Processes at membranes

Lecture notes, weeks 11–14. Nelson, chapter 7 and sections 11.1

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Throughout, $\Delta X = X_{\text{in}} - X_{\text{out}}$ is the difference across a membrane (inside minus outside), and concentrations c are number densities unless they are given in mM. With molar concentrations, replace k_B by the gas constant $R = N_A k_B$.

Osmosis



Figure 1: A box divided by a semipermeable membrane. The black (solvent) particles can cross it; the red (solute) particles are confined to the left.

A box of fixed volume is divided in two by a membrane that only the solvent (black) can cross. The red solute particles are stuck on the left, and they are few: $N_2 \ll N_1$. In a cell, the black particles are water and the red ones are ions, sugars and proteins.

- What happens? How do the water molecules distribute between left and right?
- If the solution is dilute, the solute particles hardly interact with each other. They move around in the water like the molecules of an ideal gas move around in empty space.
- So the solute exerts its own "ideal gas" pressure on the membrane, which it cannot cross. The water does not care: it can move freely across.

The extra pressure on the side with solute is then

$$\Delta P = c_2 k_B T, \qquad c_2 = \frac{N_2}{V_L}.$$

Can such a simple argument be right? Section shows that it is, for dilute solutions, from a general thermodynamic argument.

The van 't Hoff relation

$$\Delta P = k_B T \sum_i \phi_i \, \Delta c_i \qquad \text{or, in molar units,} \qquad \Delta P = RT \sum_i \phi_i \, \Delta c_i, \tag{1}$$

where ϕ_i is the number of independently moving particles that one molecule of solute i gives in solution. **It is the number of "ideal gas" particles that counts**, not their size or chemistry:

- $\text{NaCl} \rightarrow \text{Na}^+ + \text{Cl}^-$: $\phi = 2$
- glucose $\rightarrow$ glucose: $\phi = 1$
- carboxylic acid $\rightarrow$ dimers: $\phi = 1/2$



Figure 2: Two carboxylic acid molecules bind with two hydrogen bonds and move as one particle.

Numbers



Figure 3: Physiological saline: 9 g NaCl per litre.

Physiological saline contains 9 g NaCl per litre. With the molar mass $23 + 35.5 = 58.5$ g/mol this is $c = 0.15$ mol/L $= 150$ mol/m³. If a cell with this salt content were put in pure water and could not swell, the pressure would be

$$\Delta P = 2cRT = 2 \cdot 150 \cdot 8.3 \cdot 300 \text{ Pa} \approx 7.5 \times 10^5 \text{ Pa} = 7.5 \text{ bar},$$

more than in the tyres of a racing bike. A cell membrane withstands a few kPa at most. This is why cells burst in pure water.

Chemical potential and the Gibbs–Duhem relation

Equilibrium with respect to particle exchange is **equality of chemical potential**, not of concentration. At fixed T and P, the relevant definition is

$$\mu_i = \left(\frac{\partial G}{\partial N_i} \right)_{T,P,N_{j\neq i}}.$$

Adding particles at fixed T, P and composition does not change any μ_i, and each added particle of type i increases G by μ_i. Since G is extensive,

$$G = \sum_i N_i \mu_i.$$

The total differential of this expression is $dG = \sum_i \mu_i \, dN_i + \sum_i N_i \, d\mu_i$. Comparing with the thermodynamic identity $dG = -S\,dT + V\,dP + \sum_i \mu_i \, dN_i$ gives the **Gibbs–Duhem relation**:

$$\sum_i N_i \, d\mu_i = -S\,dT + V\,dP \qquad \Rightarrow \qquad \sum_i c_i \, d\mu_i = dP \quad (T \text{ constant}). \tag{2}$$

The chemical potentials of the components cannot all change independently: with I components only $I - 1$ of them are independent.

Ideal (dilute) solutions have no volume change and no heat of mixing, and

$$\mu_i = \mu_i^0(P,T) + k_B T \ln c_i$$

(see Entropy and entropic forces). **External fields** add the potential energy of each particle, $\mu_{\text{tot}} = \mu_{\text{int}} + U_{\text{ext}}$. For an ion with charge $q = ze$ in an electric potential $\mathcal{V}$, $U_{\text{ext}} = q\mathcal{V}$.

Osmotic flow

The argument at the start only gave the pressure in equilibrium. How do the flux of water and the pressure develop in time, if the two sides start at the same pressure?

Linear irreversible thermodynamics

Close to equilibrium, fluxes are linear in the thermodynamic driving forces, the gradients of chemical potential and temperature:

$$\begin{aligned} J_1 &= -l_{11}\nabla\mu_1 - l_{12}\nabla\mu_2 - l_{1q}\nabla T \\ J_2 &= -l_{21}\nabla\mu_1 - l_{22}\nabla\mu_2 - l_{2q}\nabla T \\ J_q &= -l_{q1}\nabla\mu_1 - l_{q2}\nabla\mu_2 - l_{qq}\nabla T \end{aligned}$$

The l_{ij} are the linear transport coefficients. Comparing $J_1 = -l_{11}(\partial\mu_1/\partial c_1)\nabla c_1$ with Fick's law $J_1 = -D_1\nabla c_1$ gives $l_{11} = D_1/(\partial\mu_1/\partial c_1)$, which for an ideal solution is $l_{11} = D_1 c_1/k_BT$. The off-diagonal coefficients describe species that drag each other along. Onsager showed that the matrix is symmetric, $l_{ij} = l_{ji}$.

Osmotic flux and pressure in general

Across a membrane we use differences instead of gradients. Let species 1 be water and species 2 the solute, at constant T, and let J_1 be the flux of water into the cell:

$$J_1 = -l_{11}\,\Delta\mu_1 - l_{12}\,\Delta\mu_2, \qquad J_2 = -l_{21}\,\Delta\mu_1 - l_{22}\,\Delta\mu_2.$$

The solute cannot cross, so $J_2 = 0$ for any forces: $l_{21} = l_{22} = 0$, and by Onsager symmetry $l_{12} = 0$ as well. So **only the chemical potential of water matters** for the flow of water:

$$J_1 = -l_{11}\,\Delta\mu_1.$$

To relate $\Delta\mu_1$ to the solute, use the Gibbs–Duhem relation Eq. 2, $c_1\Delta\mu_1 + c_2\Delta\mu_2 = \Delta P$:

$$J_1 = -\frac{l_{11}}{c_1}\left(\Delta P - c_2\,\Delta\mu_2\right).$$

This holds for any solution. For an ideal solution, $\Delta\mu_2 = k_BT\,\Delta\ln c_2 \approx k_BT\,\Delta c_2/c_2$, so

$$J_1 = -\frac{l_{11}}{c_1}(\Delta P - k_BT\,\Delta c_2). \tag{3}$$

Water flows into the side with more solute until the pressure there has risen to $\Delta P = k_BT\,\Delta c_2$: the van 't Hoff relation, now derived without any picture of solute particles hitting a wall. Eq. 3 also says how fast: the volume flux is proportional to $k_BT\Delta c_2 - \Delta P$, with a coefficient (the filtration coefficient L_p) set by how easily water gets through the membrane.

Charges and screening

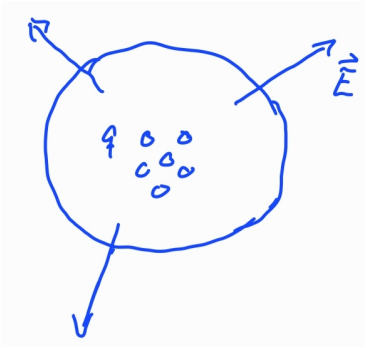


Figure 4: Charges inside a closed surface and the electric field through it.

Gauss's law and the definition of the potential, $\vec{E} = -\nabla\mathcal{V}$, give **Poisson's equation**:

$$\nabla \cdot \vec{E} = \frac{\rho}{\varepsilon}, \qquad \nabla^2\mathcal{V} = -\frac{\rho}{\varepsilon},$$

where ρ is the charge density and $\varepsilon = \varepsilon_r\varepsilon_0$ the permittivity. Oils and solids have $\varepsilon_r \sim 2$–10; water has $\varepsilon_r \approx 80$, because its molecules are strongly polar and turn to oppose an applied field.

One charge. The flux of $\vec{E}$ through any sphere around a point charge q is q/ε, so

$$\vec{E}(r) = \frac{q}{4\pi\varepsilon r^2}\hat{r}, \qquad \mathcal{V}(r) = \frac{q}{4\pi\varepsilon r}, \qquad \vec{F} = \frac{q_1 q_2}{4\pi\varepsilon r^2}\hat{r}. \tag{4}$$

A natural length scale is the **Bjerrum length** $\lambda_B = e^2/(4\pi\varepsilon k_B T)$, the distance at which two unit charges interact with energy $k_B T$. In water at room temperature $\lambda_B \approx 0.7$ nm; in oil it is 40 times longer. This is why salts dissolve in water but not in oil, and why ions cannot cross a lipid membrane without help.

Debye screening

In salt water the other ions move until they screen a charge, while thermal motion spreads them out. The Boltzmann distribution gives the concentration of ion species i (valence z_i) in a potential $\mathcal{V}(\vec{r})$ that vanishes far away:

$$c_i(\vec{r}) = c_i^{\infty}\, e^{-z_i e\mathcal{V}(\vec{r})/k_B T}.$$

The charge density $\rho = \sum_i z_i e\, c_i$ in Poisson's equation then gives the Poisson–Boltzmann equation,

$$\nabla^2\mathcal{V} = -\frac{e}{\varepsilon}\sum_i z_i c_i^{\infty}\, e^{-z_i e\mathcal{V}/k_B T}.$$

Where $e\mathcal{V} \ll k_B T$ we can expand $e^{-x} \approx 1 - x$. The zeroth-order term vanishes because the bulk is neutral, $\sum_i z_i c_i^{\infty} = 0$, and we get the linear **Debye–Hückel equation**

$$\nabla^2\mathcal{V} = \frac{\mathcal{V}}{\lambda_D^2}, \qquad \lambda_D = \left(\frac{\varepsilon k_B T}{e^2\sum_i z_i^2 c_i^{\infty}}\right)^{1/2} = \left(4\pi\lambda_B\sum_i z_i^2 c_i^{\infty}\right)^{-1/2}. \tag{5}$$

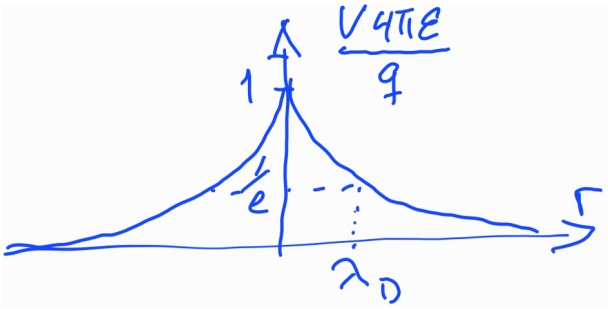
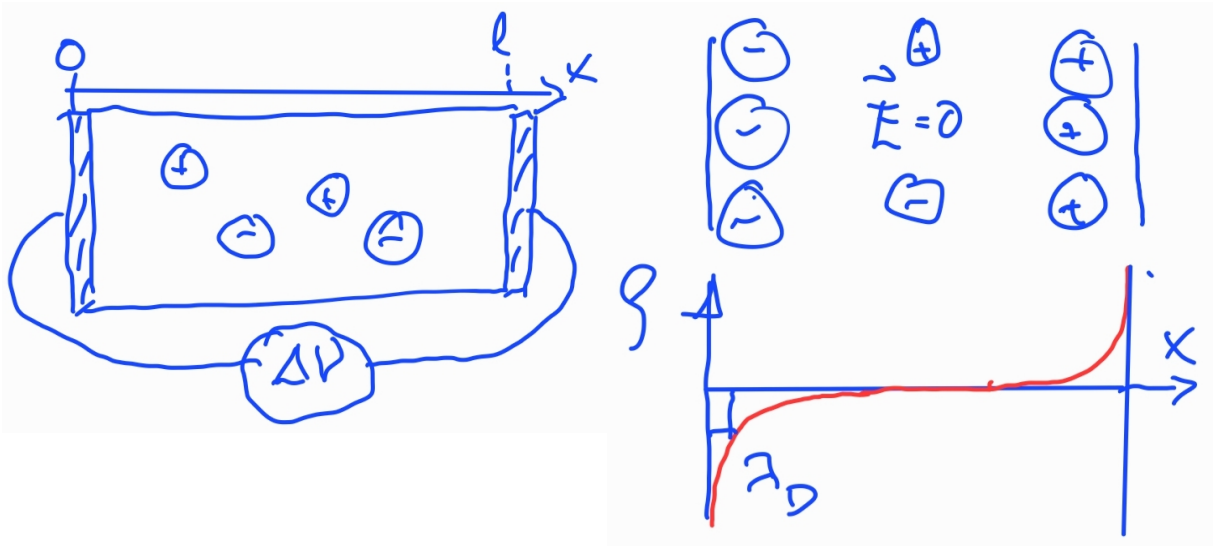


Figure 5: The potential around a point charge in salt water decays exponentially, over the Debye length.

Around a point charge the solution is $\mathcal{V}(r) = \frac{q}{4\pi\varepsilon r} e^{-r/\lambda_D}$, and near a flat charged surface $\mathcal{V}(x) = \mathcal{V}_0\, e^{-x/\lambda_D}$. Electrostatic interactions in the cell are short-ranged: in physiological saline (150 mM NaCl) $\lambda_D \approx 0.8$ nm, comparable to the size of a small molecule.

Charges at membranes: the Nernst potential



Consider an electrolyte between two electrodes with a potential difference. How do the ions distribute, and what does the field look like? In the bulk the field is screened; it is only non-zero in charged layers of thickness λ_D at the walls.

Use the chemical potential of an ion of charge $q = ze$:

$$\mu_{\text{tot}} = \mu_0 + k_B T \ln \frac{c}{c_0} + q\mathcal{V}.$$

In equilibrium $d\mu_{\text{tot}}/dx = 0$:

$$k_B T \frac{d\ln c}{dx} = -q\frac{d\mathcal{V}}{dx} \quad \Rightarrow \quad k_B T \ln \frac{c_{\text{in}}}{c_{\text{out}}} = -q\left(\mathcal{V}_{\text{in}} - \mathcal{V}_{\text{out}}\right).$$

The potential difference that balances a concentration difference of a permeant ion is the **Nernst potential**:

$$\Delta\mathcal{V} = \mathcal{V}^{\text{Nernst}} = -\frac{k_B T}{ze} \ln \frac{c_{\text{in}}}{c_{\text{out}}}. \tag{6}$$

The thermal voltage is $k_B T/e \approx 25$ mV at room temperature, so a factor 10 in concentration gives about 60 mV.

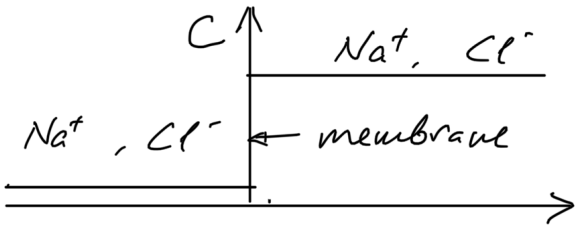


Figure 6: A salt solution on both sides of a membrane.

What happens if no ions can cross the membrane? If only one species can? If both can?

Example: only Na permeates. Far from the membrane each side is neutral, with equal Na and Cl concentrations. Sodium diffuses from high to low concentration. Each ion that crosses carries charge, and a potential difference builds up until it equals the Nernst potential of sodium. Only a tiny number of ions has to cross for this. The excess charges sit in thin layers on each side of the membrane, and chloride rearranges to screen them, within a Debye length.

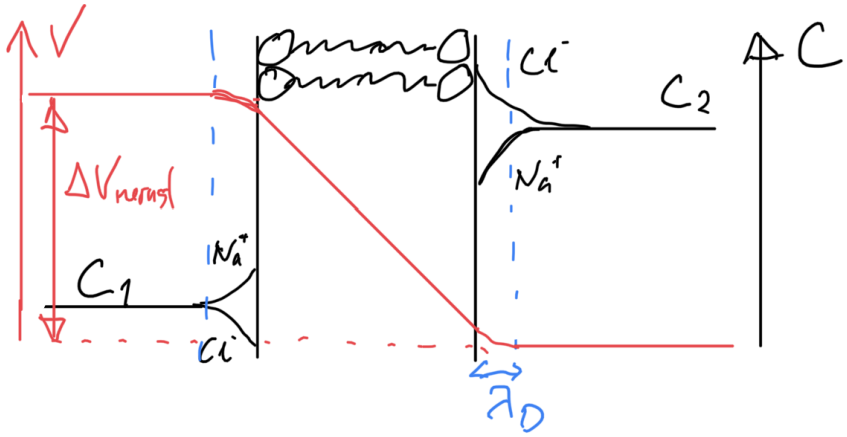


Figure 7: Concentrations and potential across a membrane that only Na can cross. The potential drop $\Delta\mathcal{V}^{\text{Nernst}}$ sits across the membrane; the charged layers have thickness λ_D.

Donnan equilibrium

A cell contains negatively charged macromolecules, mostly proteins, that cannot cross the membrane. The small ions Na , K and Cl can.

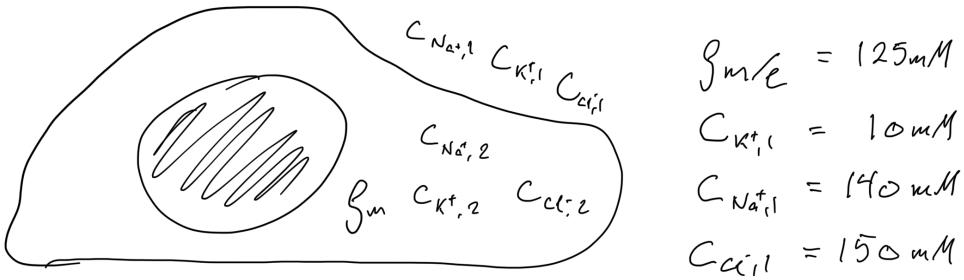


Figure 8: A cell with trapped macroions (charge density ρ_m). Outside: $c_{\text{Na},1} = 140$ mM, $c_{\text{K},1} = 10$ mM, $c_{\text{Cl},1} = 150$ mM; $\rho_m/e = -125$ mM.

In equilibrium every permeant ion obeys Eq. 6 *with the same* $\Delta\mathcal{V}$. With 1 for outside and 2 for inside:

$$\frac{e\,\Delta\mathcal{V}}{k_B T} = -\ln\frac{c_{\text{Na},2}}{c_{\text{Na},1}} = -\ln\frac{c_{\text{K},2}}{c_{\text{K},1}} = \ln\frac{c_{\text{Cl},2}}{c_{\text{Cl},1}},$$

or, exponentiated, the **Donnan relation**

$$\frac{c_{\mathrm{Na},2}}{c_{\mathrm{Na},1}} = \frac{c_{\mathrm{K},2}}{c_{\mathrm{K},1}} = \frac{c_{\mathrm{Cl},1}}{c_{\mathrm{Cl},2}} \equiv r.$$

Together with neutrality inside the cell,

$$c_{\mathrm{Na},2} + c_{\mathrm{K},2} - c_{\mathrm{Cl},2} + \frac{\rho_m}{e} = 0,$$

this gives three equations for the three unknown concentrations: $150r - 150/r - 125 = 0$, so $r = 1.5$ and

$$c_{\mathrm{Na},2} = 210 \text{ mM}, \quad c_{\mathrm{K},2} = 15 \text{ mM}, \quad c_{\mathrm{Cl},2} = 100 \text{ mM}, \qquad \Delta\mathcal{V} = -\frac{k_B T}{e} \ln 1.5 \approx -10 \text{ mV}.$$

Trapped macroions alone create a resting potential. But there is a problem. The macroions are few (each carries many charges), so the inside has $210 + 15 + 100 = 325$ mM of osmotically active particles against 300 mM outside. The resulting osmotic pressure is

$$\Delta P = RT\,\Delta c = 8.3 \cdot 310 \cdot 25 \text{ Pa} \approx 6.4 \times 10^4 \text{ Pa}$$

(25 mM = 25 mol/m³), about 0.6 bar. A cell without a cell wall would burst. Plants and bacteria have rigid walls and live with this "turgor" pressure. Animal cells instead **pump ions**, as described in Membrane potentials and ion pumps.