3 Electrodiffusion: Gauss Meets Boltzman

We previously discussed how the motion of freely dissolved ions and macromolecules is governed by diffusion, the random motion of molecules that results from fluctuating forces. This picture largely holds in the presence of weak forces that merely add a slight bias to the motion, such as the case of electric fields across membrane pores. In particular, in the presence of an electric field the motion is limited by the collisions so that the velocity, as opposed to acceleration, is proportional to the force. We have

$$\begin{aligned} \vec{v}_D(\vec{r},t) &= \mu\vec{E}(\vec{r},t) \qquad (3.1)\\ &= -\mu\vec{\nabla}V(\vec{r},t) \end{aligned}$$

where $\vec{v}_D(\vec{r},t)$ is known as the drift velocity and μ is the mobility. The joke is that life is diffusion with a small drift velocity.

How big are these terms? Without proof, we note that $|\vec{v}_D| \approx 10^1\frac{cm}{s} = 10^2\frac{\mu m}{ms}$ in membranes and $|\vec{v}_D| \approx 10^{-5}\frac{cm}{s} = 10^{-4}\frac{\mu m}{ms}$ in cytoplasm.

We can now calculate the flux due to the electric field as

$$\begin{aligned} \vec{J}_D(\vec{r},t) &= C(\vec{r},t)\vec{v}_D(\vec{r},t) \qquad (3.2)\\ &= \mu C(\vec{r},t)\vec{E}(\vec{r},t)\\ &= -\mu C(\vec{r},t)\vec{\nabla}V(\vec{r},t) \end{aligned}$$

Thus the total flux, thermal as well as force driven, is

$$\vec{J}(\vec{r},t) = -D\nabla C(\vec{r},t) - \mu C(\vec{r},t)\vec{\nabla}V(\vec{r},t) \qquad (3.3)$$

At equilibrium, $\vec{J}(\vec{r},t) = 0$ and thus

$$C(\vec{r}) = C(\vec{r}')e^{-\frac{\mu}{D}(V(\vec{r})-V(\vec{r}'))} \qquad (3.4)$$

or

$$\Delta V = V(\vec{r}) - V(\vec{r}') = -\frac{D}{\mu}ln\left(\frac{C(\vec{r})}{C(\vec{r}')}\right) \qquad (3.5)$$

but we previously showed that this equilibrium potential is just given by the Nernst formula, i.e.,

$$\Delta V = -\frac{k_BT}{e}ln\left(\frac{C(\vec{r})}{C(\vec{r}')}\right) \qquad (3.6)$$

Thus

$$\mu = D\frac{e}{k_BT} \tag{3.7}$$

We can estimate the size of $|\vec{v}_D|$ for membranes and compare it with the RMS thermal velocity, $|\vec{v}_{th}|$, since the concept of the drift velocity holds only if $|\vec{v}_D| << |\vec{v}_{th}|$. For a membrane, the electric field is of order $|\vec{E}| = \frac{V}{L} \sim \frac{k_BT}{e}\frac{1}{L}$ so that $|\vec{v}_D| = \mu|\vec{E}| \sim D\frac{e}{k_BT}\frac{k_BT}{e}\frac{1}{L} \approx \frac{D}{L}$. On the other hand, we discussed earlier that the scale of the thermal velocity is $|\vec{v}_{th}| \sim \frac{\lambda}{\tau} \approx \frac{D}{\lambda}$. Thus

$$|\vec{v}_D| \sim \frac{\lambda}{L}|\vec{v}_{th}| \sim 0.1|\vec{v}_{th}| \tag{3.8}$$

so that the thermal velocity is relatively small for distances larger than the collision length, a rather intuitive result. On the other hand, for large electric fields may may anticipate a deviation from a simple linear relationship between $|\vec{E}|$ and $|\vec{v}_D|$, a topic we will return to.

Since we previously argued that the thermal velocity can be estimated from equipartition, i.e., $|\vec{v}_{th}| \sim \sqrt{\frac{k_BT}{m}}$, we have

$$|\vec{v}_D| \sim c\sqrt{\frac{k_BT}{mc^2}}\ \frac{\lambda}{L} \tag{3.9}$$

from which we can estimate the absolute size of the drift velocity for membranes to be $|\vec{v}_{th}| \sim 10cm/s$.

We can now put all of the formalism together to get a modified flux for the diffusion equation, i.e,

$$\vec{J}(\vec{r},t) = -D\left(\nabla C(\vec{r},t) + \frac{e}{k_BT}C(\vec{r},t)\vec{\nabla}V(\vec{r},t)\right) \tag{3.10}$$

At this point, let's cool it with the general form for 3-dimensions and focus on the case of current through a pore of cross sectional area A that spans a membrane of thickness L. We further assume that the electric field is uniform (probably not true, but it allows us to make some useful progress), so that $V(x) = V(0)\frac{x}{L}$, we have an equation for the electrical current, I,

$$I = -eJ(x)A = eDA\left(\frac{dC(x)}{dx} + \frac{e}{k_BT}C(x)\frac{\Delta V}{L}\right) \tag{3.11}$$

where A is the area of the membrane. This equation is in the form of $\frac{dC(x)}{dx} + const \cdot C(x) = const'$, which we can solve directly to obtain

$$I = e\frac{D}{L}\frac{eV}{k_BT}A\frac{C(L) - C(0)e^{-\frac{eV}{k_BT}}}{1 - e^{-\frac{eV}{k_BT}}} \tag{3.12}$$

This is known as the Nernst-Plank relation. The interesting, and essential feature, is that the $I - V$ curve is nonlinear for voltage changes on the order of $\frac{k_BT}{e} \approx 25mV$ away from the reversal potential.

FIGURE - chapt-4-nernst-plank.eps

If we include the possibility of a valence, $z = \pm 1$, ± 2, ± 3, etc, the general form of the Nernst-Plank relation becomes

$$I(V) = z^2 e \frac{D}{L} \frac{eV}{k_B T} A \frac{C(L) - C(0) e^{-\frac{zeV}{k_B T}}}{1 - e^{-\frac{zeV}{k_B T}}} \tag{3.13}$$

and is particularly strong for divalents, such as Ca^{+2}.

The essential physics is that it is "easier" for currents to flow from high concentrations to low concentrations, so that the conductance (slope of the $I - V$) is larger when ions move from high to low, rather than from low to high, concentration. This property in known as rectification, and is a "normal" property of any cell membrane. The limiting currents are Ohmic, with

$$I(V) \rightarrow \begin{cases} z^2 e \frac{D}{L} \left(\frac{eV}{k_B T} \right) AC(L) & \text{if } V >> \frac{k_B T}{e} \\ \\ z^2 e \frac{D}{L} \left(\frac{eV}{k_B T} \right) AC(0) & \text{if } V << -\frac{k_B T}{e} \end{cases}$$

These asymptotic relations are often good approximations, and for the better or worse most physiologists assume that the I-V relation is Ohmic. But do this at your peril. Hagiwara made this assumption about the "Inward Rectifier" for K^+ and came to some erroneous conclusions about his data!

3.1 The resting potential of a neuron

In steady-state, the total current across the cell membrane is zero. When only a single ionic species can pass across the membrane, i.e., when the current is carried by only a single ionic species, the steady-state potential is also the equilibrium potential and we recover the Nernst potential. In general, however, multiple ions contribute to the current flow across the membrane. We focus on a cell with just 3 of these, Na^+, K^+ and Cl^-. There is a Nernst-Plank current associated with each ion, i.e.,

$$I_{Na^+}(V) = eA \left(\frac{D}{L} \right)_{Na^+} \frac{eV}{k_B T} \frac{[Na^+]_{in} - [Na^+]_{out} e^{-\frac{eV}{k_B T}}}{1 - e^{-\frac{eV}{k_B T}}} \tag{3.14}$$

$$I_{K^+}(V) = eA \left(\frac{D}{L} \right)_{K^+} \frac{eV}{k_B T} \frac{[K^+]_{in} - [K^+]_{out} e^{-\frac{eV}{k_B T}}}{1 - e^{-\frac{eV}{k_B T}}} \tag{3.15}$$

$$I_{Cl^-}(V) = eA \left(\frac{D}{L} \right)_{Cl^-} \frac{eV}{k_B T} \frac{[Cl^-]_{in} - [Cl^+]_{out} e^{\frac{eV}{k_B T}}}{1 - e^{\frac{eV}{k_B T}}} \tag{3.16}$$

In steady state, we must have

$$I_{Na^+}(V) + I_{K^+}(V) + I_{Cl^-}(V) = 0 \tag{3.17}$$

This condition is satisfied for only a single voltage. The algebra is easy to do it you recall that one should solve for $e^{\frac{eV}{k_BT}}$ rather than directly for V (it is also easy if one ignores divalents, like Ca^{+2}!). The steady state potential is given by (Goldman-Hodgkin-Katz equation)

$$V_{SS} = \frac{k_BT}{e} ln \frac{\left(\frac{D}{L}\right)_{K^+} [K^+]_{out} + \left(\frac{D}{L}\right)_{Na^+} [Na^+]_{out} + \left(\frac{D}{L}\right)_{Cl^-} [Cl^-]_{in}}{\left(\frac{D}{L}\right)_{K^+} [K^+]_{in} + \left(\frac{D}{L}\right)_{Na^+} [Na^+]_{in} + \left(\frac{D}{L}\right)_{Cl^-} [Cl^-]_{out}} \tag{3.18}$$

The fraction $\frac{D}{L}$ is often called the permeability, denoted P. Actually, the permeability is defined with the addition of a mystery fudge factor in front! We will see below that the permeability is dependent on concentration such that the channels are significantly saturated at physiological ion concentrations.

As we mentioned on the first day, V_{SS} typically has a value of about -50 mV. Ion substitution experiments that maintain a constant total ion concentration have confirmed this relation.

FIGURE - chapt-4-goldman.doc

3.2 Relations among "Diffusive" processes

Since in the linear limit (i.e., $\frac{zeV}{k_BT} \to \pm\infty$) the $I - V$ relation must reduce to Ohm's law, i.e., $I = g\frac{\pi a^2}{L}V$, we have the relation

$$g = \frac{(ze)^2 DC(L)}{k_BT} \tag{3.19}$$

In general, we recall that the diffusion constant (D), the mobility (μ), the viscosity (η), and the electrical conductance (g) are all related. We recapitulate this below,

$$D = g\frac{k_BT}{(ze)^2 C_{ions}} = \mu\frac{k_BT}{ze} = \frac{1}{\eta}\frac{k_BT}{6\pi a} \tag{3.20}$$

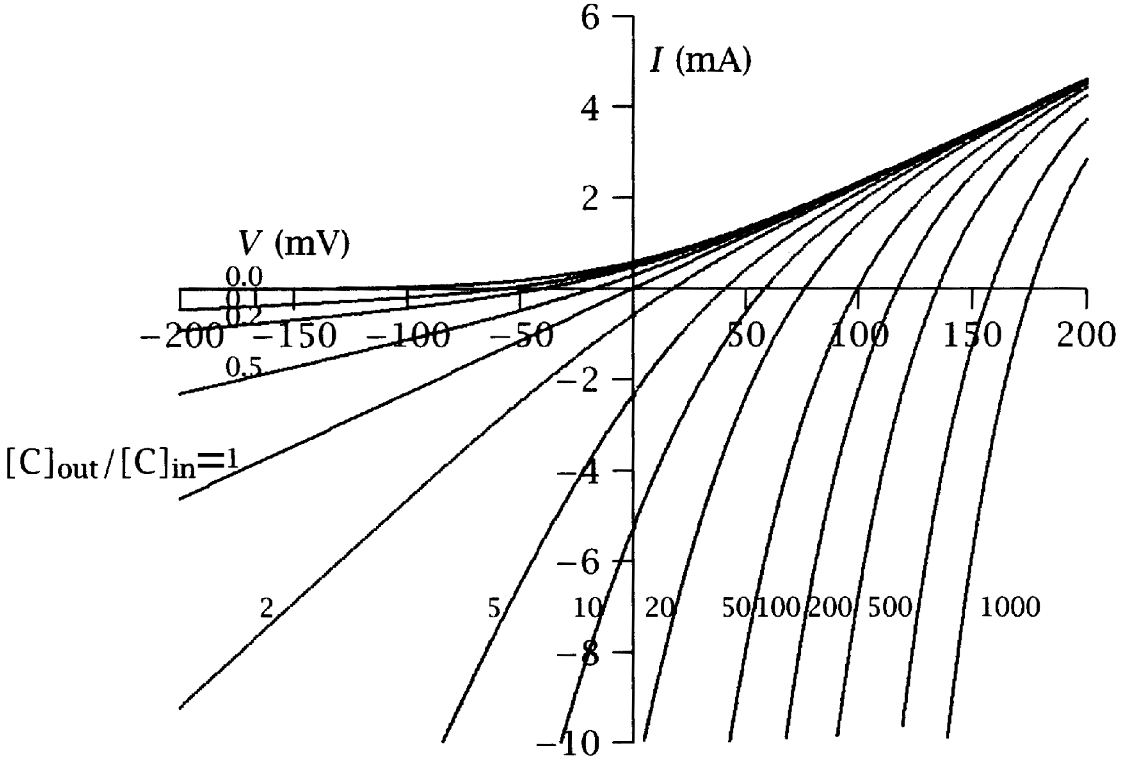
where the viscosity relation for a particle of radius a is not really useful for ions per se.

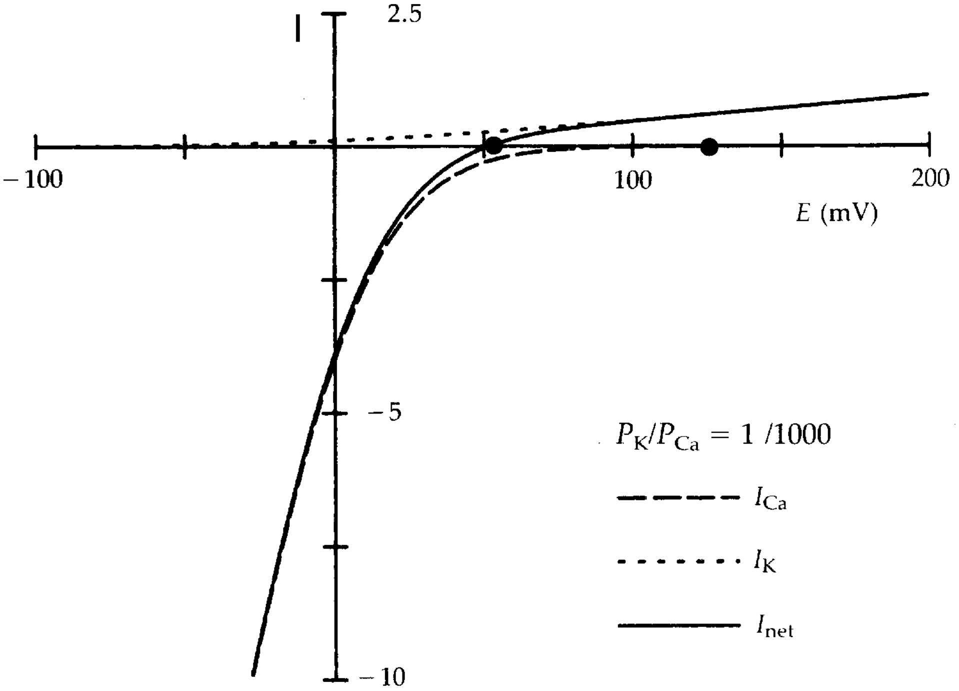
Lastly, as a practical issue, to convert from "physics" units to "chemical" units, one replaces k_B by $R = N_A \cdot k_B$ and e by $F = N_A \cdot e$ and measures concentration in molar (moles/liter) rather than ions per cm^3.

Squid Axon

External Fluid	$[K^+]_o$ in mM	$[Na^+]_o$ in mM	$[Cl^-]_o$ in mM	Measured RP (mV)	Calculated RP (mV)	Difference (mV)
ASW	10	455	587	-60	-60	0
A	0	465	587	-63	-65	+2
B	15	450	587	-58	-58	0
C	20	445	587	-56	-56	0
Sea Water	10	455	540	-59	-59	0
D	7	324	384	-59	-60	+1
E	5	227	270	-61	-61	0
F	3	152	180	-61	-61	0
G	2	91	108	-63	-62	-1
H	10	573	658	-60	-59	-1
I	10	711	796	-57	-59	+2

Adapted from Hodgkin and Katz (1949)





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