Biophysics I (BPHS 4080)

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Website: http://www.yorku.ca/cberge/4080W2018.html
Figure 2.19

- Dissolution and diffusion through lipid bilayer
- Transport through water channels
- Transport through gated ion channels
- Carrier-mediated transport
- Pumps
Steady-State Electrodiffusion through Membranes

Inside | Membrane | Outside
\[ c_i^n \quad c_n(x) \quad \psi(x) \quad c_o^n \]

\[ J_n \]

0 \quad d \quad x

Steady-state
\[ \frac{\partial c_n(x,t)}{\partial t} = 0 \]
\[ \frac{\partial J_n(x,t)}{\partial x} = 0 \]
\[ \rightarrow J_n = \text{constant} \]

\[ J_n \frac{1}{G_n} = -\left( \frac{V_n}{RT} \ln \frac{c_n(d)}{c_n(0)} + \frac{V_m}{\psi(0) - \psi(d)} \right) \]

\[ J_n = G_n(V_m - V_n) \]

\[ \rightarrow \text{Like Ohm’s law!} \]

Nernst Equilibrium Potential
\[ V_n = \frac{RT}{z_n F} \ln \frac{c_n(d)}{c_n(0)} = \frac{RT}{z_n F} \ln \frac{c_o^n}{c_i^n} \]

\[ G_n = \frac{1}{\int_{0}^{d} \frac{1}{u_n z_n^2 F^2 c_n(x)} \, dx} \geq 0 \]
Model of Steady-State Electrodiffusion through Membranes

\[ J_n = G_n (V_m - V_n) \]

if \( V_m - V_n > 0 \), then \( J_n > 0 \)
if \( V_m - V_n < 0 \), then \( J_n < 0 \)

direction of current

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

Electrical Conductivity \( G_n = \int_{0}^{d} \frac{1}{du_n z_n F^2 c_n(x)} \geq 0 \)
How is the Nernst potential generated?

**Assumption:** Single permeable ionic species (positively charged)

\[ c_1 < c_2 \]

> Note that the creation of a significant \( V_n \) need not require significant concentration changes.

**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 \( n \).
What is the basis for such a resting potential?
Temperature-dependence can affect things by several mV

\[
V_n = \frac{RT}{z_n F} \ln \left( \frac{c_n^o}{c_n^i} \right) = \frac{RT}{z_n F \log_{10} e} \log_{10} \left( \frac{c_n^o}{c_n^i} \right)
\]

\[
\frac{RT}{z_n F \log_{10} e} \sim 59 \text{ mV}
\]

(for \(z_n = +1\), room temp.)

\[\text{Figure 7.15 Variation with temperature of the factor } RT/(F \log_{10} e).\]
Resting Potential: Model considering only a single permeant ion

$\rightarrow$ Model does a decent job, but deviations apparent (e.g., low $c_K$, Na$^+$ does matter re Fig.7.23)
Resting Potential: Model considering only a **multiple permeant ions**

→ What if different ions are able to diffuse?

![Diagram of ion channels and voltage](https://via.placeholder.com/150)

**Figure 7.24**
At electrodiffusive equilibrium... (i.e., zero current densities concurrently)

\[ \frac{RT}{z_1 F} \ln \left( \frac{c_1^o}{c_1^i} \right) = \frac{RT}{z_2 F} \ln \left( \frac{c_2^o}{c_2^i} \right) = \cdots = \frac{RT}{z_n F} \ln \left( \frac{c_n^o}{c_n^i} \right) \]

Nernst potentials must be equal

Possible concentrations are constrained!

\[ \left( \frac{c_1^o}{c_1^i} \right)^{1/z_1} = \left( \frac{c_2^o}{c_2^i} \right)^{1/z_2} = \cdots = \left( \frac{c_n^o}{c_n^i} \right)^{1/z_n} \]

e.g., \( c_K^o/c_K^i = c_{Cl}^i/c_{Cl}^o \) or that \( c_K^o c_{Cl}^o = c_K^i c_{Cl}^i \)

Donnan relation
More general case

\[ J_m = \sum_n J_n \]

total membrane current is sum of all permeant charged species

\[ \sum_n G_n (V_m^o - V_n) = 0 \]

‘resting state’ condition such that membrane potential is const. (i.e., no net charge entering/leaving cell)

\[ V_m^o = \sum_n \frac{G_n}{G_m} V_n \]

where \( G_m = \sum_n G_n \)

(total conductance per unit area of membrane)
Model with three relevant “paths”:
1. K$^+$
2. Na$^+$
3. Other/Leakage (e.g., Cl$^-$, Ca$^{++}$)

\[ V_m = \sum_n \frac{G_n}{G_m} V_n \]

<table>
<thead>
<tr>
<th>Ion</th>
<th>$G_n$ (S/cm$^2$)</th>
<th>$G_n/G_m$</th>
<th>$c_n^o/c_n^i$</th>
<th>$V_n$ (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>K$^+$</td>
<td>$3.7 \times 10^{-4}$</td>
<td>0.55</td>
<td>0.05</td>
<td>$-72$</td>
</tr>
<tr>
<td>Na$^+$</td>
<td>$1 \times 10^{-5}$</td>
<td>0.016</td>
<td>9.8</td>
<td>$+55$</td>
</tr>
<tr>
<td>leakage</td>
<td>$3.0 \times 10^{-4}$</td>
<td>0.44</td>
<td>—</td>
<td>$-49$</td>
</tr>
</tbody>
</table>

‘resting’ values for squid giant axon (determined empirically)
Multiple ion model seems to take us one step closer, but still doesn't explain everything....
Chief issue is deviations at lower K⁺ concentrations (i.e., saturation in resting potential)
What if conductances were voltage-dependent?

i.e., voltage-gated ion channels
(more detail in vol.2 ch.6)

Hodgkin-Huxley model conductances

Figure 7.32

Figure 7.28
\[
\sum_{n} G_n(V_m^o - V_n) = 0
\]
Problem

7.9 Figure 7.55 shows three panels in which the distributions of Na⁺, K⁺, Cl⁻, and an impermeant anion A⁻ are shown schematically in two rigid compartments separated by a rigid semipermeable membrane. The problem concerns the distributions at electrodiffusive equilibrium for different membrane characteristics.

a. If the membrane were permeable only to K⁺, which of the three distributions would be possible at electrodiffusive equilibrium?

b. If the membrane were permeable to both K⁺ and Cl⁻, which of the three distributions would be possible at electrodiffusive equilibrium?

Figure 7.55 Two compartments separated by a membrane with different ions on the two sides of the membrane (Exercise 7.9). The three panels show different distributions of ions. The diagrams represent the compositions of the bulk solutions on the two sides of the membrane.
Problem

7.14 The intracellular and extracellular ion concentrations are given in Table 7.7 for four cells. The permeant ions are also listed for each cell. You may assume that the permeant ions are transported passively only and that there are no mechanisms of active ion transport in these cells. The temperature is 24°C. For each cell, determine whether the solutions are in electrodiffusive equilibrium across the membrane, and if they are, determine the resting membrane potential.

Table 7.7 The table shows the compositions of intracellular and extracellular ions in four different cells and also indicates which ions are permeant through the cell membranes (Exercise 7.14). Ion A is an impermeant anion.

<table>
<thead>
<tr>
<th>Cell number</th>
<th>Permeant ions</th>
<th>Intracellular</th>
<th>Extracellular</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>KCl</td>
<td>NaCl</td>
</tr>
<tr>
<td>1</td>
<td>K⁺</td>
<td>150</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>Cl⁻</td>
<td>150</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>K⁺ &amp; Cl⁻</td>
<td>150</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>K⁺ &amp; Cl⁻</td>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>
Exercise 7.9 The two solutions in (1) and (3) are electrically neutral whereas those in (2) are not. Solution 2 is an unphysical ionic solution — you cannot obtain such a solution by dissolving salts in water! Therefore, case (2) is not a possible answer to either part a or part b.

a. Both (1) and (3) are possible distributions of ions at equilibrium. In both cases, a potential appears across the membrane so that the left compartment is at a higher potential than the right compartment in order to prevent diffusion of the potassium ions from the right to the left compartment. It is interesting to note that the osmolarity of the solution in the right compartment is larger than that in the left compartment for (1). Therefore, since the walls and the membrane are rigid, a hydraulic pressure appears across the membrane such that the right compartment is at a higher hydraulic pressure than the left compartment.

b. Since both potassium and chloride are permeant, at equilibrium the potential across the membrane must equal both the potassium and the chloride equilibrium potential. But, the valences have different signs, so that

\[ V_K = \frac{RT}{F} \ln \left( \frac{c_K^r}{c_K^l} \right) = V_{Cl} = -\frac{RT}{F} \ln \left( \frac{c_{Cl}^r}{c_{Cl}^l} \right), \]

which implies that

\[ \frac{c_K^r}{c_K^l} = \frac{c_{Cl}^l}{c_{Cl}^r}, \]

where \( c_K^l, c_K^r, c_{Cl}^l, \) and \( c_{Cl}^r \) are the concentration in the left and right compartments for potassium and for chloride. Thus, the concentration ratios of potassium and chloride must be reciprocal. Therefore, only distribution (3) is possible.
Exercise 7.14 Cell #1 is permeable to $K^+$ only. The resting membrane potential will be the Nernst equilibrium potential for potassium $V_m^0 = V_K = 59 \log_{10}(10/150) = -69$ mV. Cell #2 is permeable to $Cl^-$ only. The resting membrane potential will be the Nernst equilibrium potential for chloride $V_m^0 = V_{Cl} = -59 \log_{10}(160/160) = 0$ mV. Cell#3 is permeable of both $K^+$ and $Cl^-$. Since the compositions of the solutions are the same as for Cell#1 and Cell#2, the Nernst potentials are the same as for those cells, i.e., $V_K = -69$ mV and $V_{Cl} = 0$ mV. Therefore, both ions cannot be in equilibrium and there will be net transport of each ion down its concentration gradient, and the potential across the membrane will change with time. Cell#4 is also permeable to both $K^+$ and $Cl^-$, but the compositions of these ions are different. The two Nernst equilibrium potentials are $V_K = 59 \log_{10}(10/150) = -69$ mV and $V_{Cl} = -59 \log_{10}(150/10) = -69$ mV. Therefore, both Nernst equilibrium potentials are the same and both ions will be at equilibrium at the potential $V_m^0 = -69$ mV.