Membrane potentials and ion pumps

Lecture notes, week 14. Nelson, sections 11.1–11.2

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The Donnan equilibrium explains how trapped macroions create a membrane potential, but it predicts an osmotic pressure that would burst an animal cell. Real cells are not in equilibrium. They spend a large part of their energy budget keeping themselves away from it.

The sodium anomaly

Measured ion concentrations in the squid giant axon (Nelson, Table 11.1), with the Nernst potentials from $\mathcal{V}_i^{\text{Nernst}} = -(k_B T/z_i e)\ln(c_{i,\text{in}}/c_{i,\text{out}})$:

Ion	Inside (mM)	Outside (mM)	$\mathcal{V}_i^{\text{Nernst}}$ (mV)
K	400	20	−75
Na	50	440	+54
Cl	52	560	−59

The measured resting potential is $\Delta\mathcal{V} \approx -60$ mV. Chloride is close to equilibrium and potassium not far from it. Sodium is far from equilibrium: its concentration is *lower* inside although the inside is negative and should attract it. If all three ions were in Donnan equilibrium, the three Nernst potentials would be equal. They are not, so **the resting state is not an equilibrium**.

Ion channels and the Ohmic hypothesis

Ions cross lipid membranes extremely slowly on their own (the Born energy of moving a charge from water into oil is about $100\,k_BT$, see E8). They cross through **ion channels**: proteins with a water-filled pore, often selective for one ion species, that open and close in response to voltage, ligands, temperature or mechanical stress. A single open channel passes millions of ions per second, without using metabolic energy. This is passive transport, downhill in electrochemical potential.

The driving force on ion species i is its electrochemical potential difference,

$$\Delta\mu_i = k_BT\,\Delta\ln c_i + z_i e\,\Delta\mathcal{V} = z_i e\,(\Delta\mathcal{V} - \mathcal{V}_i^{\text{Nernst}})\,.$$

Linear transport, $j_i = -g_i'\,\Delta\mu_i$ as in osmotic flow, then gives the **Ohmic hypothesis** for the electric current per area carried by species i out of the cell:

$$j_{q,i} = g_i\,(\Delta\mathcal{V} - \mathcal{V}_i^{\text{Nernst}})\,. \tag{1}$$

Each ion species is a battery $\mathcal{V}_i^{\text{Nernst}}$ in series with a conductance g_i, and all of them are in parallel across the membrane capacitance (Nelson, Figure 11.4). For the squid axon at rest,

$$g_{\text{K}} \approx 25\,g_{\text{Na}} \approx 2\,g_{\text{Cl}}. \tag{2}$$

Without pumps, a steady potential requires zero net current, $\sum_i j_{q,i} = 0$, which gives the conductance-weighted average $\Delta\mathcal{V} = \sum_i g_i\mathcal{V}_i^{\text{Nernst}}/\sum_i g_i \approx -66$ mV. But each ion still leaks, so the concentrations slowly run down towards Donnan equilibrium. Something must push them back.

Active pumping

The **sodium–potassium pump** (Na /K -ATPase) is a membrane protein that, for each ATP molecule it hydrolyses, moves 3 Na out and 2 K in. It drives sodium and potassium uphill, against their electrochemical potentials.

In a steady state no ion may accumulate, so every ion is either impermeant, in Nernst equilibrium, or pumped exactly as fast as it leaks. In the simplest model:

- Cl is not pumped, so it must be in equilibrium: $\Delta\mathcal{V} = \mathcal{V}_{\mathrm{Cl}}^{\mathrm{Nernst}} = -59$ mV.
- The leaks of Na and K must be in the ratio of the pump, $-3/2$ (the pump pushes sodium out and potassium in). From Eq. 1:

$$2\,g_{\mathrm{Na}}\,(\Delta\mathcal{V} - \mathcal{V}_{\mathrm{Na}}^{\mathrm{Nernst}}) = -3\,g_{\mathrm{K}}\,(\Delta\mathcal{V} - \mathcal{V}_{\mathrm{K}}^{\mathrm{Nernst}}) \quad \Rightarrow \quad \Delta\mathcal{V} = \frac{2g_{\mathrm{Na}}\mathcal{V}_{\mathrm{Na}}^{\mathrm{Nernst}} + 3g_{\mathrm{K}}\mathcal{V}_{\mathrm{K}}^{\mathrm{Nernst}}}{2g_{\mathrm{Na}} + 3g_{\mathrm{K}}}. \tag{3}$$

With Eq. 2 this gives $\Delta\mathcal{V} \approx -72$ mV, compared with about -60 mV measured. The linear (Ohmic) hypothesis is used for sodium, which is far from equilibrium, and other ions are left out, so moderate agreement is what we can expect. The model gets the essentials right: the resting potential lies between the Nernst potentials of potassium and sodium, much closer to potassium, because $g_{\mathrm{K}} \gg g_{\mathrm{Na}}$.

What the pump costs and what it buys

At $\Delta\mathcal{V} = -60$ mV, pushing one Na out costs $e(60 + 54)$ meV $= 114$ meV, and pulling one K in costs $e(-60+75) = 15$ meV. One cycle costs $3\cdot 114 + 2\cdot 15 = 372$ meV $\approx 15\,k_BT$. Hydrolysing one ATP releases about $19\,k_BT$ under cellular conditions, so the pump works close to its thermodynamic limit, wasting about $4\,k_BT$ per cycle as heat.

Each cycle also removes one ion from the cell (3 out, 2 in). This is what solves the osmotic problem of the Donnan equilibrium: by keeping sodium out, the pump lowers the total concentration of small ions inside until the osmotic pressure is close to zero. **Animal cells keep their volume, and a resting potential, by continuously spending free energy.** In a resting human, roughly a quarter of all ATP goes to this one pump; in neurons it is more.

Towards nerve signals

The resting state is a nonequilibrium steady state with stored free energy: the sodium battery $\mathcal{V}_{\mathrm{Na}}^{\mathrm{Nernst}}$ is held at $+54$ mV, but connected only through a small conductance. If g_{Na} suddenly increases, the membrane potential swings towards $+54$ mV. In nerve cells, the sodium and potassium channels are **voltage-gated**: their conductance depends on $\Delta\mathcal{V}$. This nonlinearity turns the leaky membrane into an excitable medium that can regenerate a sharp pulse, the action potential, and send it along an axon at constant speed and shape. That is Nelson chapter 12, the Hodgkin–Huxley model, and elective 2B Nerve signals. See the neuron demo for what it looks like.