11 Membranes

Electro-osmotic effects

Giant axon of squid *Loligo forbesi* has a diameter up to 1 mm. Our axons have $2r < d < 5 - 20 \mu m$.

Patch KCl in water inside $c_2$

outside $c_1$, an axon. If the $K^+$, but not the $Cl^-$ leak out, and if $C_2 > C_1$, then at equilibrium

Axon is slightly negative because some $K^+$ have leaked out, and so some $K^+$ hang around within a debuge length of the membrane.
The electrostatic potential $V$ is
\[ V_1 \rightarrow V_2 \rightarrow V_1 \]

If the membrane were permeable to Cl$^-$ but not to $K^+$, then we'd have
\[ c_1 \xrightarrow{\text{in membrane}} c_2 = c^- = 0, \quad \text{so} \quad \nabla \cdot \mathbf{E} = 0, \]
whence $E = E_0$, constant, and $V = \alpha n + \beta$, where $\alpha$ and $\beta$ are fitted to $V_1$ & $V_2$. 
At equilibrium, the species that can leak through, the permeant species, of valence $z$ and charge $ze$ will obey the Boltzmann distribution

$$c_1(x) \propto e^{-z e V(x)/kT}$$

so

$$\frac{c_2}{c_1} = e^{-ze(V_2-V_1)/kT}$$

or

$$\ln \frac{c_2}{c_1} = -ze \frac{(V_2-V_1)}{kT}$$

or

$$V_N = V_2 - V_1 = -\frac{kT}{ze} \ln \frac{c_2}{c_1} \quad (11.1)$$

Donnan equilibrium: Assume that $K^+$, $N_2^+$, & $Cl^-$ can move across the membrane, but that the various macromolecules, proteins, RNA, DNA stay inside.
Assume that the cell lies in a bath (body, sea, blood, puddle) with concentrations $C_{1Na^+} = 140 \text{ mM}$, $C_{1K^+} = 10 \text{ mM}$, and $C_{1Cl^-} = 150 \text{ mM}$, which makes the bath neutral. Assume that $p_q$, the charge density of big molecules is equivalent to $125 \text{ mM}$ of excess electrons. Then $p_q < 0$ and the bulk neutrality of the cell requires

$$C_{2Na^+} + C_{2K^+} - C_{2Cl^-} + p_q/e = 0, \quad (11.3)$$

The Nernst relation (11.1) then implies

$$\Delta V = V_2 - V_1 = -\frac{kT}{e} \ln \frac{C_{2Na^+}}{C_{1Na^+}} = -\frac{kT}{e} \ln \frac{C_{2K^+}}{C_{1K^+}}$$

$$= -\frac{kT}{(-e)} \ln \frac{C_{2Cl^-}}{C_{1Cl^-}} \quad (11.4)$$

which are examples of the Boltzmann distribution $\frac{C_2}{C_1} = e^{\frac{-Ze\Delta V}{kT}}$. 
This last equation implies the **Gibbs-Donnan** relations

\[
\frac{C_1 N_3^-}{C_2 N_0^+} = \frac{C_1 e^+}{C_2 K^+} = \frac{C_2 \alpha^-}{C_1 \alpha^-} \tag{1.5}
\]

in equilibrium. So, if we let

\[
x = [N^+_0]_2 = \frac{C_2 N^+_0}{m}
\]

then the G-D relations give

\[
[K^+]_1 = x \left[ \frac{[K^+]}{[N^+_0]} \right]_1 = x \frac{10}{140} = \frac{x}{14}
\]

and

\[
[C^-]_2 = \frac{[Cl^-]_1 [N^+_0]_1}{x} = \frac{(15)(14)x}{x} = 15.
\]

So, charge neutrality \((11,3)\) requires

\[
x + \frac{x}{14} - \frac{(15)(14)}{x} - 0.125 = 0
\]

\[
\frac{15}{14} x^2 - \frac{1}{8} x - 1.021 = 0
\]
\[ 15x^2 - \frac{7}{4}x - 1.294 = 0 \]

\[ x = \frac{\frac{7}{4} \pm \sqrt{\frac{49}{16} + 60(1.294)}}{30} = \frac{\frac{7}{4} \pm 4.55}{30} \]

\[ So \quad x = \frac{\frac{7}{4} + 4.55}{30} = 0.21 \]

\[ So \quad \text{C}_2\text{Na}^+ = 210 \text{ mM}, \]
\[ \text{C}_2\text{K}^+ = 15 \text{ mM} \]
\[ \text{C}_2\text{Cl}^- = 100 \text{ mM}. \]

Positive ions: 225 mM; negative ions 225 mM.

Now (11.4) gives the Donnan potential as

\[ \Delta V = V_2 - V_1 = -\frac{kT}{e} \ln \frac{\text{C}_2\text{Na}^+}{\text{C}_1\text{Na}^+} \]

\[ = -\frac{kT}{e} \ln \frac{210}{140} = -\frac{eV_1}{40} \cdot 0.4055 \]

\[ = -\frac{0.4055}{40} V = -10 \text{ mV} \] for Donnan equilibrium.
Eukaryotic cells burst when their interior ion concentrations differ from the exterior concentration by more than about 0.12 mM — as we saw on page 250. Here the interior concentrations are 325 mM while the exterior ones add to 300 mM. (We don't count the interior macromolecules because they are too few.) This Δc is

\[ Δc = \sum c_i^{\text{in}} - \sum c_i^{\text{out}} = 325 \text{ mM} - 300 \text{ mM} = 25 \text{ mM} \] (11.6)

is 200 times what would burst (lyse) a eukaryotic cell. Its Δp is nearly 1 atm:

\[ Δp = Δc k T = 25 \times 10^{-3} \times 6.1 \times 10^4 \times 4.1 \times 10^{-21} \times 10^{-3} \, \text{m}^3 = 6 \times 10^4 \, \text{Pa}. \]
Also, and more importantly, it's experimentally wrong. Real cells — e.g., the squid giant axon — have:

<table>
<thead>
<tr>
<th>Ion</th>
<th>Inside (mM)</th>
<th>Outside (mM)</th>
<th>Voltage (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K^+$</td>
<td>400</td>
<td>20</td>
<td>-75</td>
</tr>
<tr>
<td>$Na^+$</td>
<td>50</td>
<td>440</td>
<td>54</td>
</tr>
<tr>
<td>$Cl^-$</td>
<td>52</td>
<td>560</td>
<td>-59</td>
</tr>
</tbody>
</table>

The most striking departure from Donnan equilibrium is that the Nernst potential $\Delta V = V_2 - V_1 > 0$ for $Na^+$. That is, there is much more $Na^+$ outside the cell than inside. This is called the sodium anomaly. All animal cells share it. But plant and bacterial cells have rigid
cell walls and can tolerate huge Δp's. Incidentally, the reason animal cells don't have thick, rigid cell walls is that they need to communicate with each other.

Animal cells solve the Δp problem by pumping Na⁺ out and K⁺ in.

The ohmic conductance rule of thumb is that the electric-charge flux \( j_{zi} \) of an ion of valence \( z_i \) is

\[
 j_{zi} = z_i \varepsilon j_i = (\Delta V - V_i^N) g_i \tag{11.8}
\]

in which \( \Delta V = V_2 - V_1 \) is the electrical voltage drop, \( V_i^N = -\frac{kT}{Z_i e} \ln \frac{C_{2i}}{C_{1i}} \), and
$g_i$ is the conductance per area

1. The species of ion,

$$0 \leq E_{g_i} \leq m^2 \Omega^{-1}.$$ 

A resting squid axon membrane has

$$g_i \approx 5 \ m^2 \Omega^{-1}.$$ 

Here "$\Omega$" means "Ohm,"

Eq. (11.8) is a kind of Ohm's Law

$$\Delta V = IR + V'$$

where $R = 1/(g_i A)$, $A$ the area.

This ohmic rule works only within a membrane's regime of ohmic behavior. And often $g_i = g_i(\Delta V)$ varies with the voltage drop $\Delta V$. 
When $\Delta V = 0$ and $\Delta c$ is small, Eq. (11.8) gives

\[
\frac{j_0}{2e} = \frac{g}{ze} (-V^n)
\]

\[
= \frac{g}{ze} \frac{kT}{2e} \ln \left( \frac{c_2 - c_1 + c_1}{c_1} \right)
\]

\[
= \frac{g}{2e} \frac{kT}{(2e)^2} \ln (1 + \frac{\Delta c}{c}) \approx \frac{g}{(2e)^2} \frac{\Delta c}{c} \frac{kT}{c}
\]

\[
= \sigma = P_5 \Delta c \quad \text{by Eq. (4.21)}.
\]

So

\[
\sigma = P_5 \frac{(2e)^2 c}{kT} \geq 0
\]

depends upon the concentration $c$, which makes sense since $\kappa = D \frac{g^2 c}{kT}$ in Sec 4.6.4. Conductance rises with the concentration $c$. 
The conductance $g_i$ varies with the kind of ion, as well as with the kind of membrane. If $g_i = 0$, then the concentrations $C_{i1}$ and $C_{i2}$ need not be related at all.

A. Hodgkin and B. Katz found that the conductances $g_i$ in a resting squid axon were

$$g_{k^+} \approx 25 \, g_{n^+} \approx 2 \, g_{c^-}. \quad (11.9)$$

So $g_{n^+}$ is small but not zero.

Cells pump ions in and out:

$$j_{n^+} = \frac{g_{n^+}}{e} (\Delta V - V_{n^+}^N) + j_{n^+}^P. \quad (11.10)$$

cells pump $Na^+$ out (and $K^+$ in). (11.11)
The Na-K pump uses 1 ATP molecule to pump 3 \( \text{Na}^+ \) out while drawing 2 \( \text{K}^+ \) into the cell. This is coupled transport. Because one net charge is translocated, the pump is electrogenic. The pump is an active transporter.

The cost \( \Delta G \) of transporting one \( \text{Na}^+ \) can by table 11.1 be found thusly:

\[
\begin{align*}
\text{outside } & V_1, \\
\text{inside } & V_2 \quad \downarrow E \\
\Delta V = V_2 - V_1 = -60 \text{ mV}
\end{align*}
\]

is the change in the electrostatic potential. The electric field points into the cell.

The Nernst potential for \( \text{Na}^+ \) is

\[
\frac{N_{\text{Na}^+}^N}{N_{\text{Na}^+}^0} = -\frac{kT}{2e} \ln \frac{c_2}{c_1} = -\frac{kT}{e} \ln \frac{50}{440} = \frac{kT}{e} \ln \frac{44}{5}
\]

This concentration gradient pushes \( \text{Na}^+ \) into the cell.