ELEC ENG 3BB3:
Cellular Bioelectricity

Notes for Lecture 4

Tuesday, January 14, 2014

Membrane structure:

- Excitable cells are surrounded by a *plasma membrane* consisting of a lipid bilayer.
- The passage of ions through the membrane is regulated by:

1. **Pumps and exchangers**
2. **Channels**

Membrane structure (cont.):

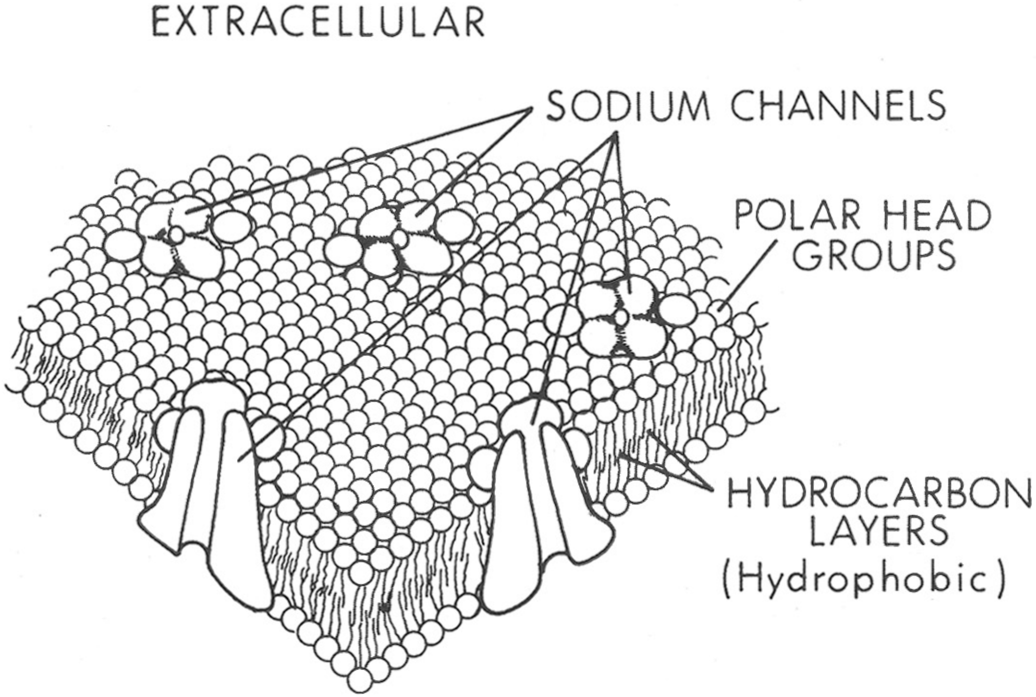

Figure 3.1. Schematic representation of the model of membrane structure showing sodium channel proteins embedded in the lipid bilayer matrix of the membrane. The channel density is unphysiologically high, for illustrative purposes. [Drawing based on W. A. Catterall et al., “Structure and modulation of voltage-gated sodium channels” in “Ion Channels in the Cardiovascular System,” P. M. Spooner and A. M. Brown, eds., Futura, Armonk, New York, 1994.

Pumps and exchangers:

- Pumps are active processes (i.e., they consume energy) that move ions against the concentration gradients.
- Exchangers use the concentration gradient of one ion to move another ion against its concentration gradient.
- The purpose of pumps and exchangers is to maintain the different intra- and extra-cellular ionic concentrations.
- The major ion transporters are: Na^+-K^+ pump, Na^+-Ca^{2+} exchanger, Ca^{2+} pump, Bicarbonate-Cl^i exchanger, Cl^i-Na^+-K^+ cotransporter.

Channels:

- Channels are passive processes that allow ions to pass through the membrane under the influence of concentration and electric potential gradients.
- Channels exhibit *selective permeability*, i.e., they only allow certain ions to pass through them.
- Ion channel *gates* regulate the permeability of channels, allowing control over the flow of particular ions.

Membrane capacitance:

- The lipid membrane itself has a specific resistance of 10^9 Ω¢cm^2, i.e., it is effectively an *insulator*.
- Consequently, charge can build up on each side of the membrane in regions where there are no channels or where channels are closed.
  Because of the thinness of the membrane, it acts as a *capacitor*, with a capacitance typically around
  $C_m = 0.9\ \mu F/cm^2$.

Ion flow through open channels:

- From the Nernst-Planck equation, the flow of the p^{th} ion will depend on both the concentration gradient of the p^{th} ion and an electric potential gradient.
- For an excitable cell, the unequal concentration of ions in the intra- versus extra-cellular spaces produces ion flow through any open ion channels.
- Ions will accumulate on the membrane because of its capacitance, producing an electrical field across and within the membrane that will in turn exert a force on all charged particles within ion channels.

Nernst equilibrium:

A *Nernst equilibrium* is achieved for a particular ion when the electric field force exactly counteracts the force of the concentration gradient for that ion, such that the net flow through an ion channel is zero:

$$\bar{J}_p = 0 = -D_p F Z_p \left[\nabla C_p + \frac{Z_p C_p F}{RT} \nabla \Phi \right], \quad (3.15)$$

and hence:

$$\nabla C_p = -\frac{Z_p C_p F}{RT} \nabla \Phi. \quad (3.16)$$

Nernst equilibrium (cont.):

Assuming that the concentration and electric potential gradients only act in the direction x, perpendicular to the membrane surface, this simplifies to:

$$\frac{\mathrm{d}C_p}{\mathrm{d}x} = -\frac{Z_p C_p F}{RT}\frac{\mathrm{d}\Phi}{\mathrm{d}x} \tag{3.17}$$

$$\Rightarrow \frac{\mathrm{d}C_p}{C_p} = -\frac{Z_p F}{RT}\mathrm{d}\Phi. \tag{3.18}$$

Nernst equilibrium (cont.):

Integrating across the membrane from the extracellular space e to the intracellular space i :

$$\int_e^i \frac{\mathrm{d}C_p}{C_p} = -\frac{Z_p F}{RT} \int_e^i \mathrm{d}\Phi \tag{3.19}$$

gives:

$$\ln\left(\frac{[C_p]_i}{[C_p]_e}\right) = -\frac{Z_p F}{RT} \left\{\Phi_i - \Phi_e\right\}, \tag{3.20}$$

where ln ´ $\log_e$.

Nernst potential:

Thus the potential difference across the membrane at equilibrium, referred to as the **Nernst potential**, is:

$$V_m^{eq} = \Phi_i - \Phi_e = \frac{-RT}{Z_p F} \ln\left(\frac{[C_p]_i}{[C_p]_e}\right), \quad (3.21)$$

where the transmembrane potential V_m is defined as the intracellular potential Φ_i minus the extracellular potential Φ_e.

Nernst potential (cont.):

In the case where the temperature is 20°C, the Nernst potential is:

$$V_m^{eq} = E_p = \frac{-25}{Z_p} \ln\left(\frac{[C_p]_i}{[C_p]_e}\right) \text{ mV}$$

$$= \frac{25}{Z_p} \ln\left(\frac{[C_p]_e}{[C_p]_i}\right) \text{ mV}, \qquad (3.22)$$

or using base 10 instead of the natural logarithm:

$$V_m^{eq} = E_p = \frac{58}{Z_p} \log_{10}\left(\frac{[C_p]_e}{[C_p]_i}\right) \text{ mV}. \quad (3.23)$$

Equilibrium potentials:

The Nernst potential for a particular ion is often referred to as the *equilibrium potential* and is given the symbol E_p.

For example, the equilibrium potentials for sodium and potassium ions are given the symbols E_{Na} and E_K, respectively.

The equilibrium potential is also sometimes referred to as the *reversal potential*, because at this potential the direction of the ionic current reverses from inwards to outwards, or vice versa.

Example equilibrium potentials:

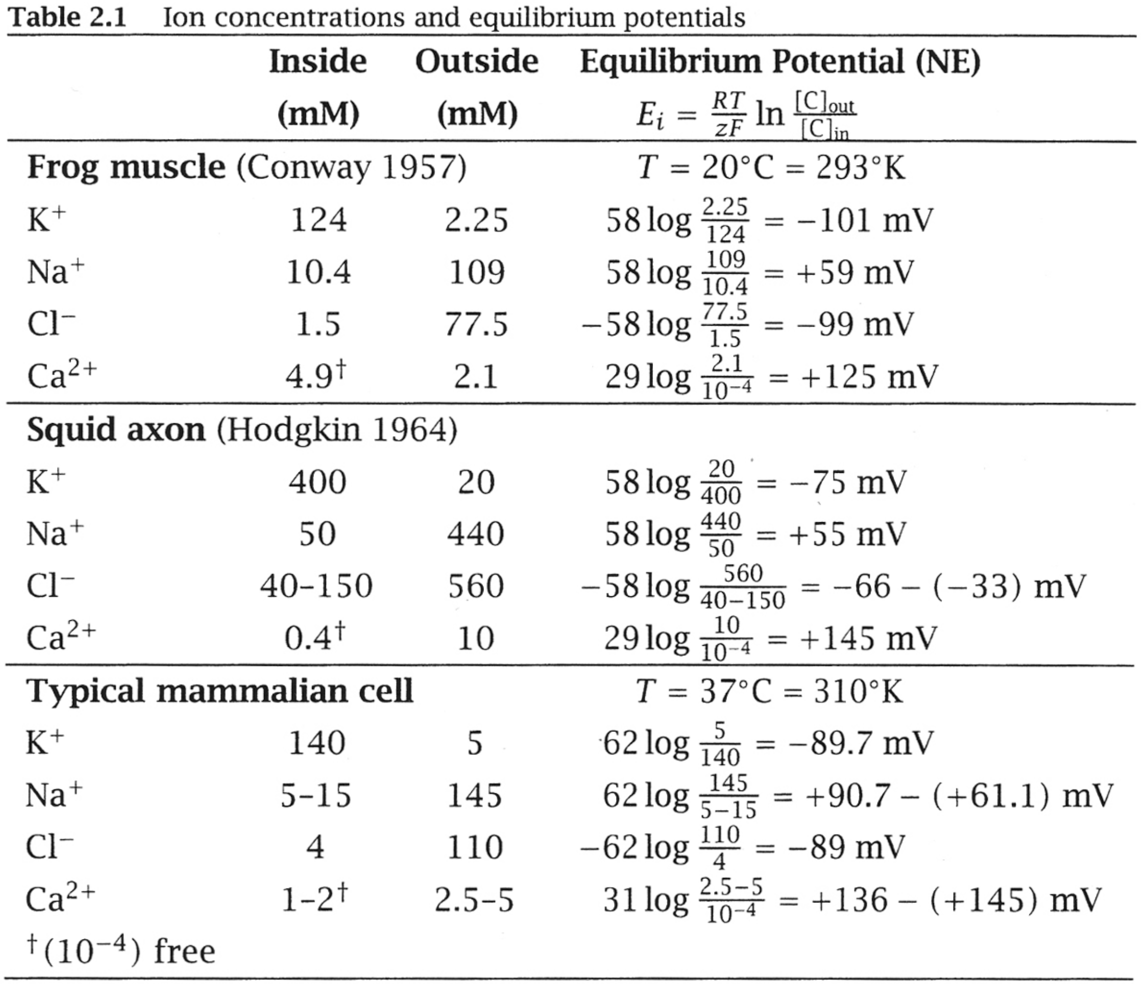

Table 2.1 Ion concentrations and equilibrium potentials

	Inside (mM)	**Outside** (mM)	**Equilibrium Potential (NE)** $E_i = \frac{RT}{zF} \ln \frac{[\mathrm{C}]_{\mathrm{out}}}{[\mathrm{C}]_{\mathrm{in}}}$
Frog muscle (Conway 1957)			$T = 20°\mathrm{C} = 293°\mathrm{K}$
K^+	124	2.25	$58 \log \frac{2.25}{124} = -101$ mV
Na^+	10.4	109	$58 \log \frac{109}{10.4} = +59$ mV
Cl^-	1.5	77.5	$-58 \log \frac{77.5}{1.5} = -99$ mV
Ca^{2+}	4.9†	2.1	$29 \log \frac{2.1}{10^{-4}} = +125$ mV
Squid axon (Hodgkin 1964)			
K^+	400	20	$58 \log \frac{20}{400} = -75$ mV
Na^+	50	440	$58 \log \frac{440}{50} = +55$ mV
Cl^-	40–150	560	$-58 \log \frac{560}{40-150} = -66 - (-33)$ mV
Ca^{2+}	0.4†	10	$29 \log \frac{10}{10^{-4}} = +145$ mV
Typical mammalian cell			$T = 37°\mathrm{C} = 310°\mathrm{K}$
K^+	140	5	$62 \log \frac{5}{140} = -89.7$ mV
Na^+	5–15	145	$62 \log \frac{145}{5-15} = +90.7 - (+61.1)$ mV
Cl^-	4	110	$-62 \log \frac{110}{4} = -89$ mV
Ca^{2+}	1–2†	2.5–5	$31 \log \frac{2.5-5}{10^{-4}} = +136 - (+145)$ mV

$^\dagger(10^{-4})$ free

(from Johnston and Wu)

Relative charge depletion and electroneutrality:

The Nernst equilibrium is achieved via movement of ions from the inside to the outside of the membrane, which might (i) deplete a particular ion and (ii) move the electrolyte away from a condition of *electroneutrality*.

However, for typical intra- and extra-cellular volumes found in excitable cells, movement of *less than 0.1%* of available ions is capable of charging up the membrane, i.e., changing the membrane potential by values on the order of 100 mV, and thus charge depletion and loss of electroneutrality are typically negligible.