Introduction to Neurobiology

BIOL 3833

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Module 2: Ion Gradients

Module 2: Ion gradients and equilibrium potentials.

Differential distribution of ions determines the membrane voltage

      As you know from previous coursework, under physiological conditions neurons maintain an uneven distribution of various ions across the cell membrane. More specifically, sodium concentrations are much higher in the extracellular space while potassium concentrations are much higher in the intracellular fluid. These concentration gradients give rise to forces that tend to drive sodium into the cell and potassium out of the cell.

      It is important to remember that the forces associated with differences in ion concentration interact with the electrical gradients created by differences in the distribution of positive and negative ions across the membrane. For example, the intracellular space is generally negative relative to the extracellular space. This would tend to attract positively charged ions like K^+ into the cell. On the other hand, the high concentration of K^+ within the cell tends to repel K^+ out of the cell. The state where the effects of the concentration gradient are balanced by the electrical gradient is known as the equilibrium potential for that ion (E_{ion}). When the membrane potential is at the equilibrium potential for that ion, there will be no net movement of that ion into or out of the cell. On the other hand, when the membrane potential deviates from the equilibrium potential, the diffusion and electromotive forces are out of balance, and the net result is a force that tends to move ions into or out of the cell depending on whether the membrane potential is above or below the equilibrium potential.

      The Nernst equation is used to calculate the equilibrium potential for any given ion species, as long as you know concentrations of that ion outside (o) of the cell and inside (i) the cell:

$$E_x = \frac{RT}{z_x F} \, ln \frac{[X]_o}{[X]_i}$$

Here E_x is the reversal potential for ion x, R = the gas constant, T = absolute temperature (in Kelvin), and F is Faraday's constant. The term z_x is the ionic charge of the ion, e.g., -1 for Chloride, +1 for potassium, +2 for calcium, etc. Because the only variable in the term RT/F is temperature, it is possible to simplify this ratio to a single value if we know the temperature. For simplicity's sake, we will assume for this class a physiological temperature of 37 °C, giving us a value of 26.73 for RT/F.

      The internal and external ionic concentrations can be estimated in most physiological systems. In the case of lab experiments, we can measure these values quite accurately because we control the concentrations of all ions in the extracellular and intracellular domains. The extracellular saline determines the extracellular concentrations, and the internal solution controls the intracellular concentrations of all ions. The composition of typical internal and external solutions is given in the following table:

Internal (Pipette) solution, in mM		ACSF (external saline), in mM:	
Potassium gluconate	130	NaCl	130
Sodium phosphocreatine	20	Glucose	20
EGTA	0.5	KCl	3
HEPES	10	NaHCO$_3$ (pH buffer)	10
MgCl$_2$	2	NaH$_2$PO$_4$	2
MgATP	2	MgCl$_2$	1
NaGTP	2	CaCl$_2$	2

While the Nernst equation allows us to calculate the equilibrium potential for each individual ion, the membrane potential actually is determined by a number of different ions. Moreover, at any given time, the membrane has different permeabilities to each type of ion. The Goldman-Hodgkin-Katz (GHK) equation allows us to predict the membrane potential given the concentration gradients and relative permeabilities for each type of ion involved:

$$V_m = \frac{RT}{F} \ln \frac{P_K[\text{K}^+]_\text{o} + P_{Na}[\text{Na}^+]_\text{o} + P_{Cl}[\text{Cl}^-]_\text{i}}{P_K[\text{K}^+]_\text{i} + P_{Na}[\text{Na}^+]_\text{i} + P_{Cl}[\text{Cl}^-]_\text{o}}$$

Note the similarities of this equation to the Nernst equation. The GHK equation is essentially the Nernst equation extended to include multiple ion species, with the addition of a term representing the relative permeabilities of those ions (P_{ion}). Again, RT/F can be simplified to 26.73 at physiological temperature.

We can consider some boundary conditions to get a feel for how equilibrium potentials and ion permeability contribute to membrane potential. For example, if the membrane is permeable only to K$^+$, that is $P_K = 1$ and both P_{Na} and P_{Cl} are equal to zero, then the membrane potential would move to E_K. By the same logic, if the membrane was only permeable to Na$^+$ then the membrane potential would be equal to E_{Na}. If the membrane is permeable to all three ions, then the membrane potential will lie somewhere between the equilibrium potentials for all three ions.

An important generalization from this discussion is that ***whenever the membrane becomes more permeable to a particular ion, the membrane potential will move toward the equilibrium potential for that ion***. More specifically, open sodium channels will pull the membrane toward E_{Na}, while open potassium channels will pull the membrane toward E_K.

<u>The driving force on any particular ion species is equal to the difference between membrane voltage and the equilibrium potential for that ion</u>

If we begin with the simple case where the membrane potential is equal to the equilibrium potential for potassium ($V_M = E_K$), we can ask what would happen if

potassium channels opened in this situation. The answer is: nothing.   Because the membrane potential is already at E_K, there would be no net movement of K^+ across the membrane. On the other hand, if the membrane potential is different from E_K, there would be a force driving potassium through any open potassium channels.

To generalize: when the membrane potential is at the equilibrium potential for an ion, there will be no net movement of that ion across the membrane, regardless of how many ion channels are open. In contrast, when the membrane potential is very different from the equilibrium potential for an ion, there is a strong driving force on that ion to cross the membrane through available ion channels. We can quantify this relationship as a variation on Ohm's Law:

$$I_{ion} = (V_m - E_{ion}) * G_{ion}$$

We are left now to examine what factors control the conductance for each particular ion species. It should be no surprise that it is the opening and closing of ion channels that control ion conductance.