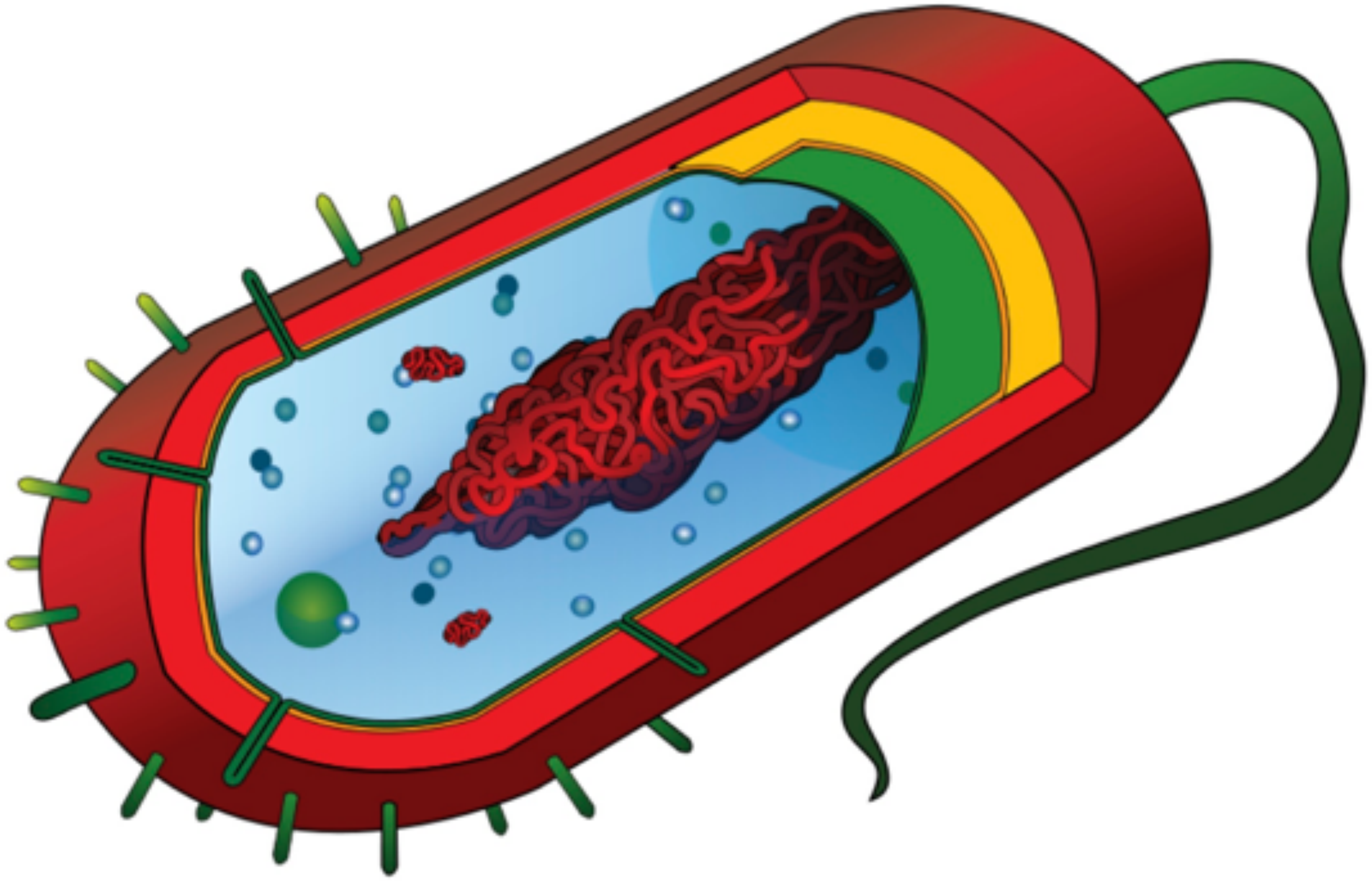
MAE 545: Lecture 11 (10/22)

Thermodynamics of the cell environment



Gibbs free energy

$$\boxed{G = E + pV - TS = \sum_i N_i \mu_i}$$

energy

pressure, volume

temperature, entropy

chemical potential of component *i*

Derivatives of system energy

$$dE = TdS - pdV + \sum_i \mu_i dN_i$$

$$T = \left(\frac{\partial E}{\partial S}\right)_{V,N_i} \qquad p = -\left(\frac{\partial E}{\partial V}\right)_{S,N_i}$$

$$\mu_i = \left(\frac{\partial E}{\partial N_i}\right)_{S,V}$$

Derivatives of Gibbs free energy

$$dG = -SdT + Vdp + \sum_i \mu_i dN_i$$

$$S = -\left(\frac{\partial G}{\partial T}\right)_{p,N_i} \qquad V = \left(\frac{\partial G}{\partial p}\right)_{T,N_i}$$

$$\mu_i = \left(\frac{\partial G}{\partial N_i}\right)_{T,p}$$

In thermodynamic equilibrium system minimizes Gibbs free energy, when temperature *T* and pressure *p* are fixed!

Charge dissociation in solution

example
NaCl salt

binding energy

$$-E_b$$

entropy

$$k_B \ln v_0 \leftarrow$$ some characteristic volume

interaction energy

$$\approx 0$$

entropy

$$k_B \ln(V/N)$$

volume of the whole system

number of dissociated pairs

Free energy change for charge dissociation

$$\Delta G = \Delta E - T\Delta S = E_b - k_B T \ln(V/N v_0)$$

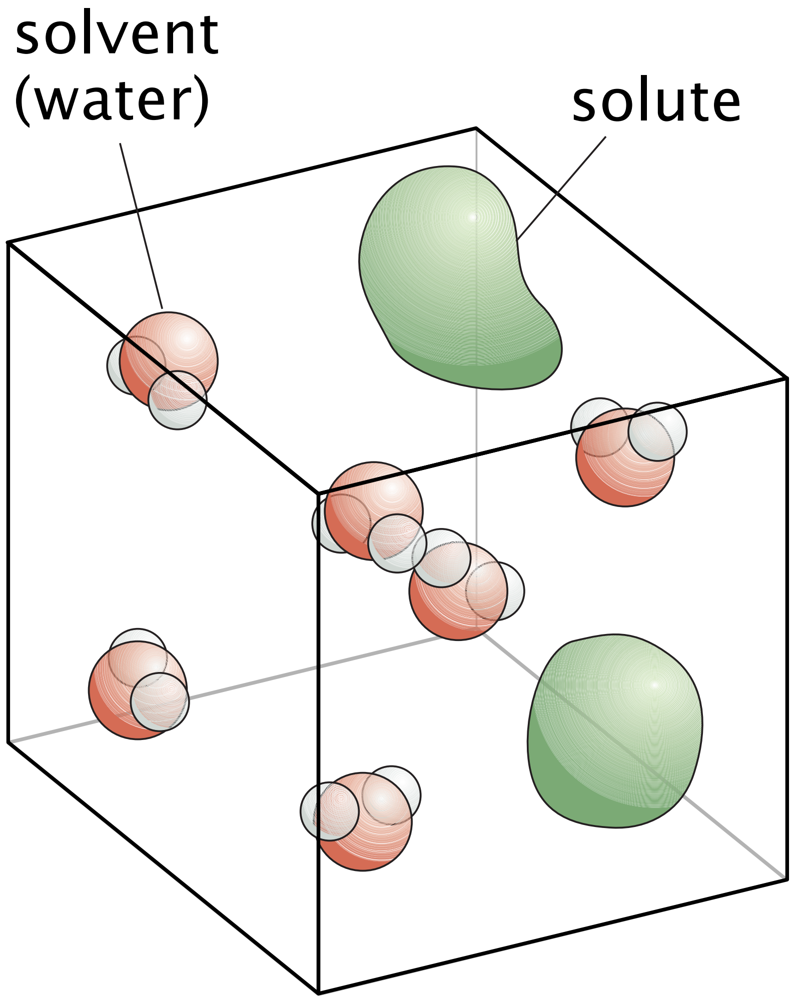
In thermodynamic equilibrium $\Delta G = 0$

$$\boxed{c = \frac{N}{V} = \frac{1}{v_0} e^{-E_b/k_B T}}$$

concentration of dissociated ions

Entropy is the reason why many molecules dissociate and ionize in solution!

Free energy of dilute solutions



Ideal solution: interactions between solute particles are negligible

Gibbs free energy of ideal solution

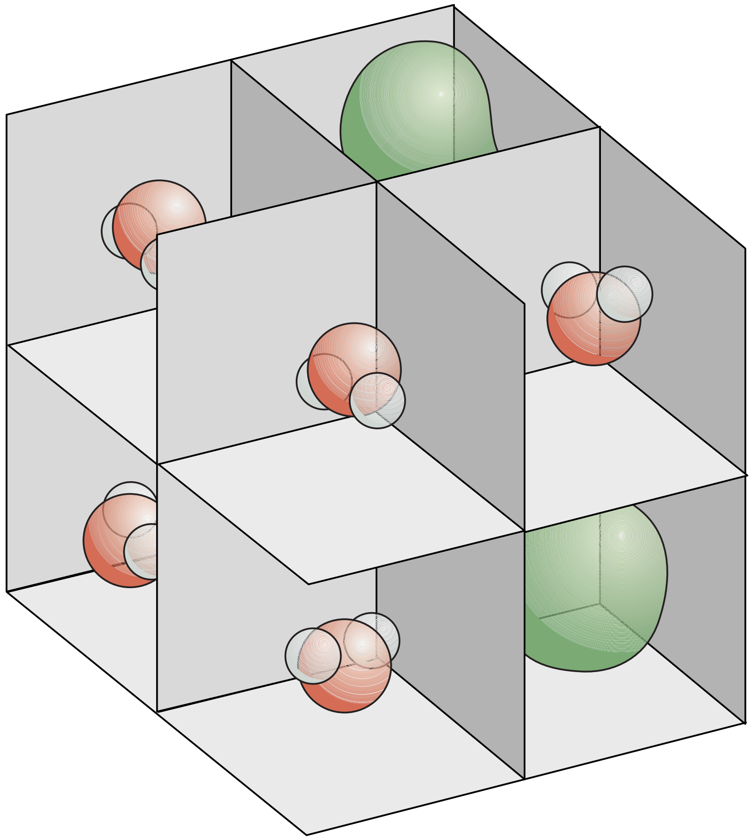
$$\boxed{G = \underbrace{N_{\mathrm{H_2O}}\mu^0_{\mathrm{H_2O}}}_{\text{water free energy}} + \underbrace{N_s\epsilon_s}_{\text{solute energy}} - \underbrace{TS_{\mathrm{mix}}}_{\text{mixing entropy}}}$$

Figure from R. Phillips et al., Physical Biology of the Cell

Mixing entropy of dilute solutions

Let's divide volume in small boxes each containing one water molecule or one solute molecule.

How many different configurations of water and solute molecules are possible?



$$\Omega = \binom{N_{\mathrm{H_2O}} + N_s}{N_s} = \frac{(N_{\mathrm{H_2O}} + N_s)!}{N_{\mathrm{H_2O}}!N_s!}$$

$$S_{\mathrm{mix}} = k_B \ln \Omega$$

Stirling approximation $\ln N! \approx N \ln N$

$$S_{\mathrm{mix}} \approx k_B \left[N_{\mathrm{H_2O}} \ln\left(\frac{N_{\mathrm{H_2O}} + N_s}{N_{\mathrm{H_2O}}}\right) + N_s \ln\left(\frac{N_{\mathrm{H_2O}} + N_s}{N_s}\right)\right]$$

Small number of solute particles $N_s \ll N_{\mathrm{H_2O}}$

$$S_{\mathrm{mix}} \approx k_B \left[N_s - N_s \ln\left(\frac{N_s}{N_{\mathrm{H_2O}}}\right)\right]$$

Figure from R. Phillips et al., Physical Biology of the Cell

Chemical potentials in dilute solution

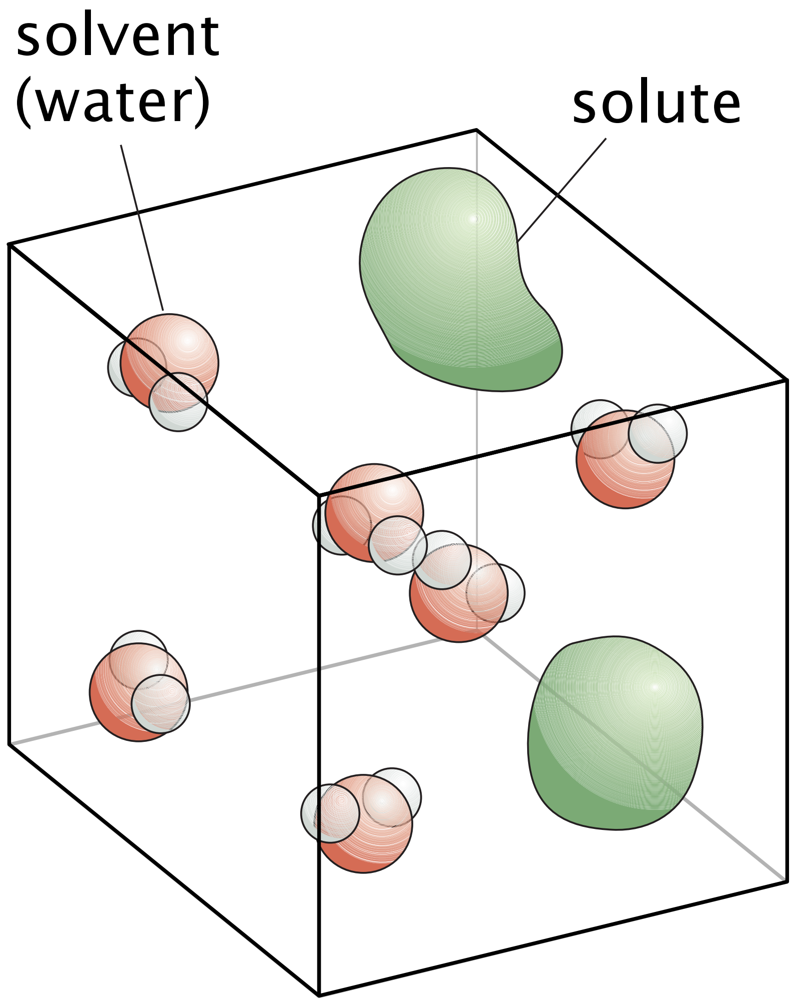


Figure from R. Phillips et al., Physical Biology of the Cell

$$G = N_{\mathrm{H_2O}}\mu^0_{\mathrm{H_2O}} + N_s\epsilon_s - TS_{\mathrm{mix}}$$

$$G \approx N_{\mathrm{H_2O}}\mu^0_{\mathrm{H_2O}} + N_s\epsilon_s + k_BT\left[N_s\ln\left(\frac{N_s}{N_{\mathrm{H_2O}}}\right) - N_s\right]$$

Chemical potential of solute

$$\mu_s = \frac{\partial G}{\partial N_s} = \epsilon_s + k_BT\ln\left(\frac{N_s}{N_{\mathrm{H_2O}}}\right)$$

$$\boxed{\mu_s(T,p,c_s) = \epsilon_s(T,p) + k_BT\ln(c_s v)}$$

solute concentration $c_s = N_s/V$

volume occupied by one water molecule $v = V/N_{\mathrm{H_2O}}$

Chemical potential of water

$$\mu_{\mathrm{H_2O}} = \frac{\partial G}{\partial N_{\mathrm{H_2O}}} = \mu^0_{\mathrm{H_2O}} - k_BT\frac{N_s}{N_{\mathrm{H_2O}}}$$

$$\boxed{\mu_{\mathrm{H_2O}}(T,p,c_s) = \mu^0_{\mathrm{H_2O}}(T,p) - k_BTc_s v}$$

Osmotic pressure

Small water molecules can pass through a semipermeable membrane, which blocks large solute macromolecules.

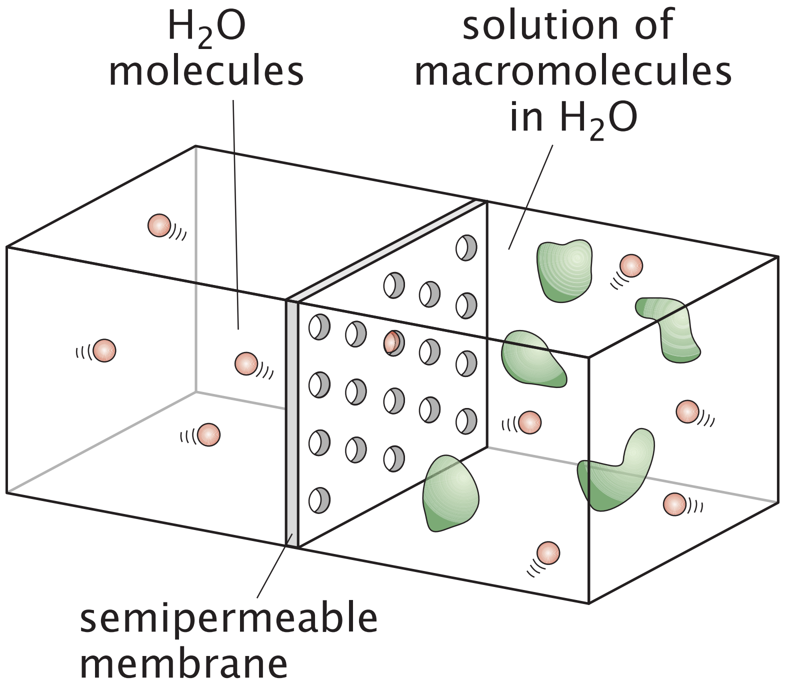


Figure from R. Phillips et al., Physical Biology of the Cell

$$G = N_1 \mu_{\mathrm{H_2O}}(T, p_1, 0) + N_2 \mu_{\mathrm{H_2O}}(T, p_2, c_s) + N_s \mu_s(T, p_2, c_s)$$

In thermodynamic equilibrium the Gibbs free energy *G* is minimized, which means that chemical potentials of water are the same on both sides of the semipermeable membrane!

$$\boxed{\mu_{\mathrm{H_2O}}(T, p_1, 0) = \mu_{\mathrm{H_2O}}(T, p_2, c_s)}$$

Osmotic pressure

Water flows from region of low concentration of macromolecules to region of large concentrations. This additional water increases pressure and the water stops flowing once the osmotic pressure is reached.

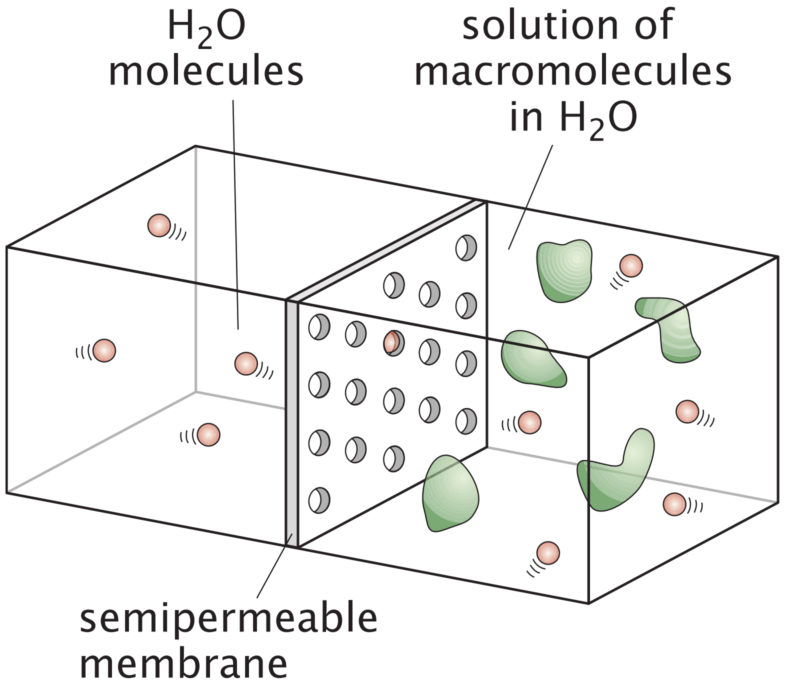


Figure from R. Phillips et al., Physical Biology of the Cell

$$\mu_{\mathrm{H_2O}}(T,p_1,0)=\mu_{\mathrm{H_2O}}(T,p_2,c_s)$$

v

$$\mu_{\mathrm{H_2O}}(T,p_2,c_s)=\mu^0_{\mathrm{H_2O}}(T,p_2)-k_BTc_sv$$

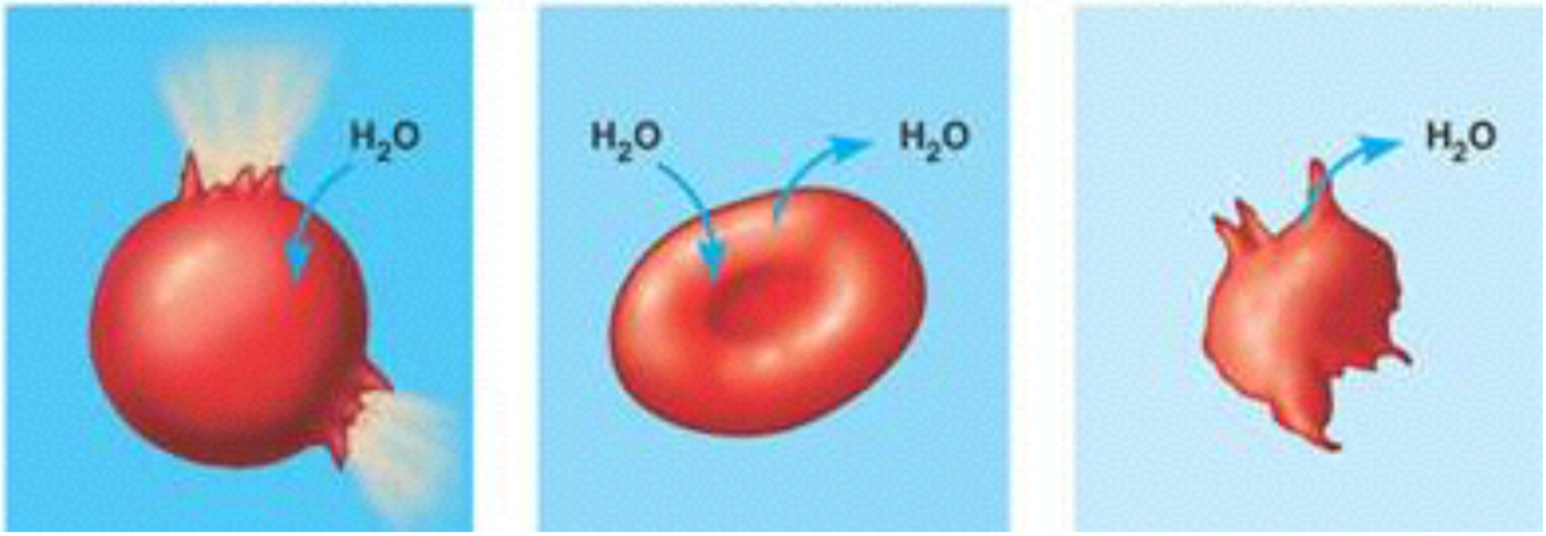
$$\mu_{\mathrm{H_2O}}(T,p_2,c_s)\approx\mu^0_{\mathrm{H_2O}}(T,p_1)+\left(\frac{\partial\mu^0_{\mathrm{H_2O}}}{\partial p}\right)(p_2-p_1)-k_BTc_sv$$

$$\boxed{\Pi=p_2-p_1=k_BT\Delta c_s}$$

Osmotic pressure depends only on temperature and concentration difference across the membrane!

Osmotic pressure in cells

If extracellular solution has different concentration of ions from the interior of cells, then the resulting flow of water can cause the cell to shrink or swell and even burst.



hypotonic solution

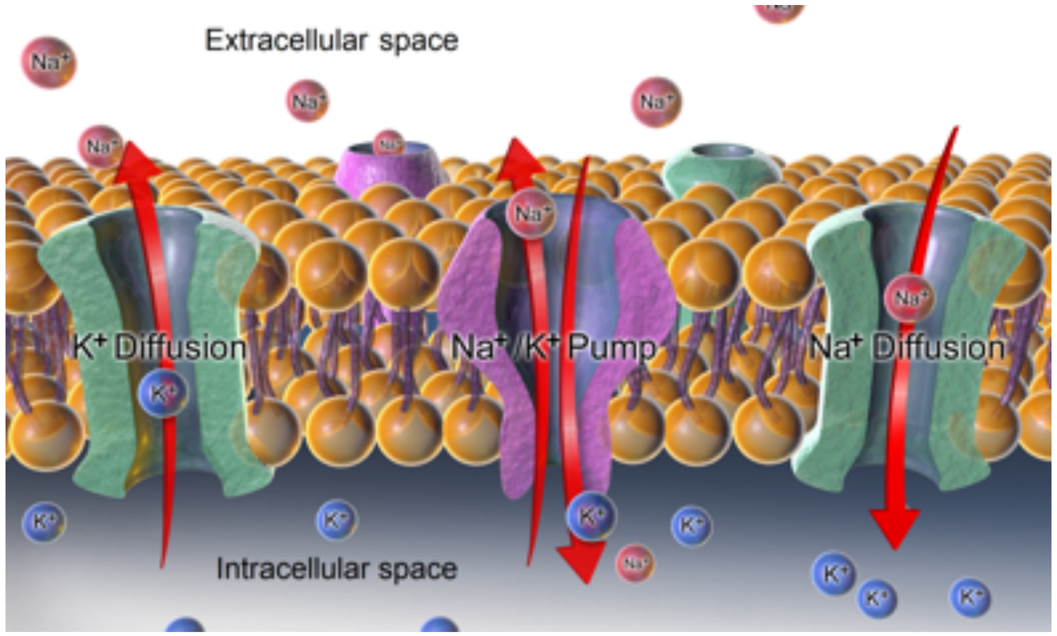
$c_{s,\mathrm{out}} \ll c_{s,\mathrm{in}}$

isotonic solution

$c_{s,\mathrm{out}} \sim c_{s,\mathrm{in}}$

hypertonic solution

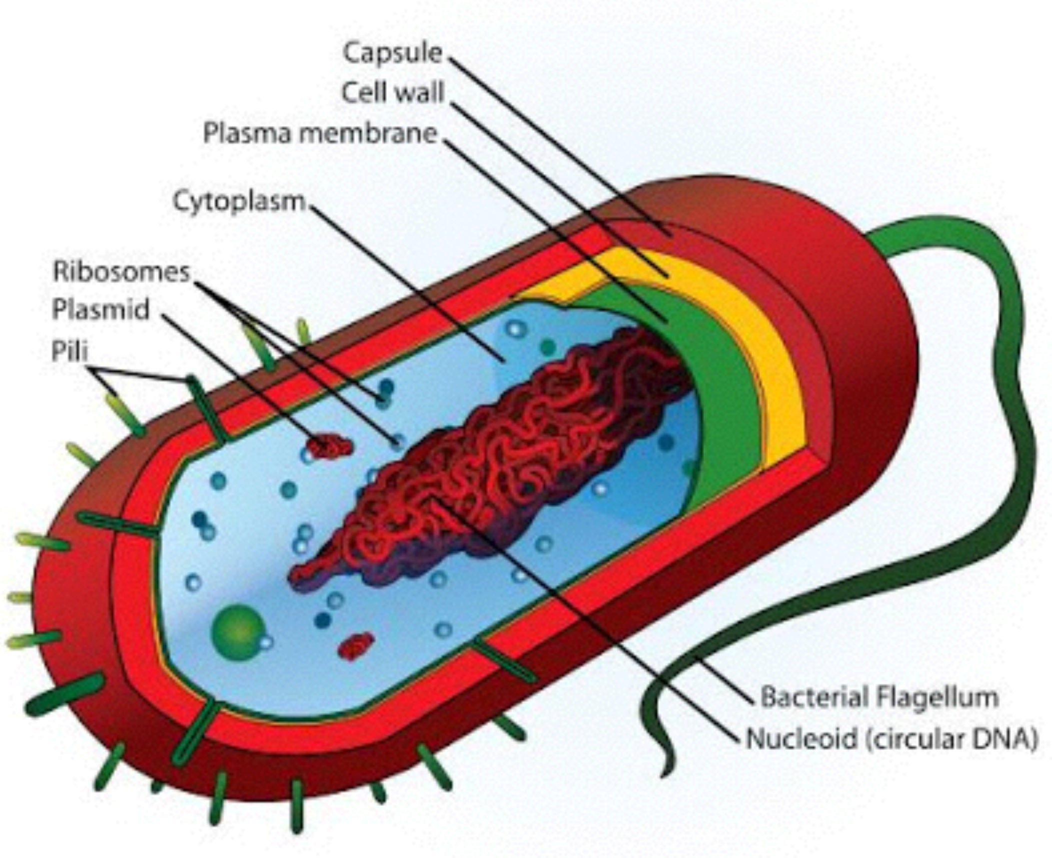
$c_{s,\mathrm{out}} \gg c_{s,\mathrm{in}}$



Cells use ion channels and ion pumps to regulate concentration of ions and therefore also the cell volume.

(Note: cell membrane is impermeable for charged particles)

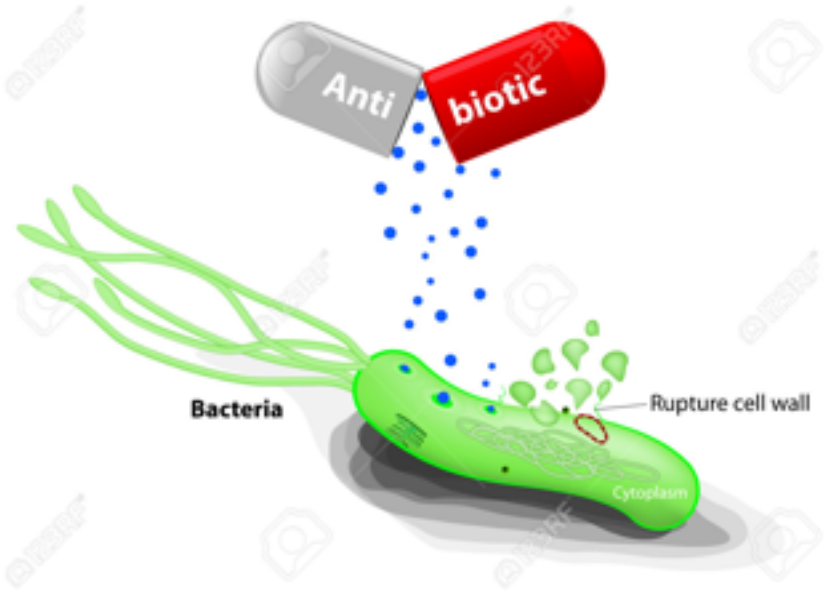
Osmotic pressure in bacteria



Bacteria have strong cell wall that can support large osmotic pressure (Turgor pressure).

$$\Pi \sim 10^5 \mathrm{Pa} \sim 1 \mathrm{bar}$$

Antibiotics cause damage to cell wall and as a result cells rupture due to large Turgor pressure.



Energetics of ATP hydrolysis

How much energy is released during ATP hydrolysis?

$$\mathrm{ATP} \longrightarrow \mathrm{ADP} + \mathrm{P_i}$$

$$\Delta G = \mu_{\mathrm{ADP}} + \mu_{\mathrm{P}} - \mu_{\mathrm{ATP}}$$

$$\Downarrow$$

$$\boxed{\Delta G = \underbrace{\mu^0_{\mathrm{ADP}} + \mu^0_{\mathrm{P}} - \mu^0_{\mathrm{ATP}}}_{-12.5 k_B T} + k_B T \ln\left(\frac{[\mathrm{ADP}][\mathrm{P_i}]}{[\mathrm{ATP}]c_0}\right)}$$

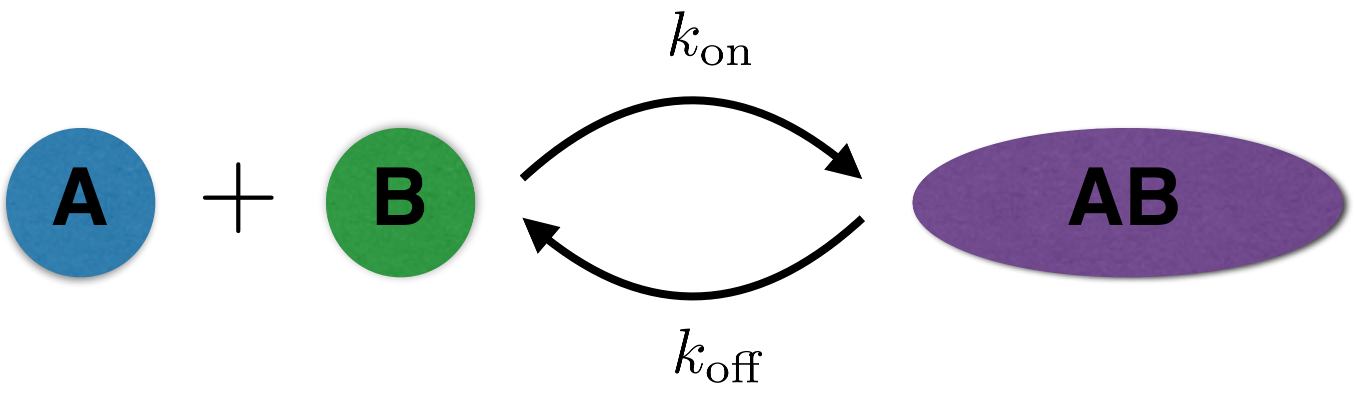
Under physiological conditions: $\Delta G \sim -20 k_B T$

$([\mathrm{ATP}], [\mathrm{ADP}], [\mathrm{P}_i] \sim 1\mathrm{mM})$

Chemical potentials are typically defined relative to concentration c_0 ~ 1 M.

$$\mu_s(c_s) = \mu_s(c_0) + k_B T \ln(c_s/c_0)$$

Law of mass action



example

$$\mathrm{Na^+ + Cl^-} \longleftrightarrow \mathrm{NaCl}$$
$$\mathrm{H^+ + Cl^-} \longleftrightarrow \mathrm{HCl}$$
$$\mathrm{Na^+ + OH^-} \longleftrightarrow \mathrm{NaOH}$$
$$\mathrm{H^+ + OH^-} \longleftrightarrow \mathrm{H_2O}$$

In thermodynamic equilibrium

$$\Delta G = \mu_{AB} - \mu_A - \mu_B = 0$$

$$\boxed{\frac{[\mathrm{A}][\mathrm{B}]}{[\mathrm{AB}]} = c_0 e^{-\left(\mu^0_{\mathrm{A}} + \mu^0_{\mathrm{B}} - \mu^0_{\mathrm{AB}}\right)/k_B T} = K_{\mathrm{eq}}(T, p) = \frac{k_{\mathrm{off}}}{k_{\mathrm{on}}}}$$

For general chemical reaction

$$a_1 \mathrm{R}_1 + a_2 \mathrm{R}_2 + \cdots \longleftrightarrow b_1 \mathrm{P}_1 + b_2 \mathrm{P}_2 + \cdots$$

$$\boxed{\frac{\prod_i [\mathrm{R}_i]^{a_i}}{\prod_j [\mathrm{P}_j]^{b_j}} = c_0^{\left(\sum_i a_i - \sum_j b_j\right)} e^{-\left(\sum_i a_i \mu^0_{\mathrm{R}_i} - \sum_j b_j \mu^0_{\mathrm{P}_j}\right)/k_B T} = K_{\mathrm{eq}}(T, p)}$$

Chemical potentials are typically defined relative to concentration c_0 ~ 1 M.

$$\mu_s(c_s) = \mu_s(c_0) + k_B T \ln(c_s / c_0)$$

pH value of solutions

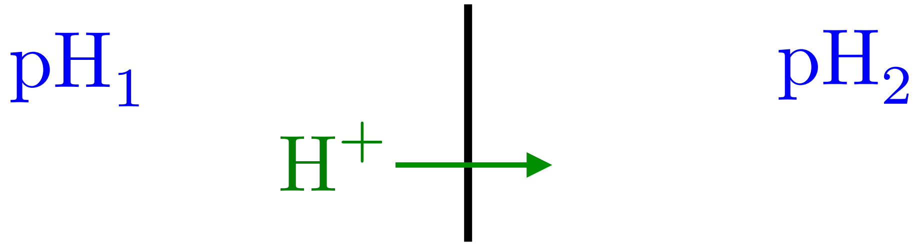
$$\frac{[\mathrm{H}^+][\mathrm{OH}^-]}{c_0^2} = \frac{[\mathrm{H_2O}]K_{\mathrm{eq}}(T,p)}{c_0^2} \approx 10^{-14}$$

$$c_0 = 1\mathrm{M}$$

at room temperature

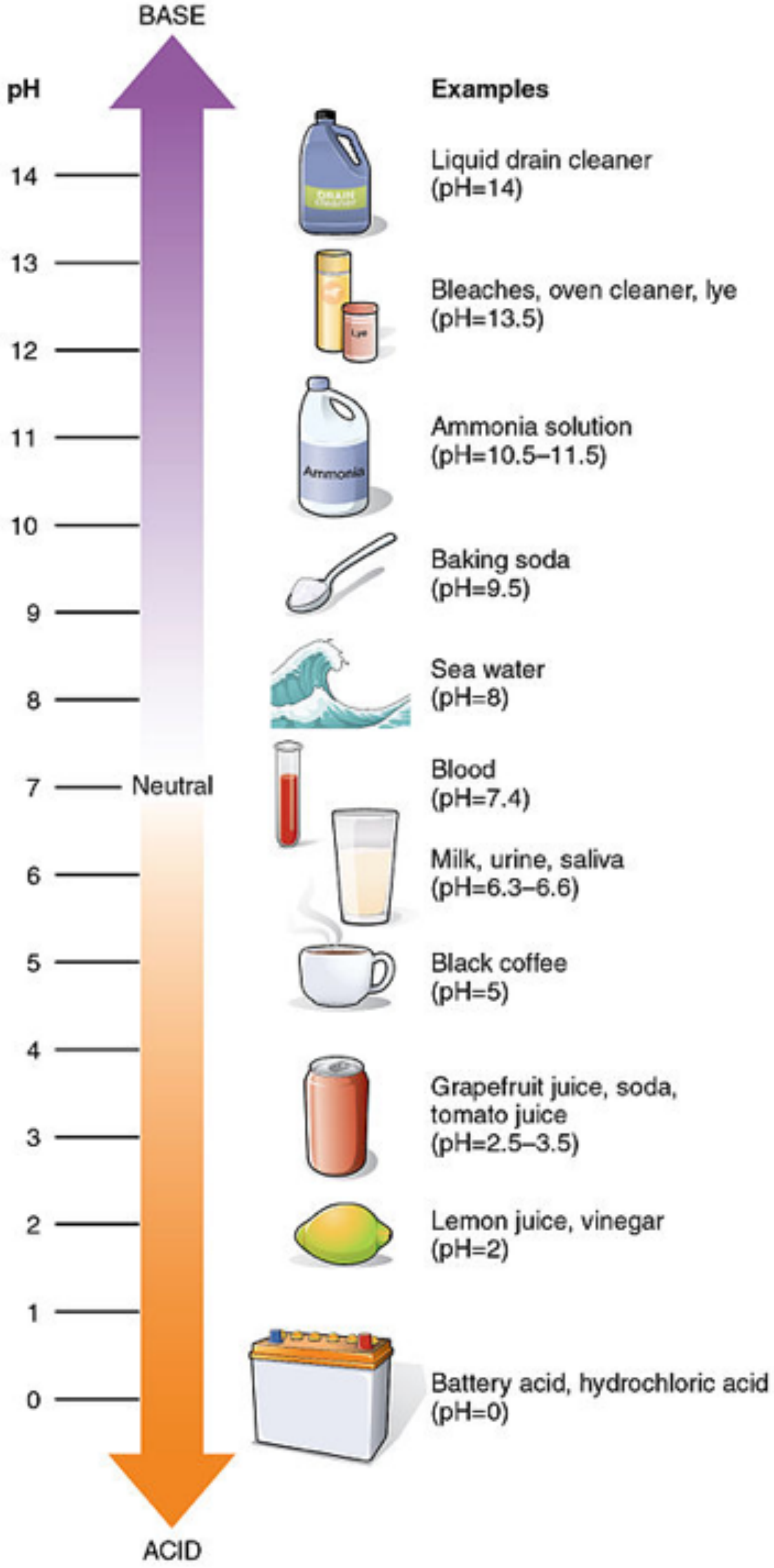
$$\boxed{\begin{aligned} \mathrm{pH} &= -\log_{10}\left([\mathrm{H}^+]/c_0\right) \\ \mathrm{pOH} &= -\log_{10}\left([\mathrm{OH}^-]/c_0\right) \approx 14 - \mathrm{pH} \end{aligned}}$$

How much free energy is changed when H⁺ goes to environment with different pH?

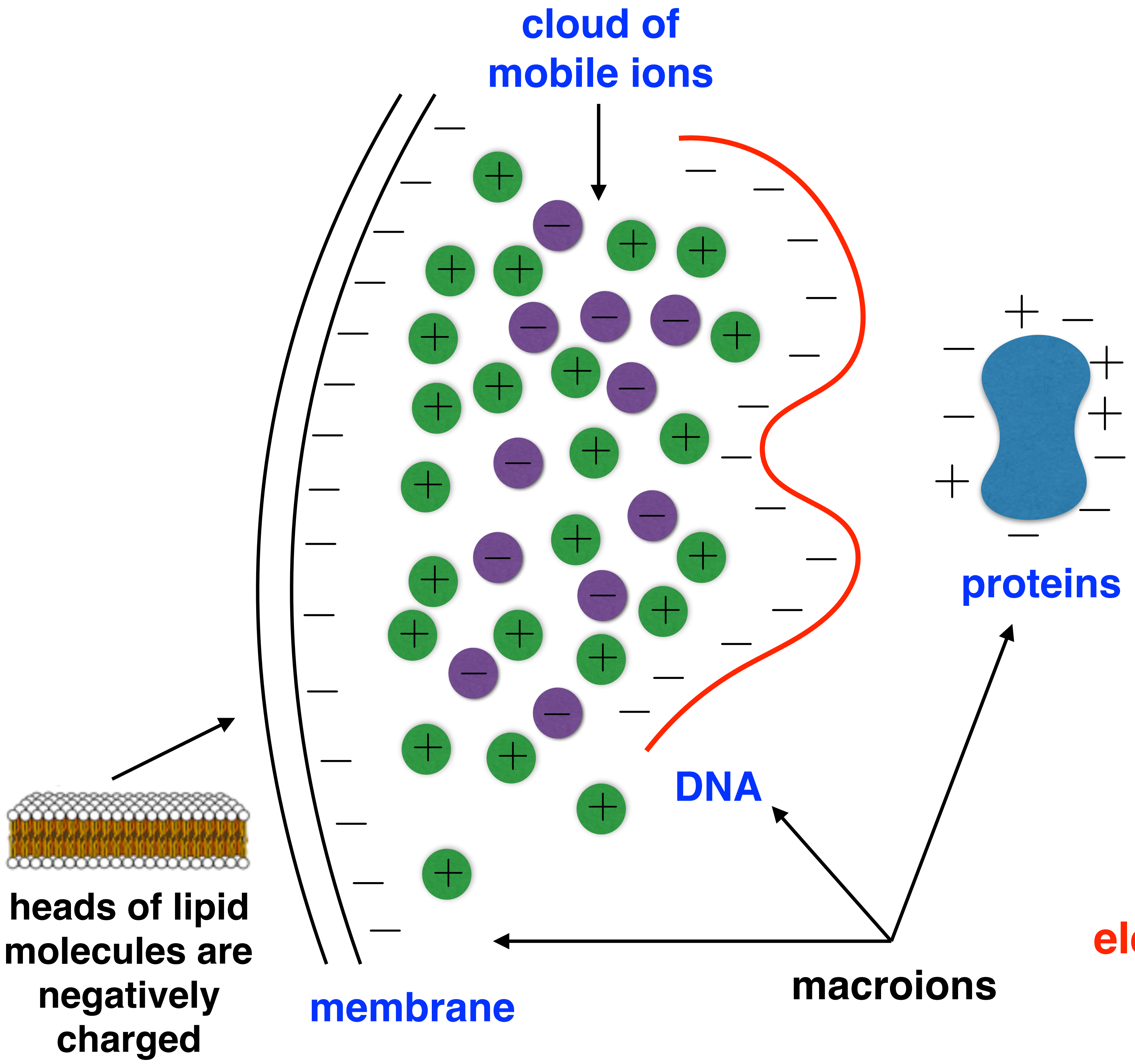


$$\boxed{\begin{aligned} \mu_2 - \mu_1 &= k_B T \ln\left([\mathrm{H}^+]_2/[\mathrm{H}^+]_1\right) \\ E = \frac{\mu_2 - \mu_1}{e_0} &\approx -\frac{2.3026\, k_B T}{e_0}(\mathrm{pH}_2 - \mathrm{pH}_1) \end{aligned}}$$

Nernst electric potential *E*



Charge environment of the cell



cloud of mobile ions

proteins

DNA

heads of lipid molecules are negatively charged

membrane

macroions

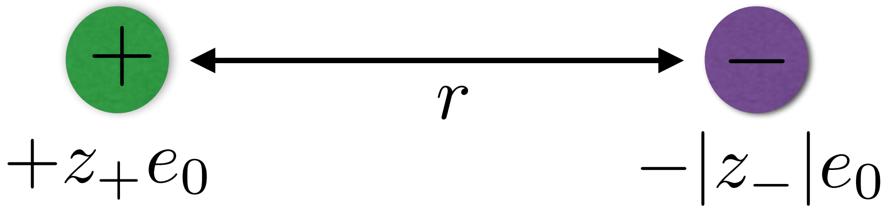
in water some salts completely dissociate

cations	anions
+	–
Na^+	Cl^-
K^+	Cl^-
Ca^{2+}	$2\mathrm{Cl}^-$
Mg^{2+}	$2\mathrm{Cl}^-$

besides salt ions there are also other mobile ions (H^+, electrons, phosphates, …)

Mobile ions screen electrostatic interactions between macroions!

Electrostatic energy



Coulomb's law

$$E_c = \frac{q_1 q_2}{\epsilon r} = \frac{z_+ z_- e_0^2}{\epsilon r}$$

Gaussian units

$$E_c = \frac{q_1 q_2}{4\pi\epsilon_0 \epsilon r} = \frac{z_+ z_- e_0^2}{4\pi\epsilon_0 \epsilon r}$$

SI units

water dielectric constant

$$\epsilon \approx 81$$

vacuum permittivity

$$\epsilon_0 = 8.85 \times 10^{-12} \mathrm{As/Vm}$$

Electrostatic interaction is small for large separation

$$\frac{E_c}{k_B T} = \frac{z_+ z_- \ell_B}{r}$$

Bjerrum length

$$\ell_B = \frac{e_0^2}{k_B T \epsilon}$$

Bjerrum length in water at room T

$$\ell_B \approx 0.7 \mathrm{nm}$$

Poisson-Boltzmann equation

Let's assume some mean-field electric potential $\phi(\vec{r})$ throughout the cell.

Local density of mobile ions carrying charge $z_\alpha e_0$.

$$n_\alpha(\vec{r}) = \overline{n}_\alpha e^{-z_\alpha e_0 \phi(\vec{r})/k_B T}$$

$$\int d^3\vec{r}\, \overline{n}_\alpha e^{-z_\alpha e_0 \phi(\vec{r})/k_B T} = N_\alpha$$

Charge density of mobile ions

$$\rho_{\text{mobile ions}}(\vec{r}) = \sum_\alpha z_\alpha e_0 \overline{n}_\alpha e^{-z_\alpha e_0 \phi(\vec{r})/k_B T}$$

Poisson equation

$$\nabla^2 \phi(\vec{r}) = -\frac{4\pi}{\epsilon} \rho(\vec{r})$$

Poisson-Boltzmann equation

$$\boxed{\nabla^2 \phi(\vec{r}) = -\frac{4\pi}{\epsilon} \left[\rho_{\text{macroions}}(\vec{r}) + \sum_\alpha z_\alpha e_0 \overline{n}_\alpha e^{-z_\alpha e_0 \phi(\vec{r})/k_B T} \right]}$$

For a given distribution of macroions Poisson-Boltzmann equation must be solved self-consistently for the electric potential $\phi(\vec{r})$.

Debye-Hückel approximation

Let's assume that electrostatic energy due to the mean field electric potential is small compared to *$k_B T$*.

Local density of mobile ions carrying charge $z_\alpha e_0$.

$$n_\alpha(\vec{r}) = \overline{n}_\alpha e^{-z_\alpha e_0 \phi(\vec{r})/k_B T}$$

$$n_\alpha(\vec{r}) \approx \overline{n}_\alpha \left(1 - \frac{z_\alpha e_0 \phi(\vec{r})}{k_B T}\right)$$

$$\int d^3\vec{r}\; \overline{n}_\alpha e^{-z_\alpha e_0 \phi(\vec{r})/k_B T} = N_\alpha$$

$$\overline{n}_\alpha \approx N_\alpha / V$$

Charge neutrality

$$\sum_\alpha z_\alpha \overline{n}_\alpha = 0$$

Charge density of mobile ions

$$\rho_{\text{mobile ions}}(\vec{r}) = \sum_\alpha z_\alpha e_0 \overline{n}_\alpha e^{-z_\alpha e_0 \phi(\vec{r})/k_B T}$$

$$\rho_{\text{mobile ions}}(\vec{r}) \approx -\frac{e_0^2 \phi(\vec{r})}{k_B T} \sum_\alpha z_\alpha^2 \overline{n}_\alpha = -\ell_B \epsilon \phi(\vec{r}) \sum_\alpha z_\alpha^2 \overline{n}_\alpha$$

Debye-Hückel approximation

Charge density of mobile ions

$$\rho_{\text{mobile ions}}(\vec{r}) \approx -\frac{e_0^2\phi(\vec{r})}{k_BT}\sum_\alpha z_\alpha^2 \overline{n}_\alpha = -\ell_B\epsilon\phi(\vec{r})\sum_\alpha z_\alpha^2\overline{n}_\alpha$$

Poisson equation

$$\nabla^2\phi(\vec{r}) = -\frac{4\pi}{\epsilon}\left[\rho_{\text{macroions}}(\vec{r}) + \rho_{\text{mobile ions}}(\vec{r})\right]$$

$$\boxed{\nabla^2\phi(\vec{r}) = -\frac{4\pi}{\epsilon}\rho_{\text{macroions}}(\vec{r}) + \frac{\phi(\vec{r})}{\lambda_D^2}}$$

Debye screening length

$$\boxed{\lambda_D^{-2} = 4\pi\ell_B\sum_\alpha z_\alpha^2\overline{n}_\alpha}$$

Electric potential for a point charge

$$\rho_{\text{macroions}}(\vec{r}) = ze_0\delta(\vec{r})$$

$$\boxed{\phi(\vec{r}) = \frac{ze_0}{\epsilon r}e^{-r/\lambda_D}}$$

Electrostatic interaction between macroions

$$\rho_{\text{macroions}}(\vec{r}) = \sum_m z_m e_0\delta(\vec{r}-\vec{r}_m)$$

$$\phi(\vec{r}) = \sum_m \frac{z_m e_0}{\epsilon|\vec{r}-\vec{r}_m|}e^{-|\vec{r}-\vec{r}_m|/\lambda_D}$$

$$\frac{E_{\text{interactions}}}{k_BT} = \ell_B\sum_{m<n}\frac{z_m z_n}{|\vec{r}_m-\vec{r}_n|}e^{-|\vec{r}_m-\vec{r}_n|/\lambda_D}$$