the equilibrium membrane potential and what is given are known the intracellular and extracellular concentrations of potassium at equilibrium. So, how do you connect the known to the needed? We know from equation 6.1.2 - 1 or Nernst equation that is, it relates to the equilibrium membrane potential to the concentrations. So, this is the equation that relates that, so, as long as we find all the terms here, we would have whatever we need.

The left hand side is the membrane potential potassium is the only ion under consideration and therefore, the Nernst potential of potassium is the membrane potential. In rare case, we are looking only at 1 ion to understand it better. So, Nernst potential of potassium equals the membrane potential in this case this is the Nernst potential by the way. And if we substitute the given values, we get intracellular potential electrical potential minus extracellular potential R is 8.314.

$$(\mathbf{V}_{\text{int}} - \mathbf{V}_{\text{ext}}) = -\frac{RT}{z_n F}\ln\left(\frac{c_{n,\text{int}}}{c_{n,\text{ext}}}\right)$$

where the LHS gives the membrane potential.

Substituting the values given and known, we get

$$(\mathbf{V}_{\text{int}} - \mathbf{V}_{\text{ext}}) = -\frac{8.314\times 310}{1\times 96487}\ln\left(\frac{120}{2.5}\right)$$

$$(\mathbf{V}_{\text{int}} - \mathbf{V}_{\text{ext}}) = -\,0.1034\text{ V} = -\,103.4\text{ mV}$$

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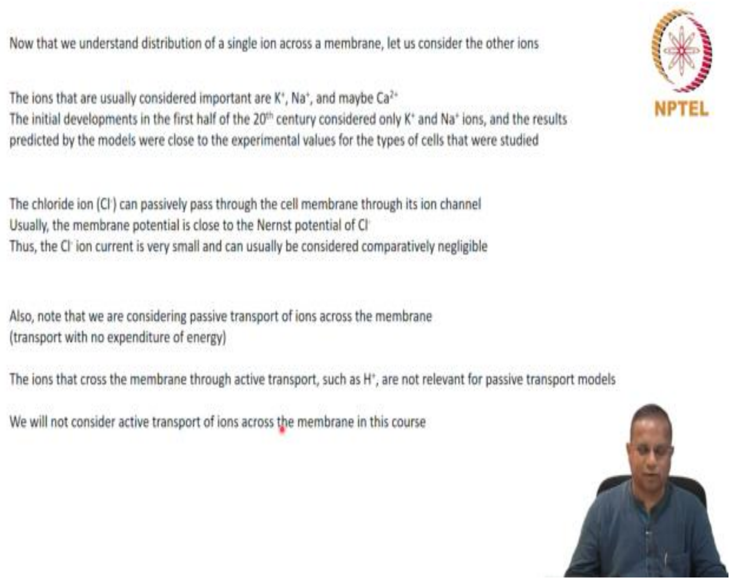

Now that we understand distribution of a single ion across a membrane, let us consider the other ions

The ions that are usually considered important are K^+, Na^+, and maybe Ca^{2+}
The initial developments in the first half of the 20th century considered only K^+ and Na^+ ions, and the results predicted by the models were close to the experimental values for the types of cells that were studied

The chloride ion (Cl^-) can passively pass through the cell membrane through its ion channel
Usually, the membrane potential is close to the Nernst potential of Cl^-
Thus, the Cl^- ion current is very small and can usually be considered comparatively negligible

Also, note that we are considering passive transport of ions across the membrane
(transport with no expenditure of energy)

The ions that cross the membrane through active transport, such as H^+, are not relevant for passive transport models

We will not consider active transport of ions across the membrane in this course

So, this is a typical value not a typical value, but if you consider 1 ion it is a typical value especially potassium. Now that we understand the distribution of a single ion across the membrane, let us consider the other ions also. We have time we do and I do not think we are too tired. So, let us consider the other ions also. The ions that are usually considered important are potassium, sodium, maybe calcium chloride under extreme cases, there are reasons for each one of these.

In fact, most of the initial development in this field of neuro physiology happened only with potassium and sodium, and then calcium came in under certain circumstances, chloride is rarely used. And beyond this nothing else is used in normally speaking an undergraduate do not even go beyond these. So the initial developments in the first half of the 20th century consider only potassium and sodium ions.

And the results predicted by the models were close to the experimental values for the type of cells that were studied. That is the reason this is this is good enough for a model. The chloride ion can pass can passively pass through the cell membrane through its ion channel, of course, and usually the membrane potential is close to the Nernst potential of chloride when it is close to the Nernst potential of chloride, the movement of chloride ions.

Then there is not going to be no net movement of chloride ions. That is the reason why chloride is not considered too important it is considered at times, but not usually, the chloride ion current is very small and thus can be usually considered to be comparatively negligible. Also note that we are considering only passive transport of ions across the membrane. These models that we are looking at are developing sort of, they have already been developed.

We are covering in this course considering in this course, discussing in this course, these are all for passive transport of ions that is transport with no expenditure of energy. The ions that cross the membrane through active transport such as the hydrogen ion are not relevant for passive transport models, they cannot be explained by passive transport models because just not in the scope of things itself.

We will not consider the active transport of ions across the membrane in this course, of course, it is very important, only thing is that for our purpose, which is transport and so on so forth. We are not going to get into the complications of the active transport. So, if needed of course as a whole body huge body of information on this you can go and read up we will not consider active transport we will limit ourselves to passive transport.

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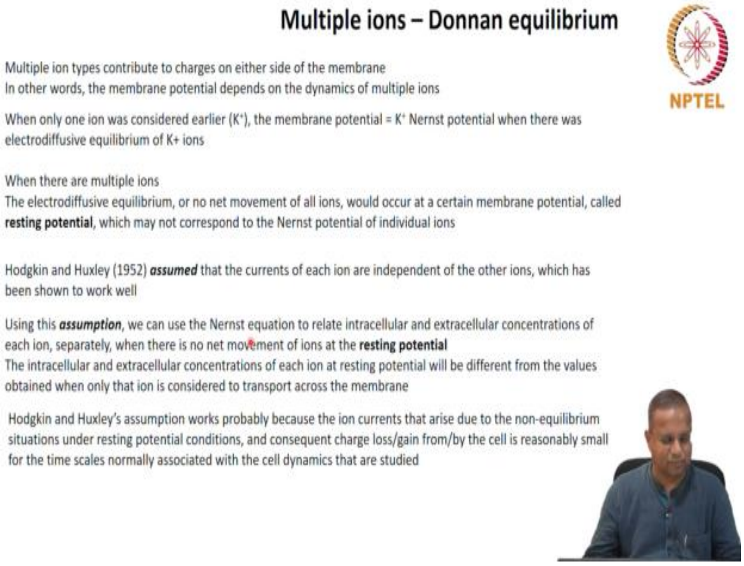

Multiple ions – Donnan equilibrium

Multiple ion types contribute to charges on either side of the membrane
In other words, the membrane potential depends on the dynamics of multiple ions

When only one ion was considered earlier (K^+), the membrane potential = K^+ Nernst potential when there was electrodiffusive equilibrium of K+ ions

When there are multiple ions
The electrodiffusive equilibrium, or no net movement of all ions, would occur at a certain membrane potential, called **resting potential**, which may not correspond to the Nernst potential of individual ions

Hodgkin and Huxley (1952) ***assumed*** that the currents of each ion are independent of the other ions, which has been shown to work well

Using this ***assumption***, we can use the Nernst equation to relate intracellular and extracellular concentrations of each ion, separately, when there is no net movement of ions at the **resting potential**
The intracellular and extracellular concentrations of each ion at resting potential will be different from the values obtained when only that ion is considered to transport across the membrane

Hodgkin and Huxley's assumption works probably because the ion currents that arise due to the non-equilibrium situations under resting potential conditions, and consequent charge loss/gain from/by the cell is reasonably small for the time scales normally associated with the cell dynamics that are studied

Now, let us consider multiple ions and when the equilibrium occurs we look at it a certain way with certain assumptions which turned out to be valid and such an equilibrium is called Donnan equilibrium after the person who is known for it. So, this is a typical situation with multiple ions or at least sodium, potassium, calcium. Multiple ion types contribute to charges on either side of the membrane we all know this in other words the membrane potential depends on the dynamics of multiple ions.

When only 1 ion was considered, that is potassium, the membrane potential was the potassium Nernst potential, we saw that when there was electro diffusive equilibrium of potassium ions, so that itself was good enough for us to predict and that we said that is only for an understanding when there are multiple ions, which is usually the case closer to real, I mean, it is reality, the electro diffusive equilibrium or no net movement of all ions.

They could be individual ions moving only thing is that if you take the sum of ions going to the side, or the rate at which ions move to the side, equals the rate at which is moved to this side, both in terms of charge and the numbers and so on. So I will put a this is essentially charged movement that we are looking at, so at the electro diffusive equilibrium or no net movement of all ions would occur at a certain membrane potential called the resting potential which, may not correspond to the Nernst potential of energy levels.

So, Nernst potential means that for that particular ion, the forces cancel out, so there is no net movement whereas now there are multiple ions that are contributing to the membrane potential. So, that may not equal the Nernst potential of any 1 ion. So, they are at some potential membrane potential, there is going to be no net movement of any ion across the surface. There will be individual movements, but there is no net movement.

Hodgkin and Huxley in 1952 for a totally different purpose they assumed that the currents of each ion are independent of the other ions and this assumption worked very well. So this was assumed that the currents of each ion are independent of the other ions, which means the current of sodium does not interfere with the current of potassium that in turn does not interfere with the current of calcium that does not interfere the current of chloride is what they assumed.

There is no strong basis for this that is an assumption, but that assumption was a very turned out to be a very good assumption. So, with this assumption, you could get a nice handle on the treatment or the understanding of this. Using this assumption, we can use the Nernst equation to relate the intracellular and extracellular concentrations of each ion separately when there is no net movement of ions at the resting potential.

Because each ion is independent Nernst potential for the Nernst equation for each ion must be added separately. So that would take care of those things. Let us go for then the significance of this will become clearer the intracellular and extracellular concentrations of each ion at resting potential will be different from the values obtained when only 1 of that ion or only when only that ion is considered for transport across the membrane.

Let me read this again the intracellular and extracellular concentrations of each ion at resting potential will of course be different from the values obtained and only that ion is considered to transport or move across the membrane and Hodgkin and Huxley assumption works probably because the ion currents that arise due to non equilibrium situations and the resting potential conditions.

And consequent charge loss or gain from or by the cell is reasonably small for the time scales normally associated with the cell dynamics that are studied I will leave you the sentence with you, when you get to a certain comfort level in understanding, you can go back to this sentence and try to understand why this could be happening? You had just about getting comfortable so I do not want to confuse you, load you further with this also. So I am not going to take too much time to explain the reason why this works it works.

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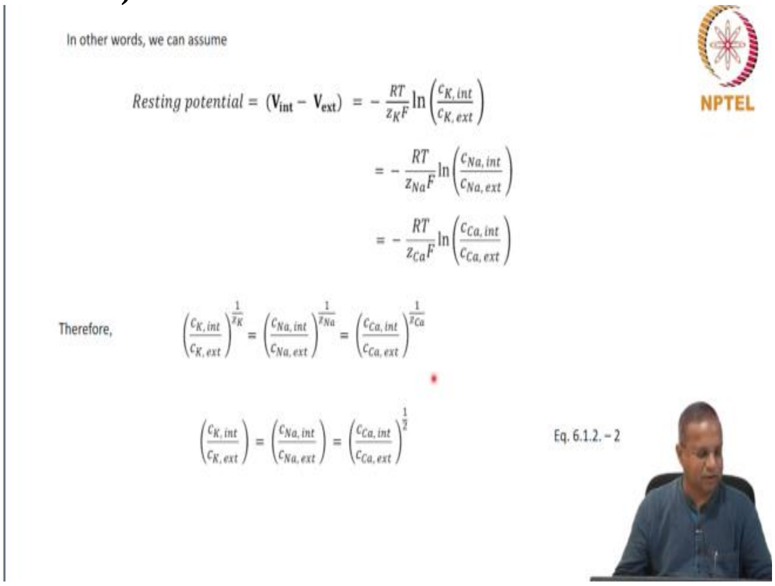

In other words, we can assume

$$\text{Resting potential} = (\mathbf{V_{int}} - \mathbf{V_{ext}}) = -\frac{RT}{z_K F}\ln\left(\frac{c_{K,int}}{c_{K,ext}}\right)$$

$$= -\frac{RT}{z_{Na} F}\ln\left(\frac{c_{Na,int}}{c_{Na,ext}}\right)$$

$$= -\frac{RT}{z_{Ca} F}\ln\left(\frac{c_{Ca,int}}{c_{Ca,ext}}\right)$$

Therefore,

$$\left(\frac{c_{K,int}}{c_{K,ext}}\right)^{\frac{1}{z_K}} = \left(\frac{c_{Na,int}}{c_{Na,ext}}\right)^{\frac{1}{z_{Na}}} = \left(\frac{c_{Ca,int}}{c_{Ca,ext}}\right)^{\frac{1}{z_{Ca}}}$$

$$\left(\frac{c_{K,int}}{c_{K,ext}}\right) = \left(\frac{c_{Na,int}}{c_{Na,ext}}\right) = \left(\frac{c_{Ca,int}}{c_{Ca,ext}}\right)^{\frac{1}{2}}$$

Eq. 6.1.2. – 2

$(V_{int} - V_{ext}) = - RT/z_K F \ln(c_{K,int} / c_{K,ext}) = - RT/z_{Na} F \ln(c_{Na,int} / c_{Na,ext}) = -RT/z_{Ca} F \ln(c_{Ca,int} / c_{Ca,ext})$

Because each ion is independent we can write the Nernst potential for each ion separately but whatever is intracellular minus extracellular of voltage is the same situation, whatever you consider that is, for that condition, we are writing these equations, so the left hand side would be the same, which again equals minus RT / z_{Ca} F ln of intracellular calcium concentration divided by the extracellular calcium concentration.

Therefore, we could equate all these left hand side as same therefore, we could equate all these. If you do that, you know, if you are going to equate this, then A ln B is ln B^A. And therefore, this goes to the index here, it gets raised to the power here, raise the power here raised the power here, and then the augments can be equated because they are all natural logs.

If you equate the augments, $c_{K,int}$ / $c_{K,ext}$, raised to the power of (1 / z_K). RT / F is going to cancel throughout equals intracellular sodium concentration divided by the extracellular sodium concentration raised to the power of (1/z_{Na}) equals the intracellular calcium concentration divided by the extracellular calcium concentration raised to the power of 1 / z_{Ca}, this is how we got it.

$$\left(\frac{c_{\mathrm{K,int}}}{c_{\mathrm{K,ext}}}\right)^{\frac{1}{z_{\mathrm{K}}}} = \left(\frac{c_{\mathrm{Na,int}}}{c_{\mathrm{Na,ext}}}\right)^{\frac{1}{z_{\mathrm{Na}}}} = \left(\frac{c_{\mathrm{Ca,int}}}{c_{\mathrm{Ca,ext}}}\right)^{\frac{1}{z_{\mathrm{Ca}}}}$$

or

$$\left(\frac{c_{\mathrm{K,int}}}{c_{\mathrm{K,ext}}}\right) = \left(\frac{c_{\mathrm{Na,int}}}{c_{\mathrm{Na,ext}}}\right) = \left(\frac{c_{\mathrm{Ca,int}}}{c_{\mathrm{Ca,ext}}}\right)^{\frac{1}{2}} \qquad (6.1.2\text{-}2)$$

If chloride had been considered, the exponent for the ratio of intracellular to extracellular chloride concentrations would have been – 1.

And this is the condition for Donnan equilibrium, which arose out of the application of the approximation by Hodgkin and Huxley that the fluxes of ions are independent of each other across a membrane under conditions of equilibrium. I think we will stop here in this class, where we looked at Donnan equilibrium and continue in the next class. See you.