

Lecture 1: Membrane Potential, Nernst & Goldman Equations

I. Membrane Potential

A. In a typical animal cell, potassium, chloride & sodium are in unequal distribution

1. Potassium is higher inside than outside; sodium & chloride are higher outside than inside

B. The unequal distribution of potassium & chloride can be explained using a model called the Donnan equilibrium (the following is somewhat simplified from a rigorous examination of the Donnan equilibrium)

1. The distribution of ions across the membrane depends not only on concentration gradients (& diffusion), but also on electrical gradients

a) *An electrical gradient of sufficient magnitude & polarity can oppose the movement of a charged molecule down its concentration gradient*

2. If we start out with a chamber divided into two compartments by a semipermeable membrane (the left compartment will be analogous to the inside of the cell)

a) *The membrane is permeable to K^+ , but not to A^-*

b) *If we place equal concentrations of KA on both sides of the membrane there will be not net movement of K^+*

3. **Compartment I has a higher concentration of K^+ than does Compartment II**

a) *K^+ moves down its concentration gradient into Compartment II*

(1) However, since A^- can't cross the membrane, it is left behind

(2) We have a net movement of positive charge into Compartment II – this produces a voltage between the two compartments

b) *You might think that K^+ will eventually be equally distributed between the chambers – WRONG!!!*

(1) The negative charges of the anions attract the positive charges of the potassium ions

(a) This attraction produces an electrochemical force (electromotive force [emf]; emf is the same as voltage) that tries to pull potassium ions back into Compartment I from Compartment II

c) Eventually the mechanical force trying to move potassium down its chemical gradient is balanced by the emf trying to move potassium back into Compartment I

(1) At this point of equilibrium we end up with a higher concentration of potassium in Compartment I than II

(2) Compartment I is also negative relative to compartment II

(a) This voltage difference is known as the equilibrium potential – at this potential, there will be no net movement of the ion even though there is a concentration gradient

(b) An important corollary – if the voltage across the membrane is perturbed from the equilibrium potential, current (ions) will flow in an attempt to reestablish the equilibrium potential

II. The Nernst Equation

- A. **The unequal distribution of ions described by the Donnan equilibrium also gives rise to an electrical potential**
- B. **How does Donnan equilibrium cause electrical potential?**
- C. **When K^+ is unequally distributed across the membrane, there is a force which causes the movement of K^+ down its concentration gradient - a chemical force**
- D. **Since opposite charges attract, there is an electrical force trying to pull the K^+ back into the cell**
- E. **At equilibrium there is no net movement of K^+**
 - 1. **Therefore the chemical force trying to move the K^+ out of the cell is balanced by the electrical force trying to move the K^+ into the cell**
- F. **There are equations that describe both the chemical work & the electrical work (mostly derived from thermodynamics)**
 - 1. **If you substitute these equations in the simple equation at equilibrium:**

Chemical work = Electrical work, & then invoke the mysteries of algebra to rearrange the equation you get:

$$E = 2.3 \frac{RT}{zF} \log \frac{[K^+]_{OUT}}{[K^+]_{INSIDE}}$$

G. Where:

1. **R = the gas constant (a measure of the energy contained in a substance [per Kelvin per mole])**
2. **T = Absolute temperature in degrees Kelvin**
3. **z = the valance of the ion (give examples)**
4. **F = Faraday's constant (a measure of electrical charge per mole of substance = 96500 coulombs)**
5. **Concentrations are expressed in moles/liter**
6. **The 2.3 is a fudge factor for using base 10 log rather than natural log**

H. *This is the Nernst Equation - the most important equation in neurobiology - it describes the electrical potential produced by the unequal distribution of ions across a membrane*

1. **Although we used K^+ , the Nernst equation can be used to describe the electrical potential produced by any other membrane permeable ion**

I. *Example using K^+*

1. **Since 2.3 (RT/zF) are all constants at a given temperature**
 - a) ***For an ion with a valance of 1 at room temp., this term = 58 mV and the equation will produce results in mV***

2. **The Nernst equation for potassium now becomes:**

$$E_K = 58 \log \frac{[K^+]_{OUT}}{[K^+]_{INSIDE}} \text{ mV}$$

3. **For the case of the squid giant axon (explain importance):**

$$\begin{aligned} a) \quad E_K &= 58 \log \frac{20mM}{400mM} \text{ mV} \\ &= -75.4 \text{ mV} \end{aligned}$$

J. *E* is the potential at which there is no net flux of the ion in question (in this case potassium)

1. Even if the membrane poses no resistance to movement of that ionic species, there is no net flux if the potential across the membrane is equal to this value

K. *This potential is called the equilibrium potential = E_K*

L. *If a membrane is permeable to that particular ion, the potential across the membrane will tend to go to the equilibrium potential*

1. An important corollary is that if the membrane potential is moved from the equilibrium potential, current will flow and the membrane potential will return to the equilibrium potential

M. *Unlike the assumption we made for the Donnan equilibrium, the cell membrane is slightly permeable to Na^+ ; so let's determine the sodium equilibrium potential*

$$E_{Na} = 58 \log \frac{[Na^+]_{OUT}}{[Na^+]_{INSIDE}} \text{ mV}$$

N. *Again for the squid giant axon:*

$$\begin{aligned} E_{Na} &= 58 \log \frac{460 \text{ mM}}{50 \text{ mM}} \text{ mV} \\ &= 58 \log (9.2) \text{ mV} \\ &= 58 * 0.96 \text{ mV} \\ &= +55.9 \text{ mV} \end{aligned}$$

O. *+56 mV = sodium equilibrium potential*

III. The overall membrane potential of a cell is dependent on all of the equilibrium potentials for permeant ions and their relative permeability

A. *The equation that describes this is a modification of the Nernst equation called the Goldman Hodgkin Katz constant-field equation (also known as the GHK or Goldman equation):*

$$E_m = 58 \log \frac{P_K [K^+]_{OUT} + P_{Na} [Na^+]_{OUT} + P_{Cl} [Cl^-]_{INSIDE}}{P_K [K^+]_{INSIDE} + P_{Na} [Na^+]_{INSIDE} + P_{Cl} [Cl^-]_{OUT}}$$

B. *Where:*

1. E_m = membrane potential
2. P = relative permeability

a) *Units of cm/sec*

C. Note chloride term is inverse of sodium and potassium

1. Due to chloride being negatively charged

D. If we ignore Cl and use $P_K = 1$ and $P_{Na} = 0.04$ (1/25)

1. Cl is near equilibrium and thus doesn't contribute to membrane potential very much

a) *Chloride is also passively distributed while Na^+ and K^+ are actively distributed via the sodium potassium pump*

- (1) Chloride concentrations will change depending on membrane potential, but Na^+ and K^+ do not

2. Can use permeability ratios rather than real values

E. A rearrangement of the GHK equation produces the chord conductance equation

$$V_m = \frac{(E_K \times g_K) + (E_{Na} \times g_{Na}) + (E_{Cl} \times g_{Cl})}{g_K + g_{Na} + g_{Cl}}$$