Biophysics I (BPHS 4080)

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Website: http://www.yorku.ca/cberge/4080W2018.html

York University
Winter 2018
Lecture x

Reference/Acknowledgement:
- TF Weiss (Cellular Biophysics)
- D Freeman

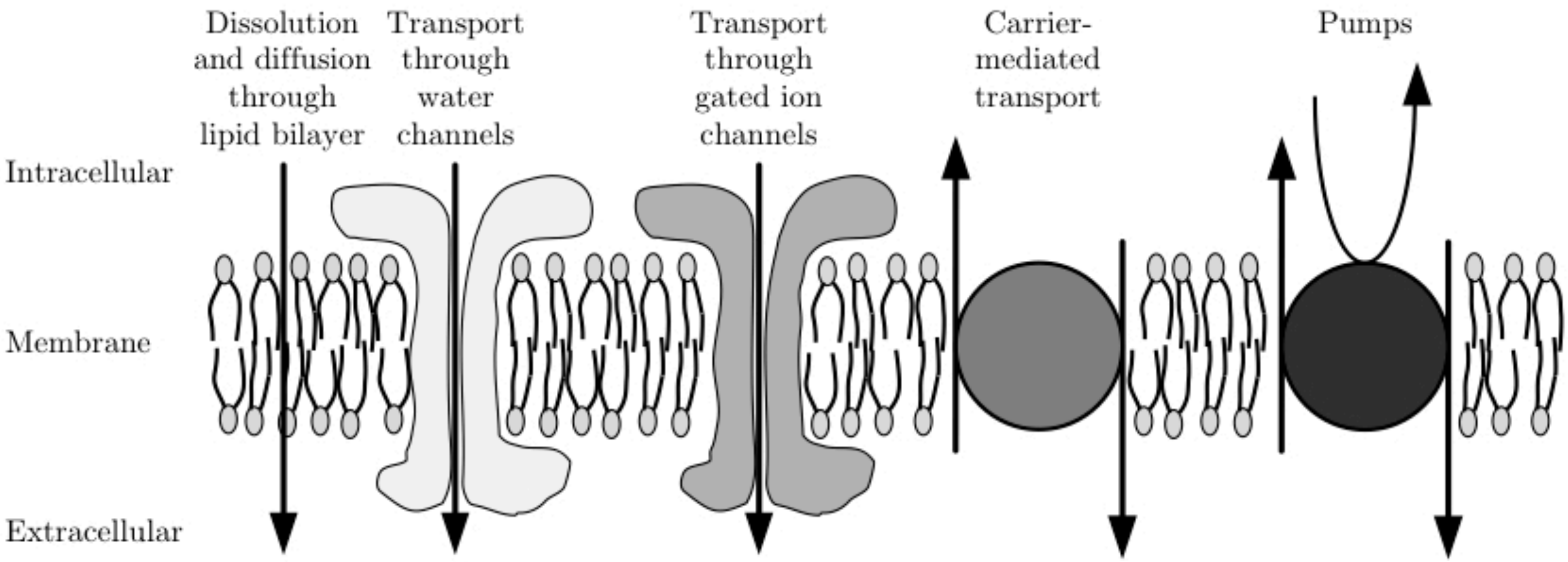
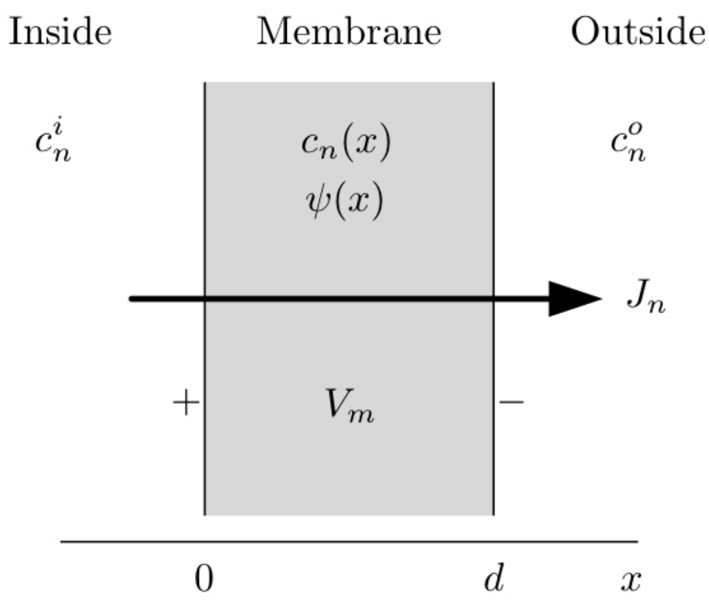

Dissolution and diffusion through lipid bilayer
Transport through water channels
Transport through gated ion channels
Carrier-mediated transport
Pumps
Intracellular
Membrane
Extracellular

Figure 2.19

Steady-State Electrodiffusion through Membranes



Steady-state

$$\rightarrow \quad \frac{\partial c_n(x,t)}{\partial t} = 0$$

$$\rightarrow \quad \frac{\partial J_n(x,t)}{\partial x} = 0$$

$$\rightarrow \quad J_n = \text{constant}$$

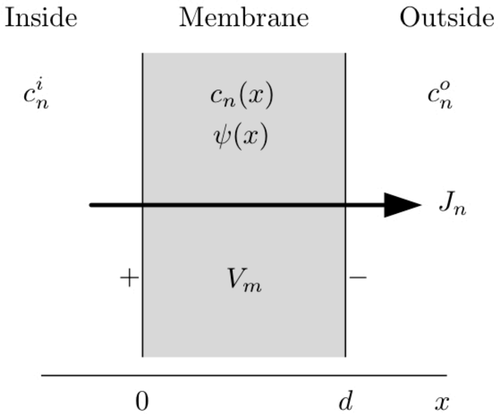
Electrolyte solutions $\rightarrow$ Electroneutrality

$$\text{if} \quad t >> \tau_r \quad \text{and} \quad x >> \Lambda_D \quad \text{then} \qquad \sum_n z_n F c_n(x,t) = 0$$

$$\frac{\partial^2 \psi(x,t)}{\partial x^2} = -\frac{1}{\epsilon} \sum_n z_n F c_n(x,t)$$

→ Simplifies Poisson's equation such that ψ is a linear function across the membrane

Steady-State Electrodiffusion through Membranes



Steady-state

$$\rightarrow \frac{\partial c_n(x,t)}{\partial t} = 0$$

$$\rightarrow \frac{\partial J_n(x,t)}{\partial x} = 0$$

$$\rightarrow J_n = \text{constant}$$

Mobility & Stokes-Einstein Relation

$$D_n = u_n RT$$

Rearrange Nernst-Plank Equation

$$J_n = -z_n F D_n \frac{dc_n(x)}{dx} - u_n z_n^2 F^2 c_n(x) \frac{d\psi(x)}{dx} = -u_n z_n^2 F^2 c_n(x) \left[\frac{D_n}{u_n z_n F c_n(x)} \frac{dc_n(x)}{dx} + \frac{d\psi(x)}{dx} \right]$$

Integrate across membrane

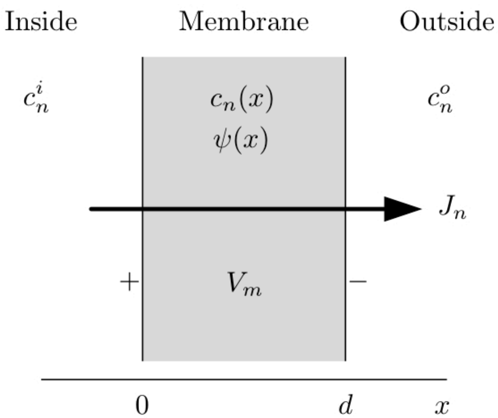
$$J_n \underbrace{\int_0^d \frac{dx}{u_n z_n^2 F^2 c_n(x)}}_{\frac{1}{G_n}} = -\int_0^d \frac{d}{dx} \left[\frac{RT}{z_n F} \ln c_n(x) + \psi(x) \right] dx$$

Solve/Rearrange/Rename

$$J_n \frac{1}{G_n} = -\overbrace{\frac{RT}{z_n F} \ln \frac{c_n(d)}{c_n(0)}}^{V_n} + \overbrace{\psi(0) - \psi(d)}^{V_m}$$

$$\rightarrow \boxed{J_n = G_n(V_m - V_n)}$$

Steady-State Electrodiffusion through Membranes



Steady-state

$$\rightarrow \frac{\partial c_n(x,t)}{\partial t} = 0$$

$$\rightarrow \frac{\partial J_n(x,t)}{\partial x} = 0$$

$$\rightarrow J_n = \text{constant}$$

$$J_n \frac{1}{G_n} = -\overbrace{\frac{RT}{z_n F} \ln \frac{c_n(d)}{c_n(0)}}^{V_n} + \overbrace{\psi(0) - \psi(d)}^{V_m}$$

$$J_n = G_n(V_m - V_n)$$

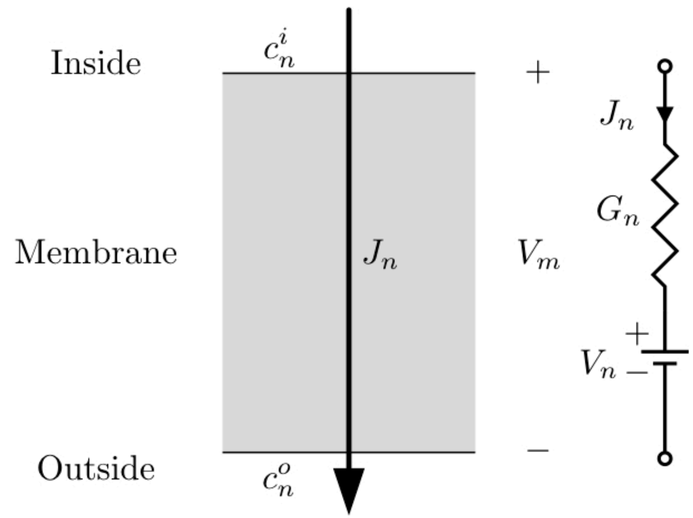
→ Like Ohm's law!

Nernst Equilibrium Potential

$$V_n = \frac{RT}{z_n F} \ln \frac{c_n(d)}{c_n(0)} = \frac{RT}{z_n F} \ln \frac{c_n^o}{c_n^i}$$

$$G_n = \frac{1}{\displaystyle\int_o^d \frac{dx}{u_n z_n^2 F^2 c_n(x)}} \geq 0$$

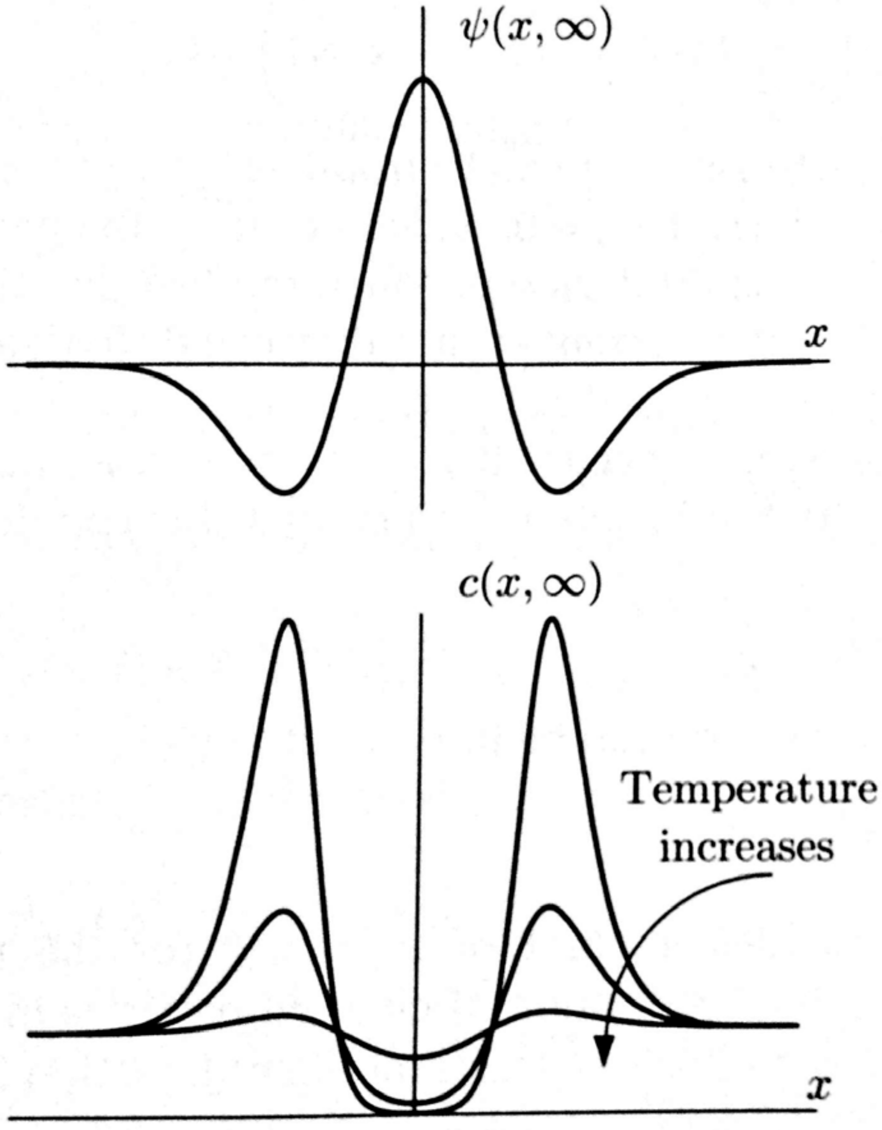
Model of Steady-State Electrodiffusion through Membranes



$$\text{Nernst Equilibrium Potential } V_n = \frac{RT}{z_n F} \ln \frac{c_n^o}{c_n^i}$$

$$\text{Electrical Conductivity } G_n = \frac{1}{\displaystyle\int_o^d \frac{dx}{u_n z_n^2 F^2 c_n(x)}} \geq 0$$

Mechanical analog for electrodiffusive equilibrium



Analog to gravitational potential energy
(no negative concentrations!)

$$\frac{\partial^2 \psi(x,t)}{\partial x^2} = -\frac{1}{\epsilon} \sum_n z_n F c_n(x,t)$$

Figure 7.6 The spatial distribution of electric potential and ion concentration at electrodiffusive equilibrium for different temperatures.

How is the Nernst potential generated?

Assumption: Single permeable ionic species (positively charged)

$c_1 < c_2$

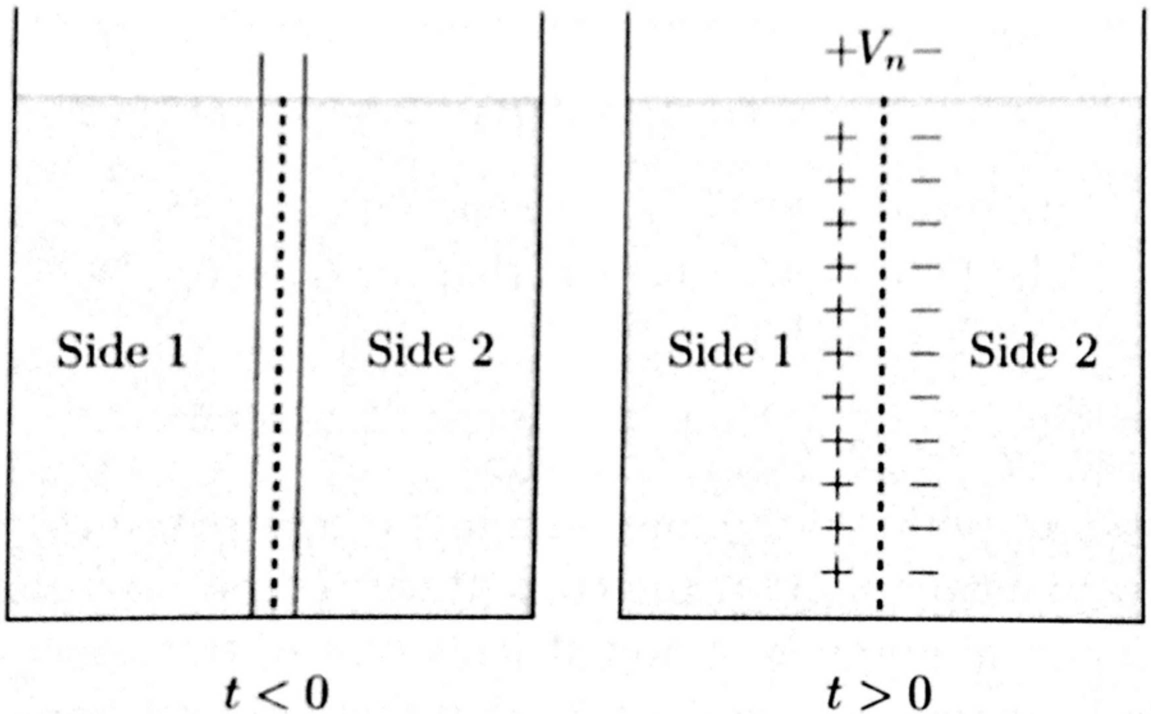


Figure 7.16 Illustration of the generation of the Nernst equilibrium potential. A bath is separated into two compartments by a membrane permeable only to ion n.

→ Note that the creation of a significant V_n need not require significant concentration changes

Resting Potential

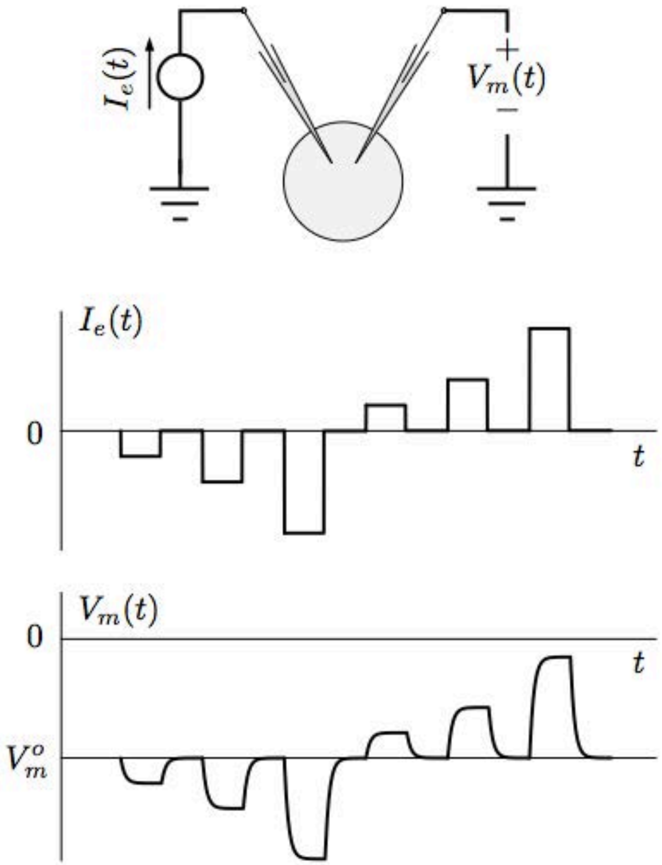


Figure 1.1

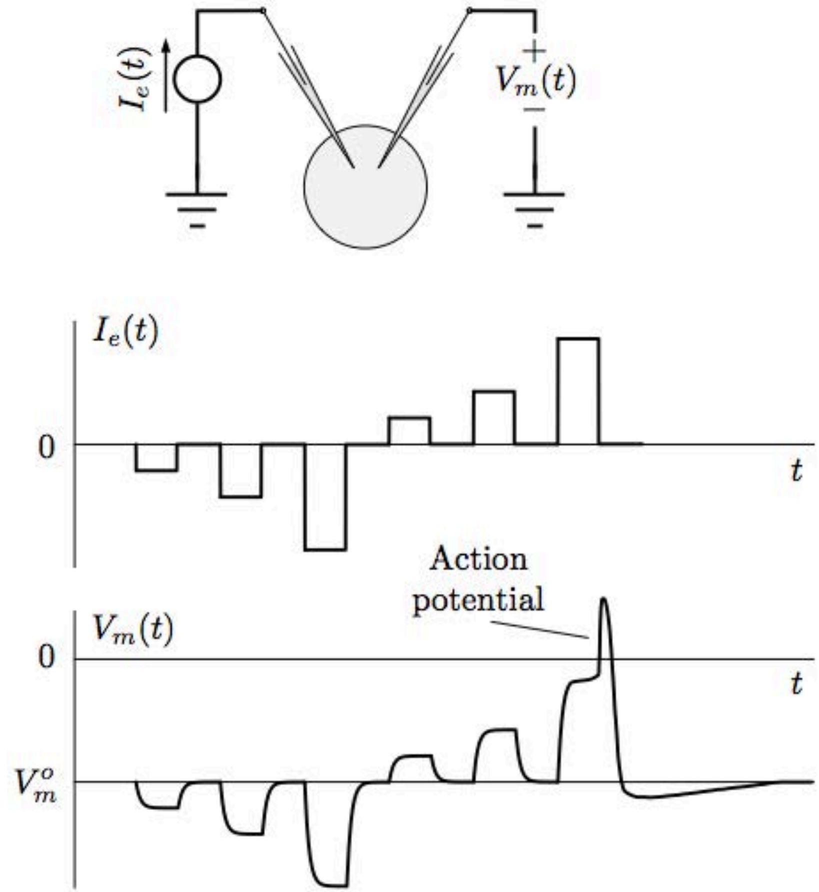


Figure 1.8

→ Independent of whether a cell "fires" an action potential or not, note that there is a baseline trans-membrane potential ("resting potential") V_m^o

Resting Potential

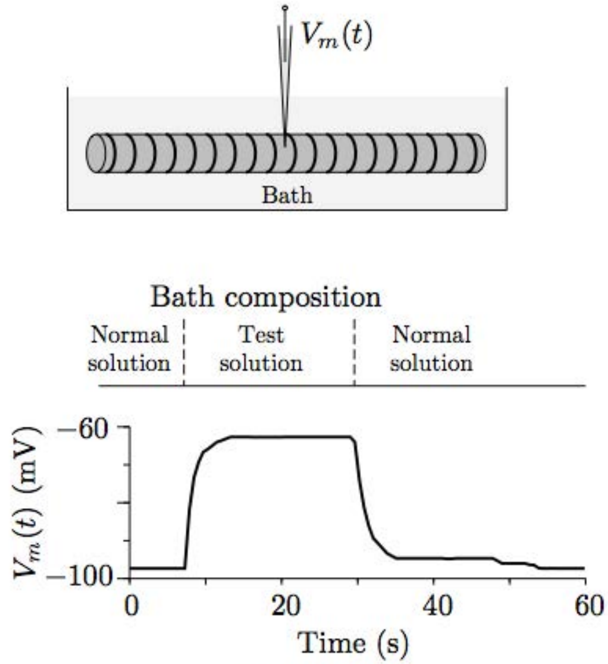


Figure 1.2

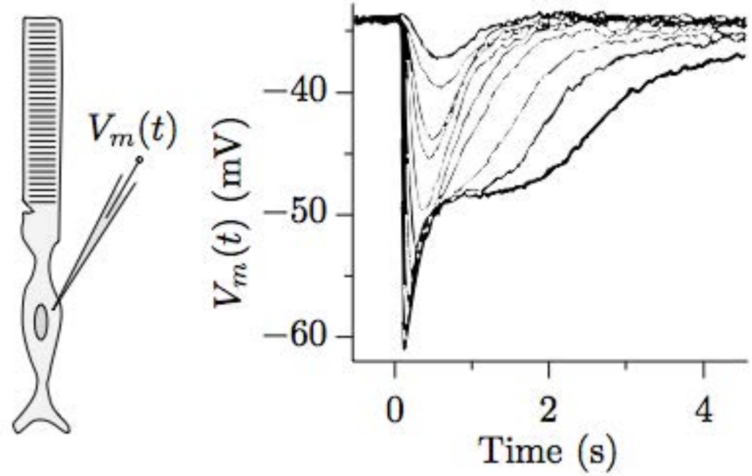


Figure 1.3

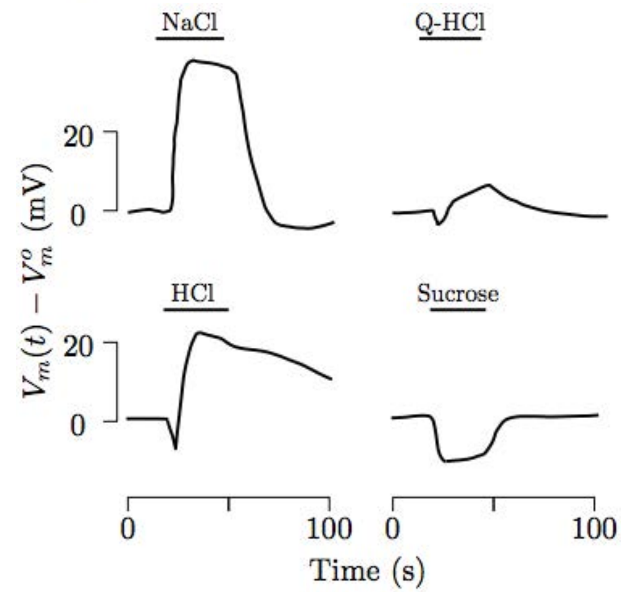


Figure 1.6

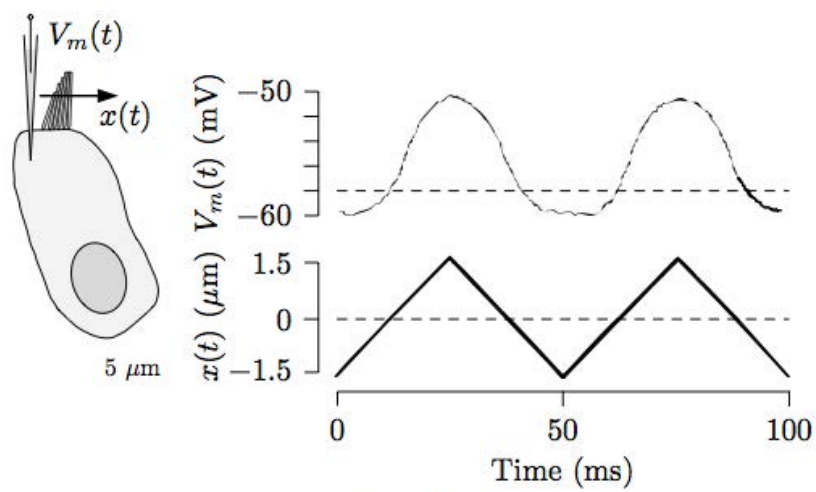


Figure 1.5

→ What is the basis for such a resting potential?

Resting Potential: Model considering only a *single permeant ion*

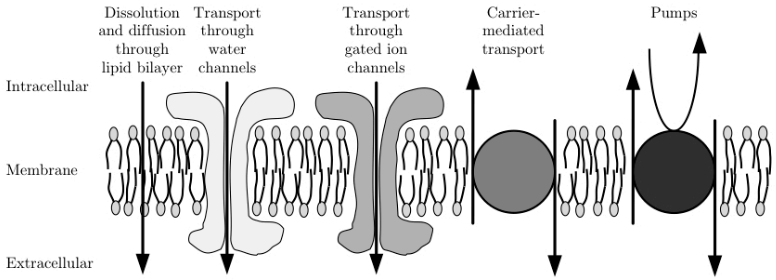


Figure 2.19

Emipirical observation:
Inside cell: high [K+], low [Na+]
Outside cell: low [K+], high [Na+]

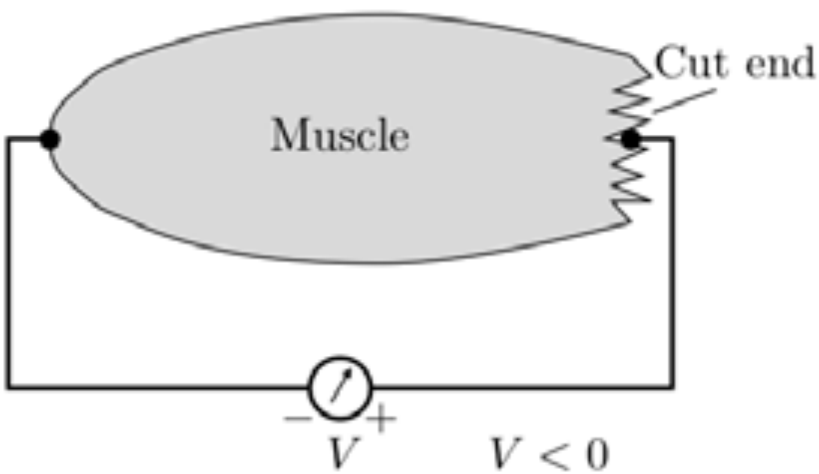


Figure 7.17

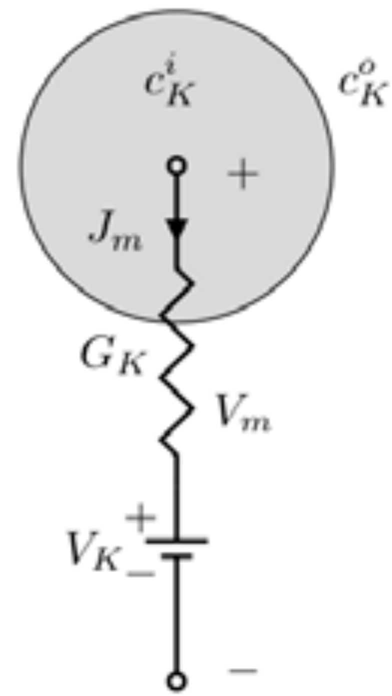


Figure 7.18

→ Bernstein's idea (1902) was that membrane was permeable to potassium only, thereby K^+ determined resting potential

<u>Resting Potential:</u> Model considering only a *single permeant ion*

Nernst Equilibrium Potential

$$V_n = \frac{RT}{z_n F} \ln \frac{c_n(d)}{c_n(0)} = \frac{RT}{z_n F} \ln \frac{c_n^o}{c_n^i}$$

$$G_n = \frac{1}{\int_o^d \frac{dx}{u_n z_n^2 F^2 c_n(x)}} \geq 0$$

Bernstein model:

$$V_m^o = V_K = \frac{RT}{F \log_{10} e} \log_{10} \left(\frac{c_K^o}{c_K^i} \right)$$

$$\frac{RT}{z_n F \log_{10} e}$$ ~ 59 mV

(for z_n=+1, room temp.)

Inside cell: high [K+], low [Na+]

Outside cell: low [K+], high [Na+]

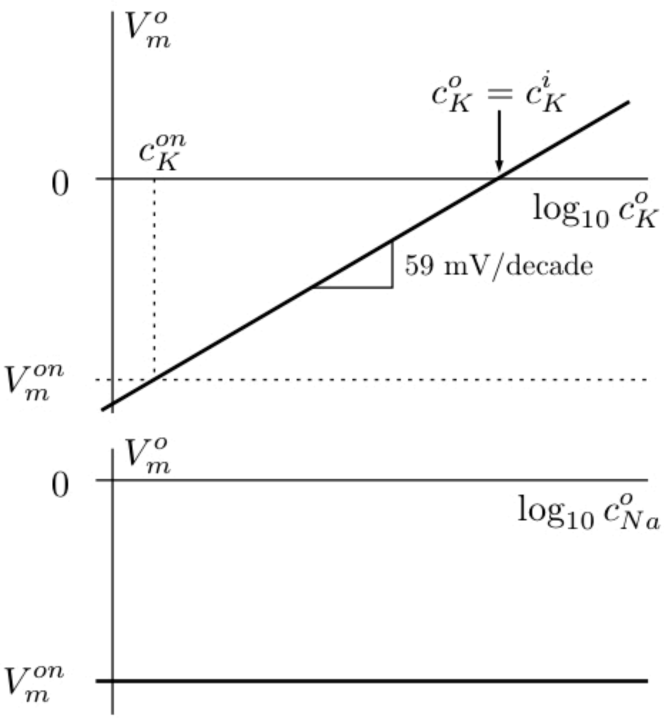


Figure 7.19

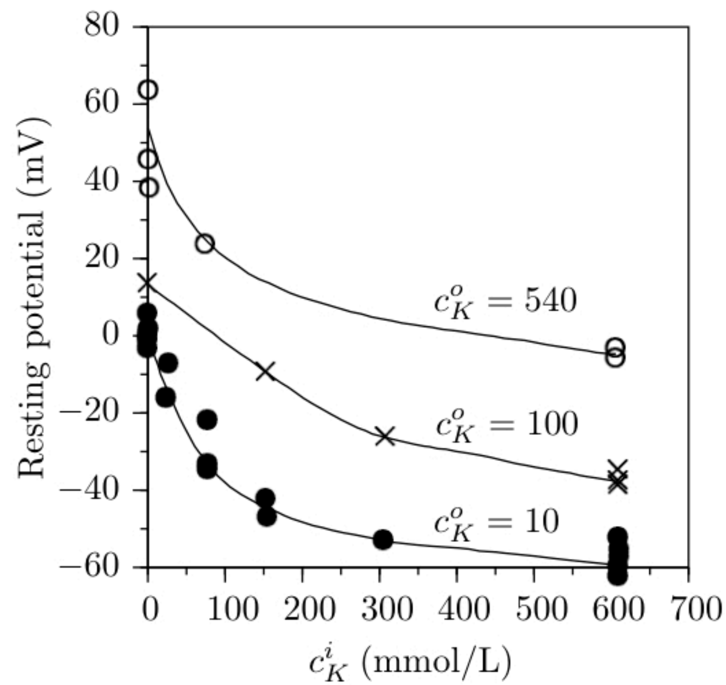


Figure 7.20

Resting Potential: Model considering only a *single permeant ion*

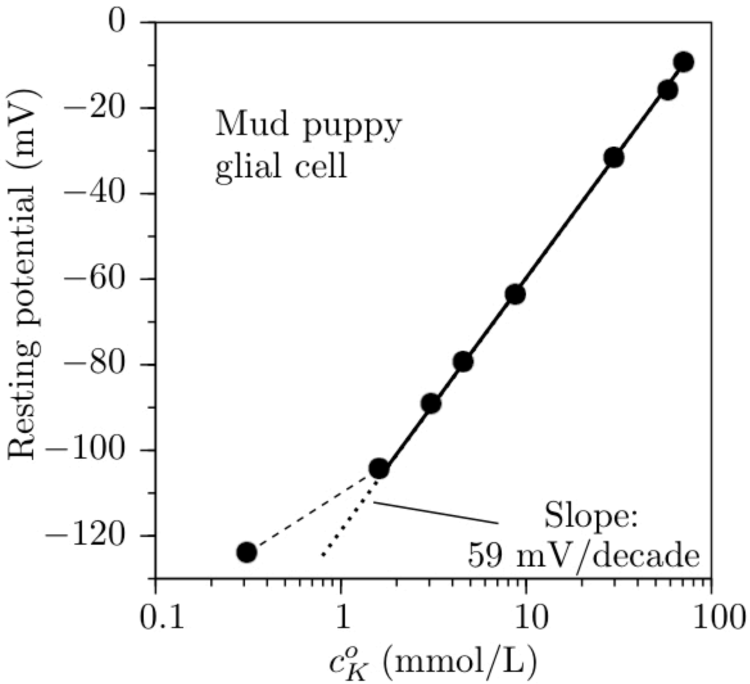


Figure 7.21

→ Model does a decent job, but deviations apparent (e.g., low c_K, Na^+ does matter re Fig.7.23)

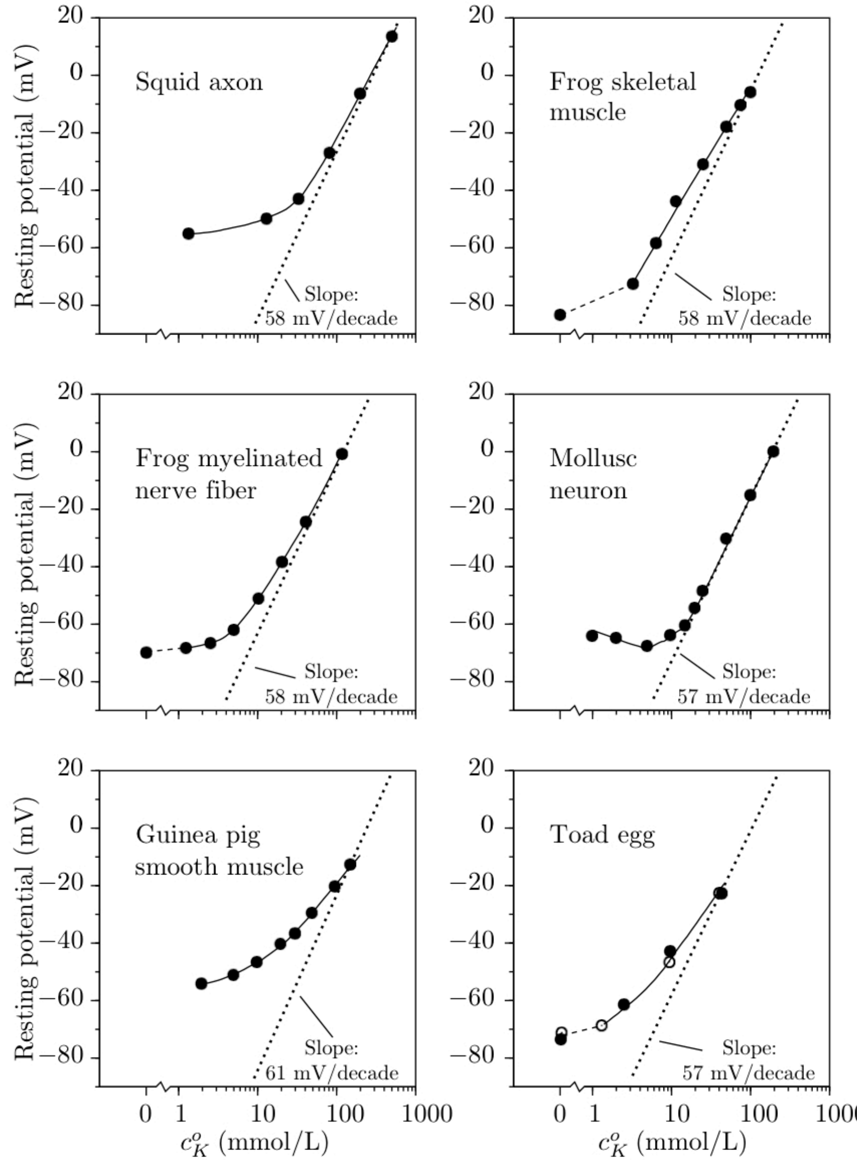
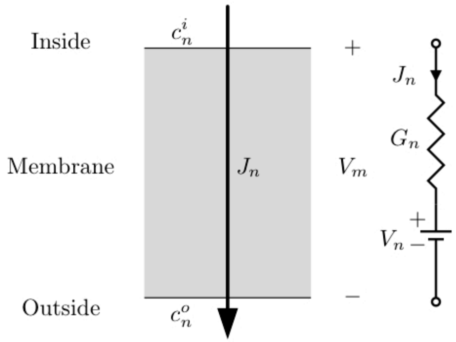


Figure 7.22

Stepping back a moment....



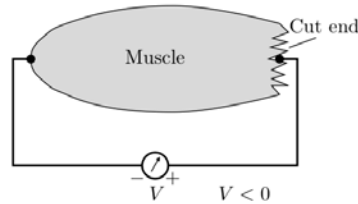


Figure 7.17

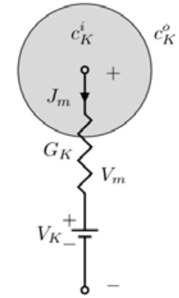
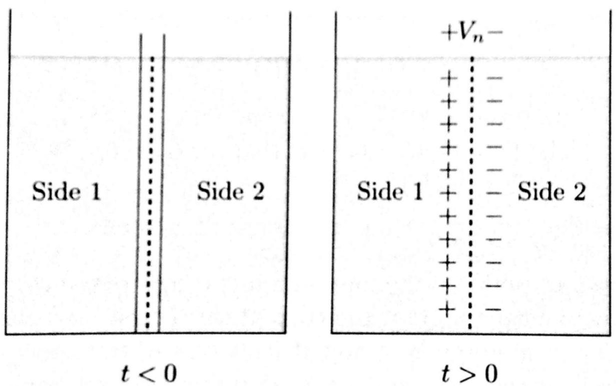
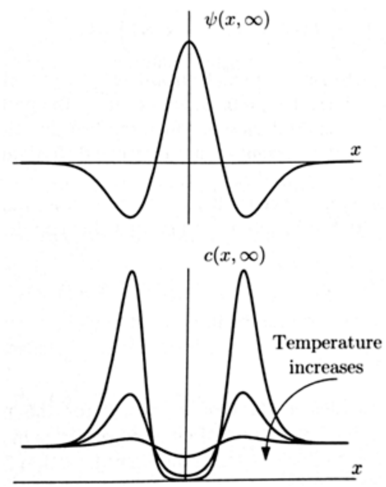


Figure 7.18

$$J_n(x,t) = -z_n F D_n \frac{\partial c_n(x,t)}{\partial x} - u_n z_n^2 F^2 c_n(x,t) \frac{\partial \psi(x,t)}{\partial x}$$





$$V_m^o = V_K = \frac{RT}{F \log_{10} e} \log_{10}\left(\frac{c_K^o}{c_K^i}\right)$$

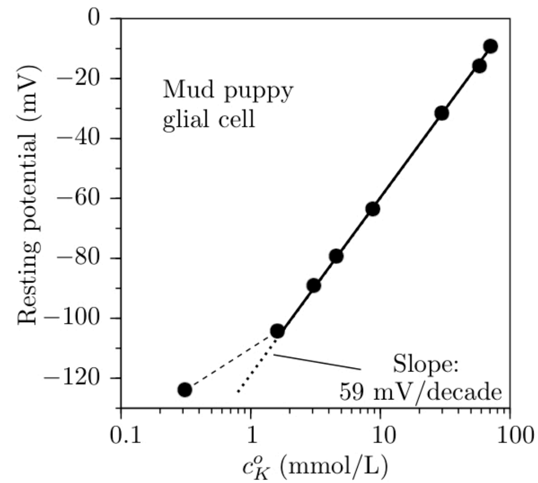


Figure 7.21

→ Different ways of looking at/describing the same thing!

Resting Potential: Model considering only a ***multiple*** *permeant ions*

→ What if different ions are able to diffuse?

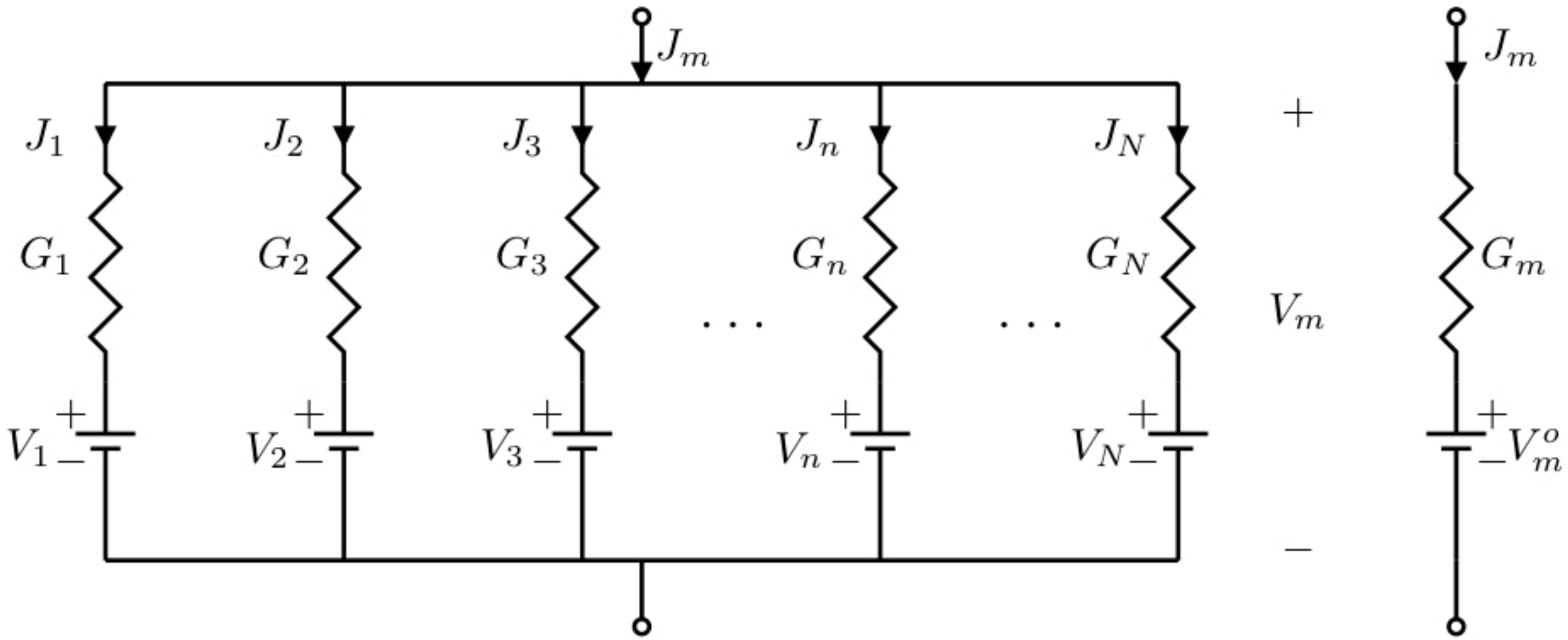


Figure 7.24

Problems

7.5 Describe the distinctions between the following terms that refer to ion transport across a cellular membrane: electrodiffusive equilibrium, steady state, resting conditions, and cellular quasi-equilibrium.

7.6 The following is a discussion of electroneutrality (Nicholls et al., 1992):

The intracellular and extracellular solutions must each be electrically neutral. For example, a solution of chloride ions alone cannot exist; their charges must be balanced by an equal number of positive charges on cations such as sodium or potassium (otherwise electrical repulsion would literally blow the solution apart).

Briefly critique this discussion of electroneutrality.

Exercise 7.5 In steady state the ionic flux through the membrane, the concentration of ions in the membrane, and the voltage across the membrane are all constant with respect to time. Electrodiffusive equilibrium requires all of the conditions for steady state plus the condition that the ionic flux through the membrane is zero. At equilibrium, the potential across the membrane equals the Nernst equilibrium potentials of each permeant ionic species. Rest requires all of the conditions for steady state plus the condition that the net current through the membrane (total across ionic species) is zero. Quasi-equilibrium requires all of the conditions for steady state plus that the net flux of each ionic species (summed across all of the transport mechanisms for that species) is zero.

As an example, suppose external electrodes pass a constant current through the membrane of a cell. For this case, the membrane could come to a steady-state condition. It could be at electrodiffusive equilibrium if the membrane contains active transport mechanisms to carry all of the current from the external electrodes through the membrane. By definition, the cell is not at rest. Furthermore, the cell could not be in quasi-equilibrium, since the external current must be carried through the membrane by some ionic species.

Exercise 7.6 The statement is largely correct except for the parenthetical phrase. The solution would not blow up. The excess charges would repel each other and would ultimately reside on the boundaries of the vessel enclosing the solution.