“Life” (or Molecular biology) exists at low Reynolds number, in salty water, and in a thermal bath!

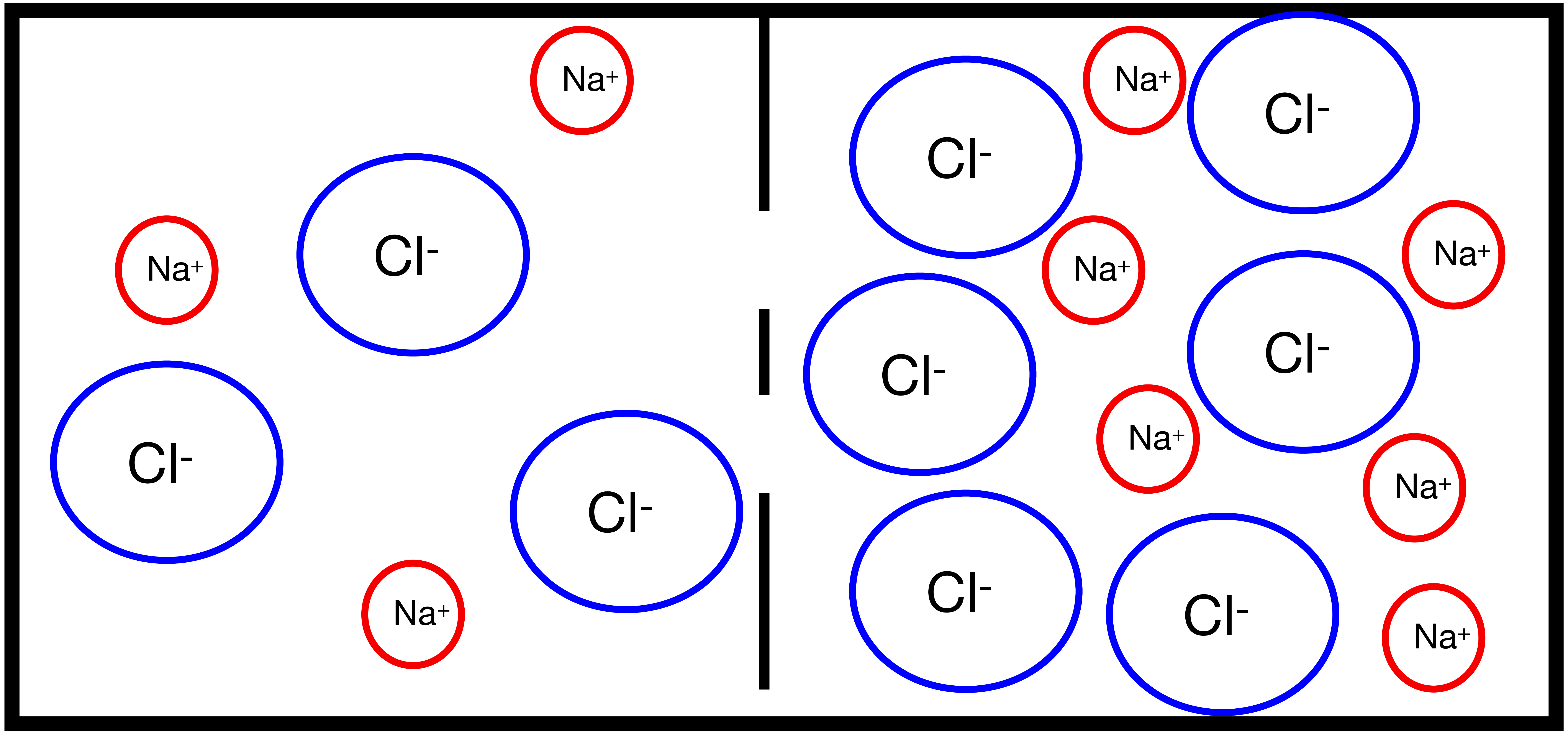
What is the consequence of molecular biology happening in salty water?

Nerve signals! And Coulomb’s law is not the same!

Consider a cell separated by a semi-permeable membrane

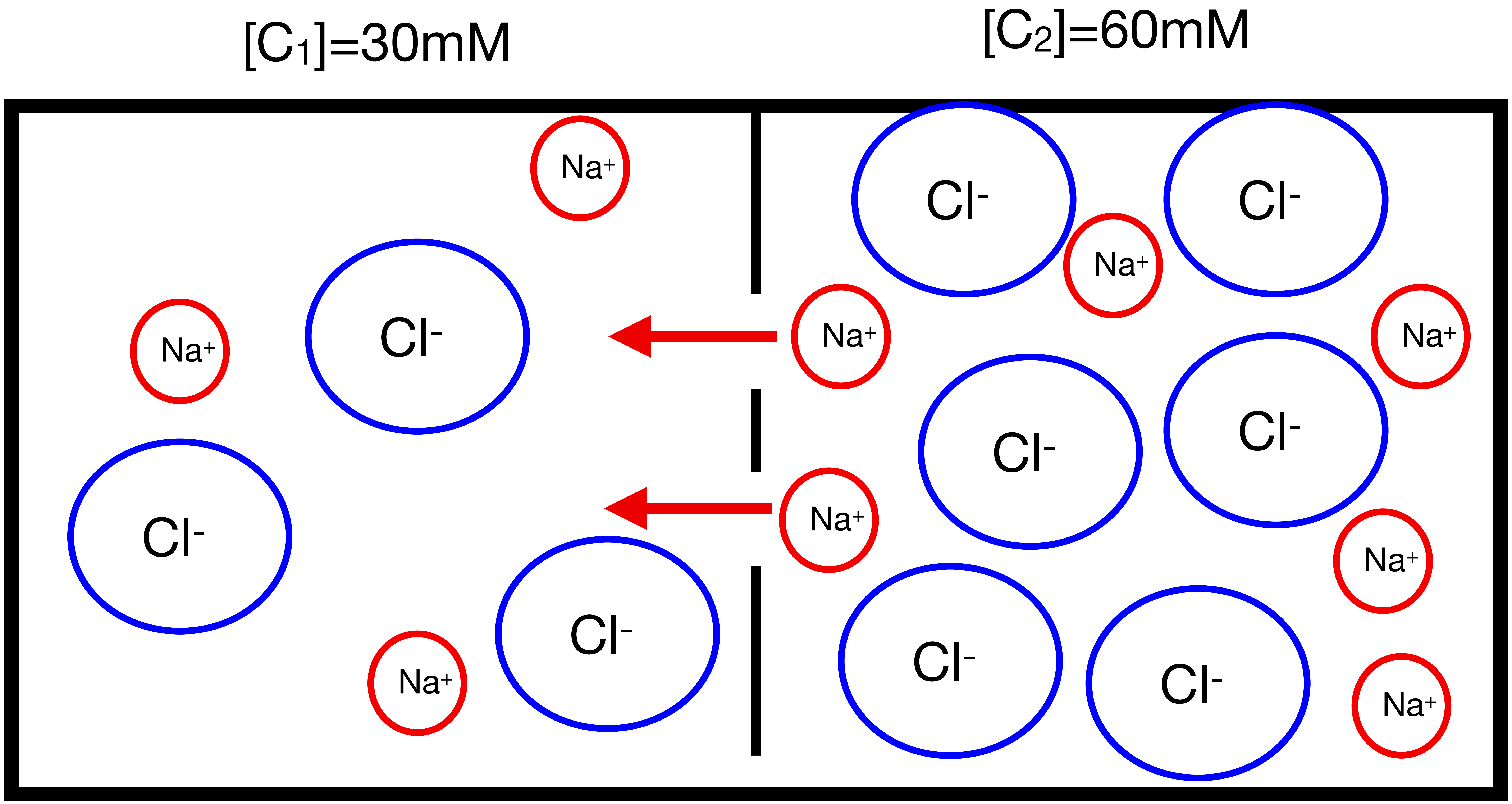
Having two concentration of ions. Only [Na] can diffuse across the membrane. Cl- cannot

$[C_1]=30mM$ $[C_2]=60mM$



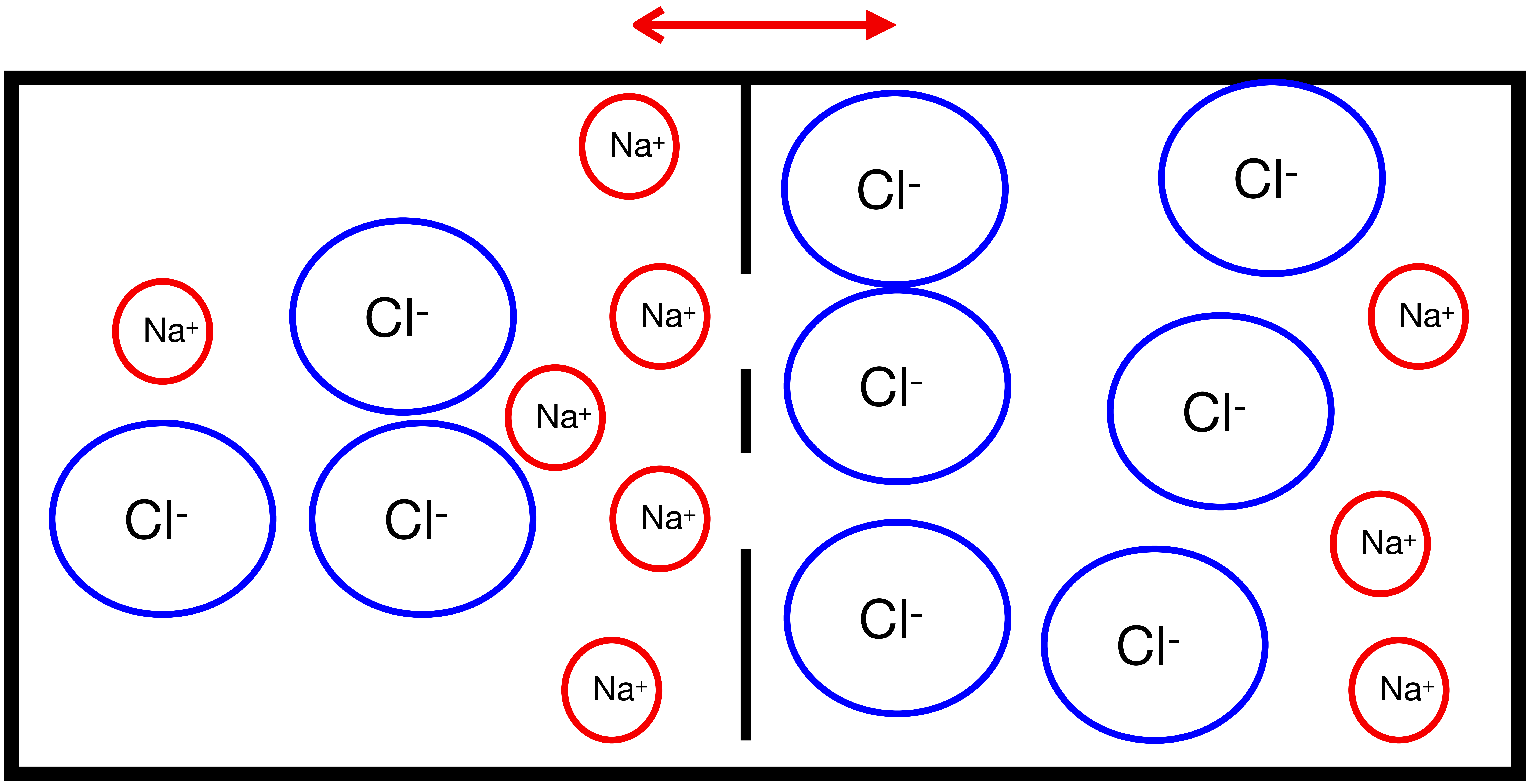
Charge neutral on both sides

Na will diffuse from higher concentration to lower concentration

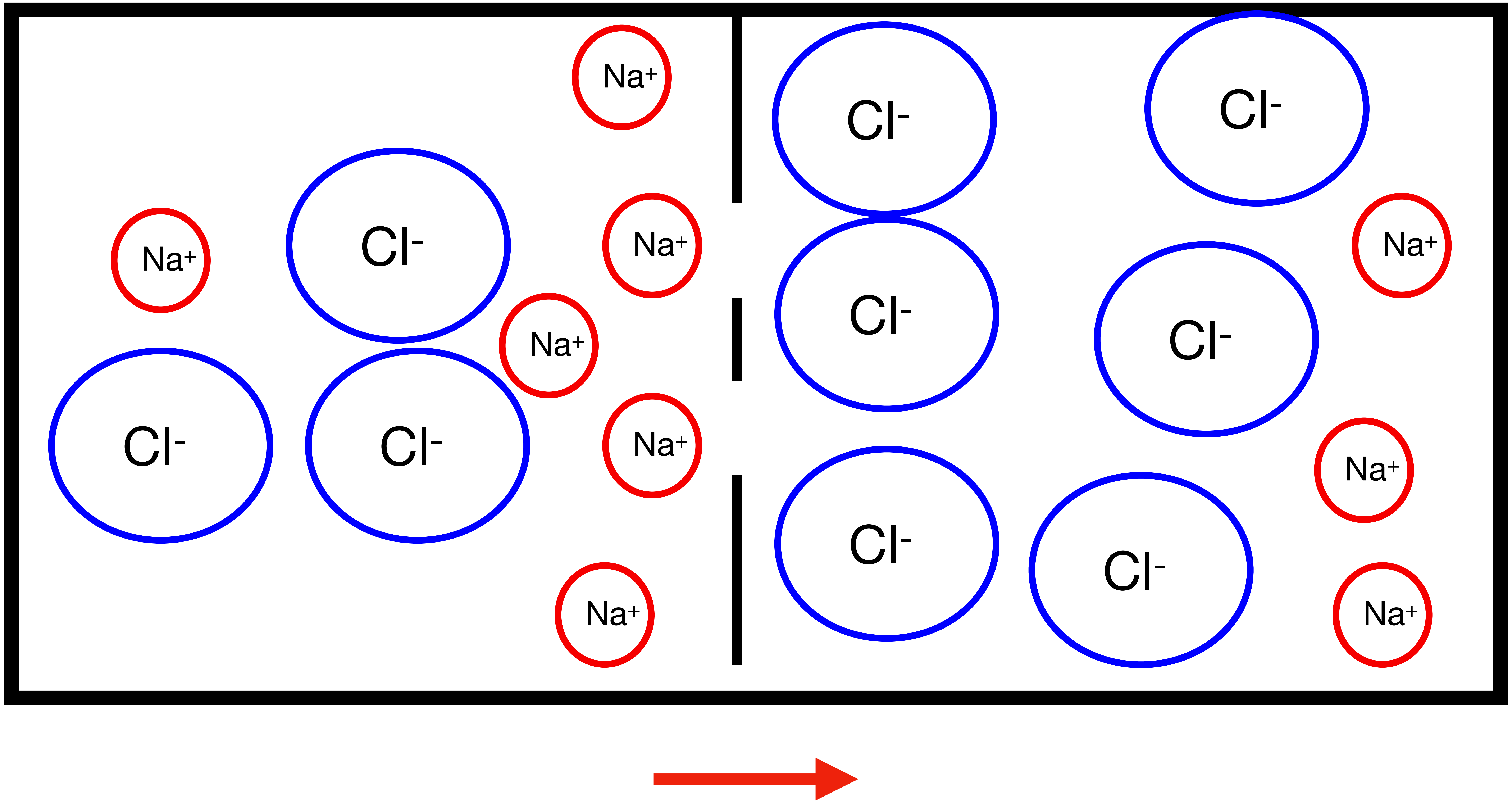


Cl- cannot diffuse through the pore

Opposite charges build up across the membrane

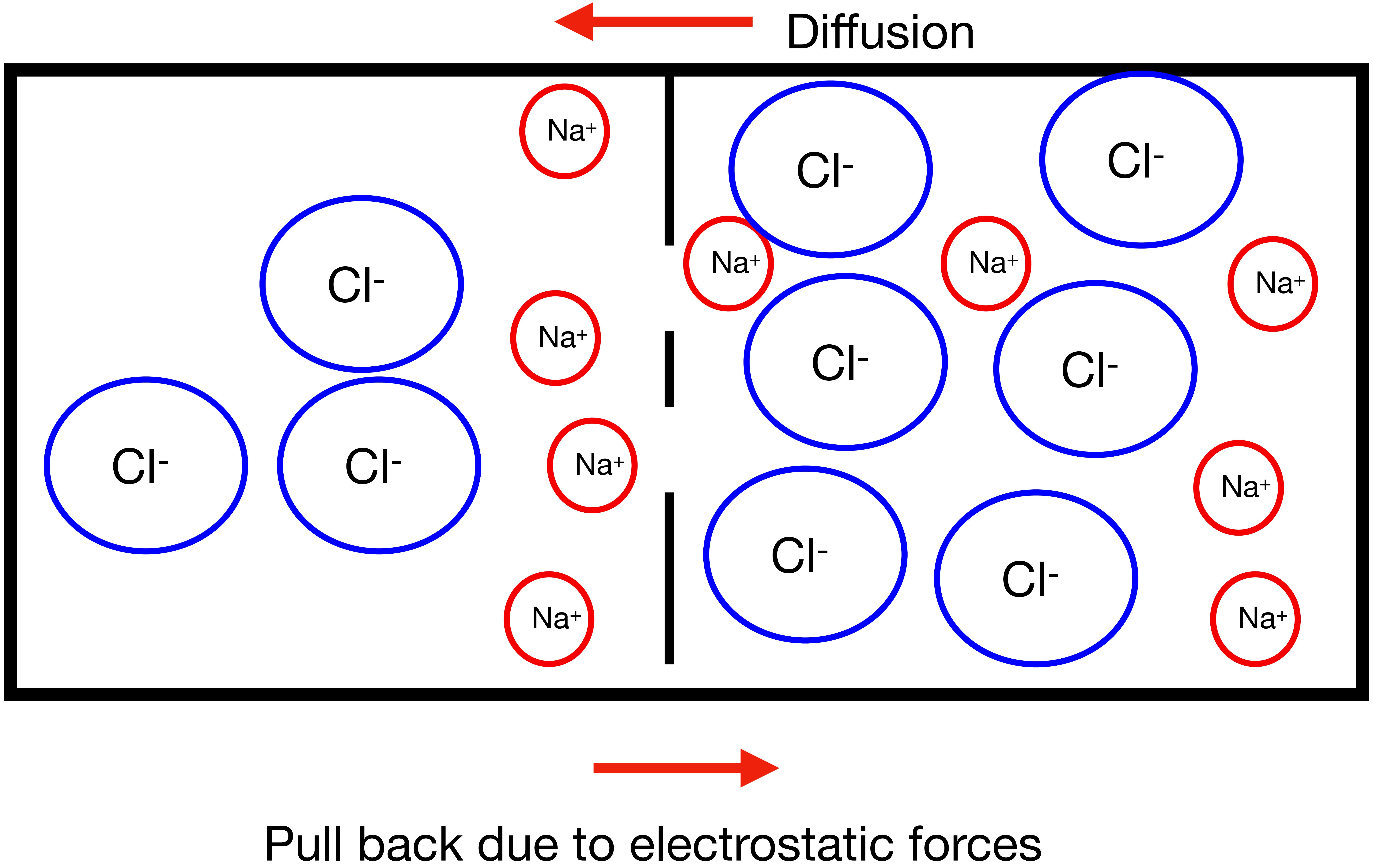


Opposite charges build up across the membrane

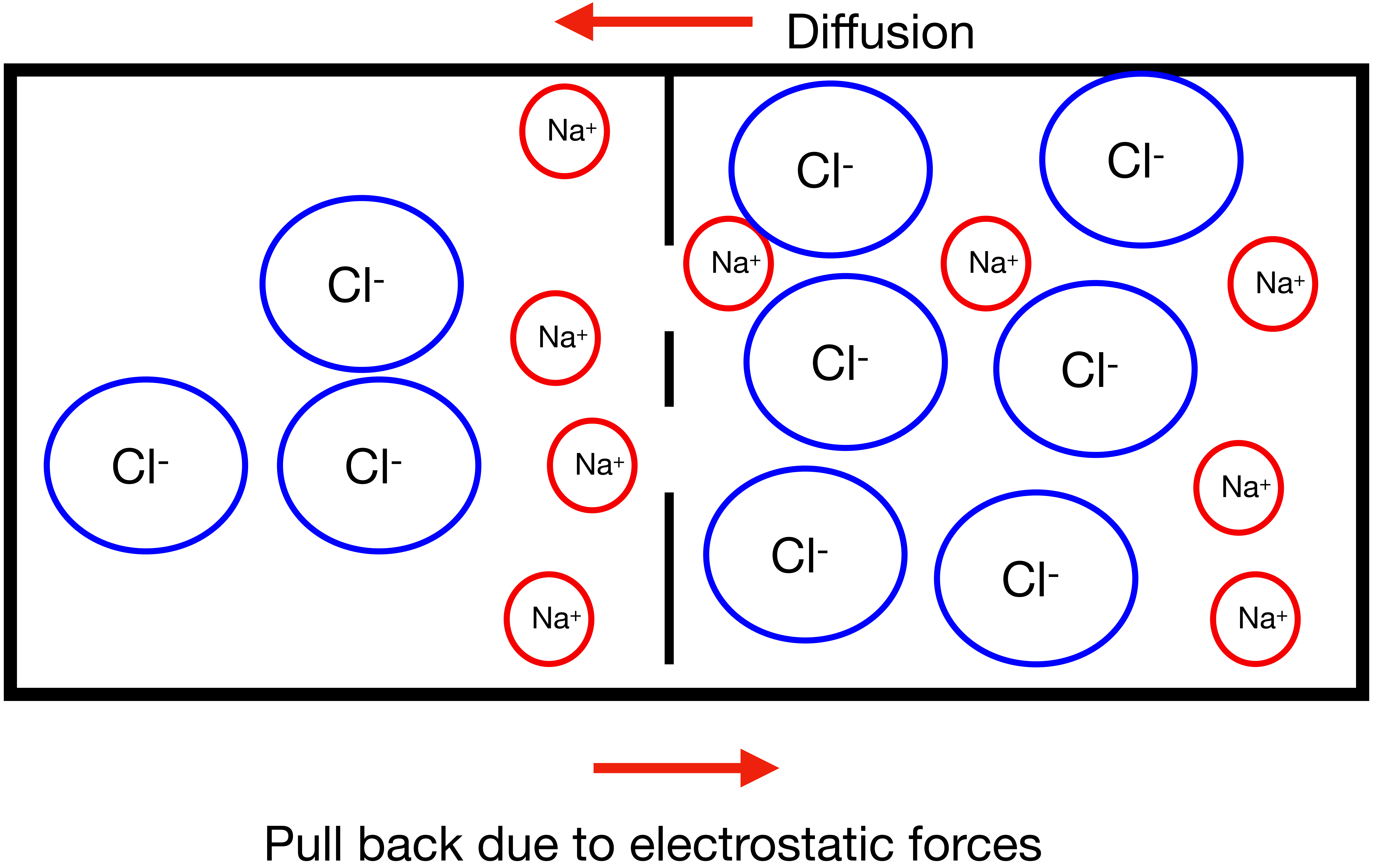


Some Na ions will be pulled back due to electrostatic potential difference

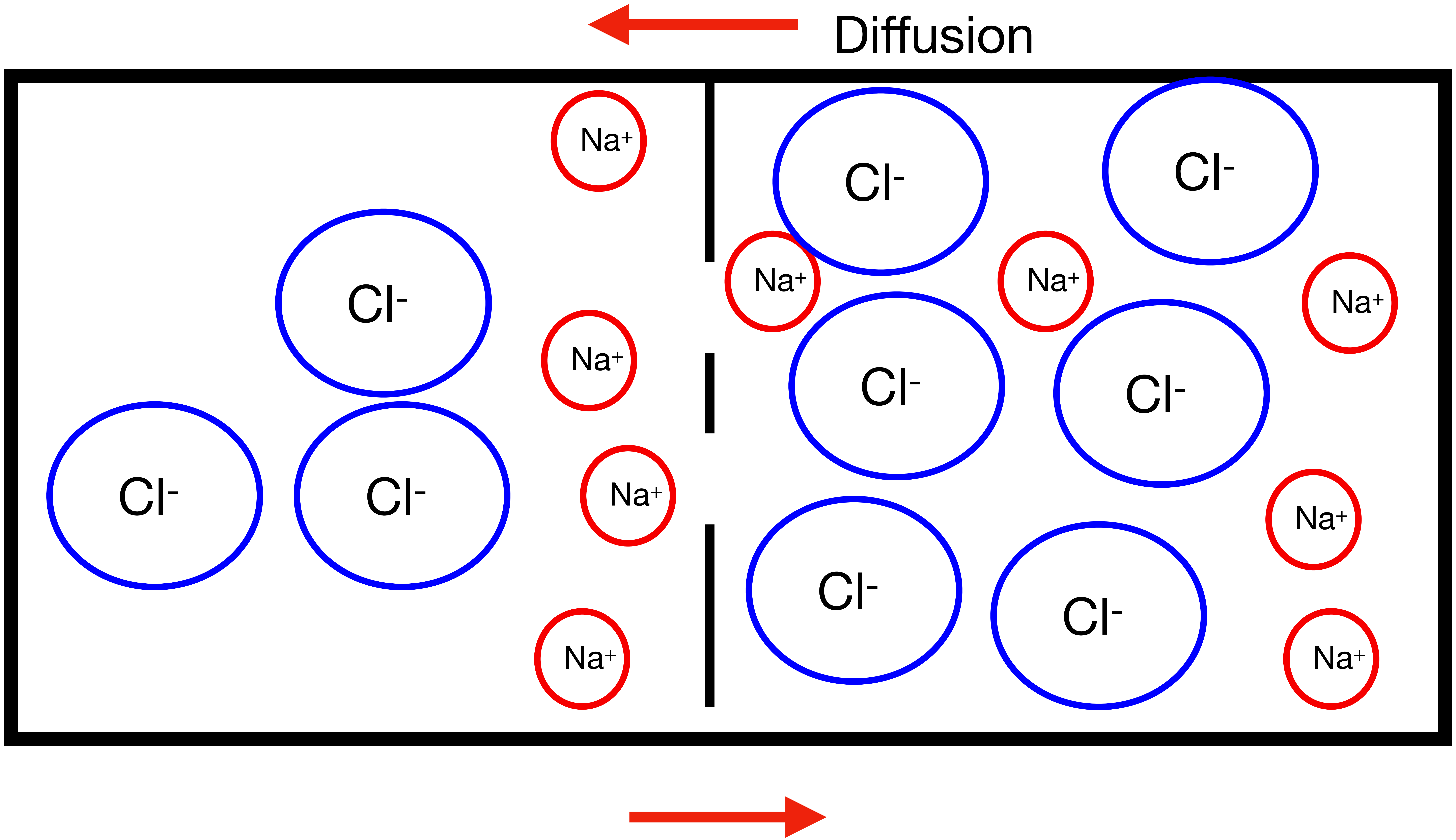
Two flows in the opposite direction



These two opposite flows balance => equilibrium



$$\text{Diffsion flow } \vec{J}_D = -D\frac{\partial C}{\partial x}\hat{x}$$



$$\text{Flow due to electrostaticpotential } \vec{J}_E = c\vec{v} = c\frac{\vec{f}}{6\pi\eta a}$$

These two opposite flows balance => equilibrium

$$D\frac{\partial C}{\partial x} = c\frac{f}{6\pi\eta a}$$

These two opposite flows balance => equilibrium

$$D\frac{\partial C}{\partial x} = c\frac{f}{6\pi\eta a}$$

$$D\frac{\partial C}{\partial x} = c\frac{q\frac{\partial V}{\partial x}}{6\pi\eta a}$$

These two opposite flows balance => equilibrium

$$D\frac{\partial C}{\partial x} = c\frac{q\frac{\partial V}{\partial x}}{6\pi\eta a}$$

$$\frac{dC}{C} = \frac{-q}{D6\pi\eta a}\frac{dV}{dx}dx$$

Integrate both sides

(Note: Converted the partial derivatives to ordinary derivatives because, at equilibrium, the system is independent time, and only position (x) matters)

These two opposite flows balance => equilibrium

$$D\frac{\partial C}{\partial x} = c\frac{q\frac{\partial V}{\partial x}}{6\pi\eta a}$$

$$\int_{x_1}^{x_2} \frac{dC}{C} = \int_{x_1}^{x_2} \frac{q}{D6\pi\eta a}\frac{dV}{dx}dx$$

Integrate both sides

These two opposite flows balance => equilibrium

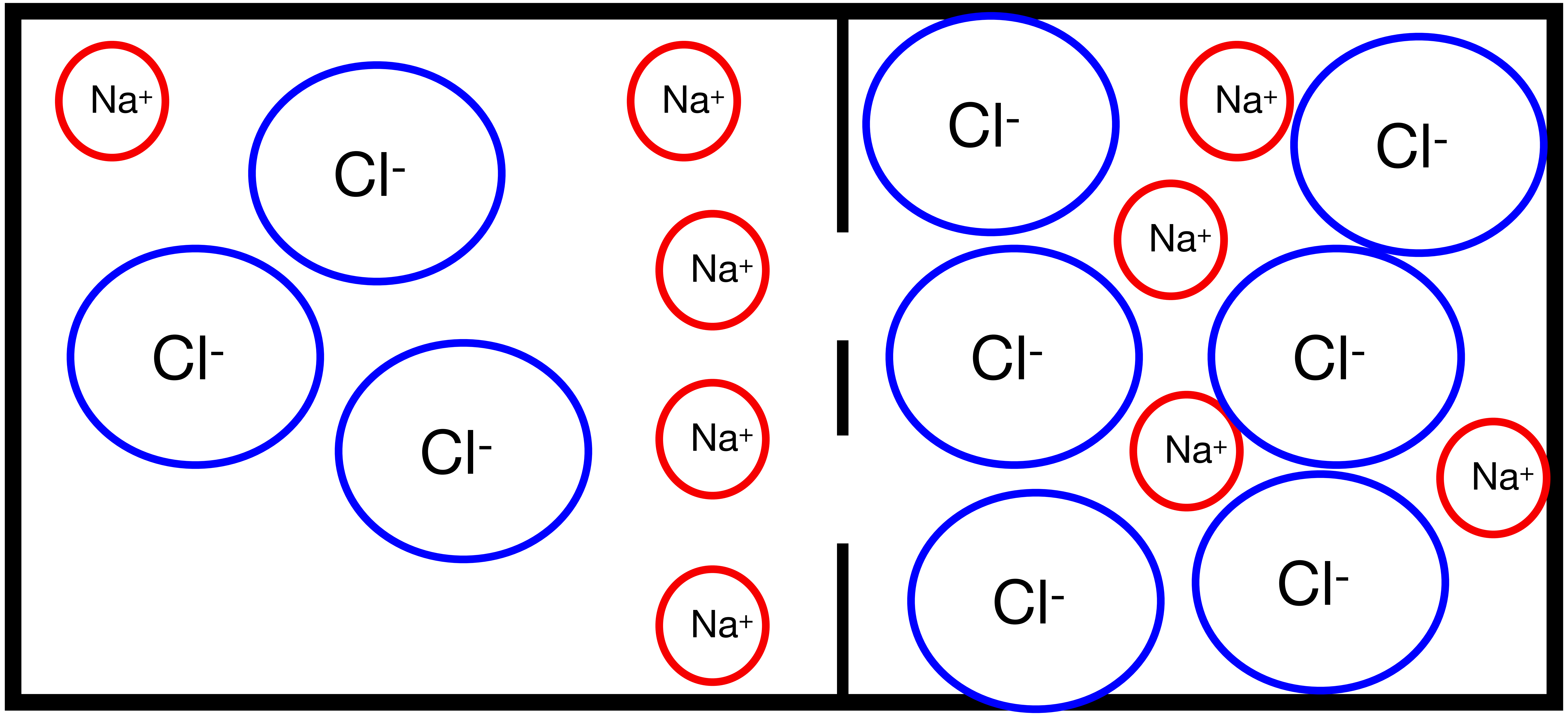
$$\int_{x_1}^{x_2} \frac{dC}{C} = \int_{x_1}^{x_2} \frac{q}{D6\pi\eta a} \frac{dV}{dx} dx$$

$$\frac{k_B T}{q} \ln \frac{C_1}{C_2} = V_1 - V_2$$

Einstein, $D = \dfrac{k_B T}{6\pi\eta a}$

At equilibrium, we get a potential difference across the membrane

$$V_2 - V_1 = \Delta V = \frac{k_B T}{q} \ln \frac{C_1^{eq}}{C_2^{eq}}$$

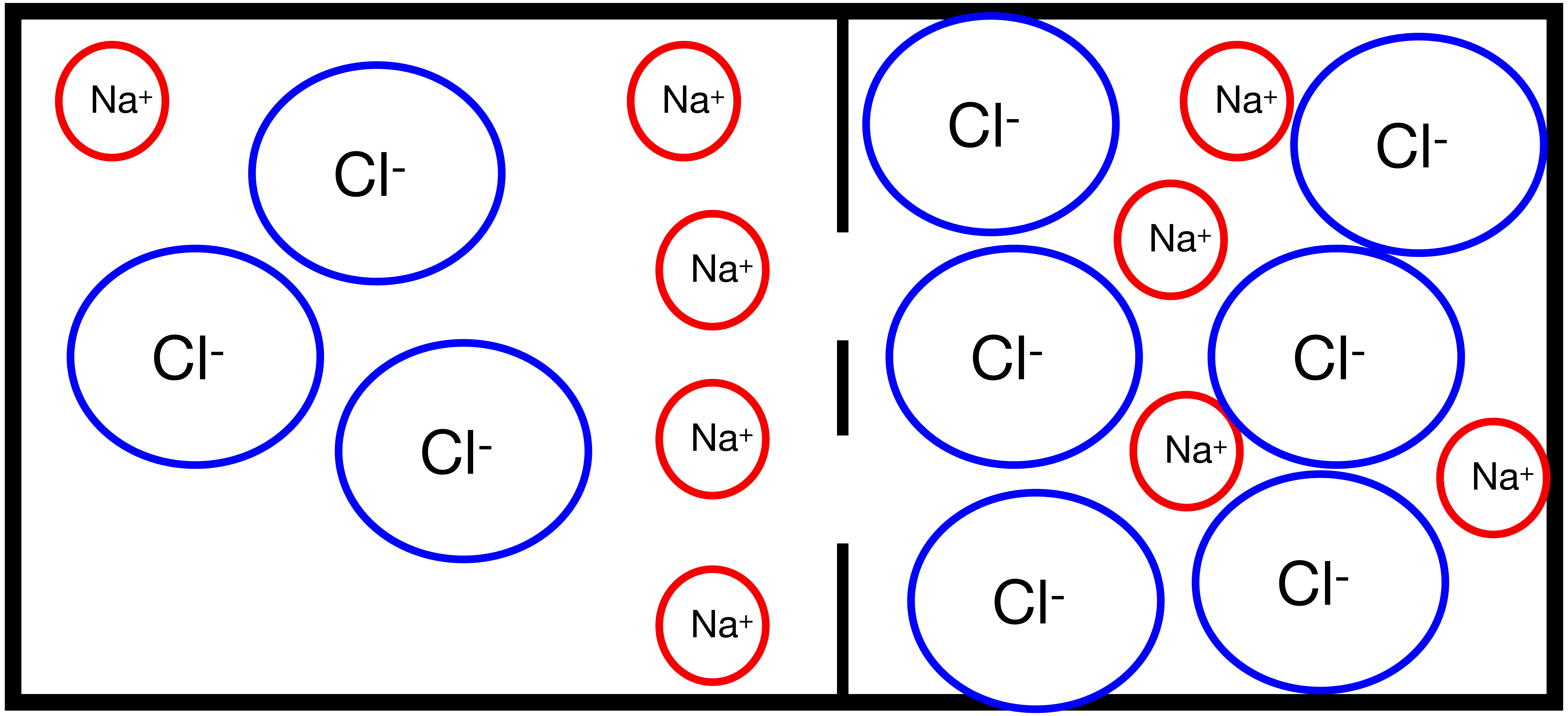


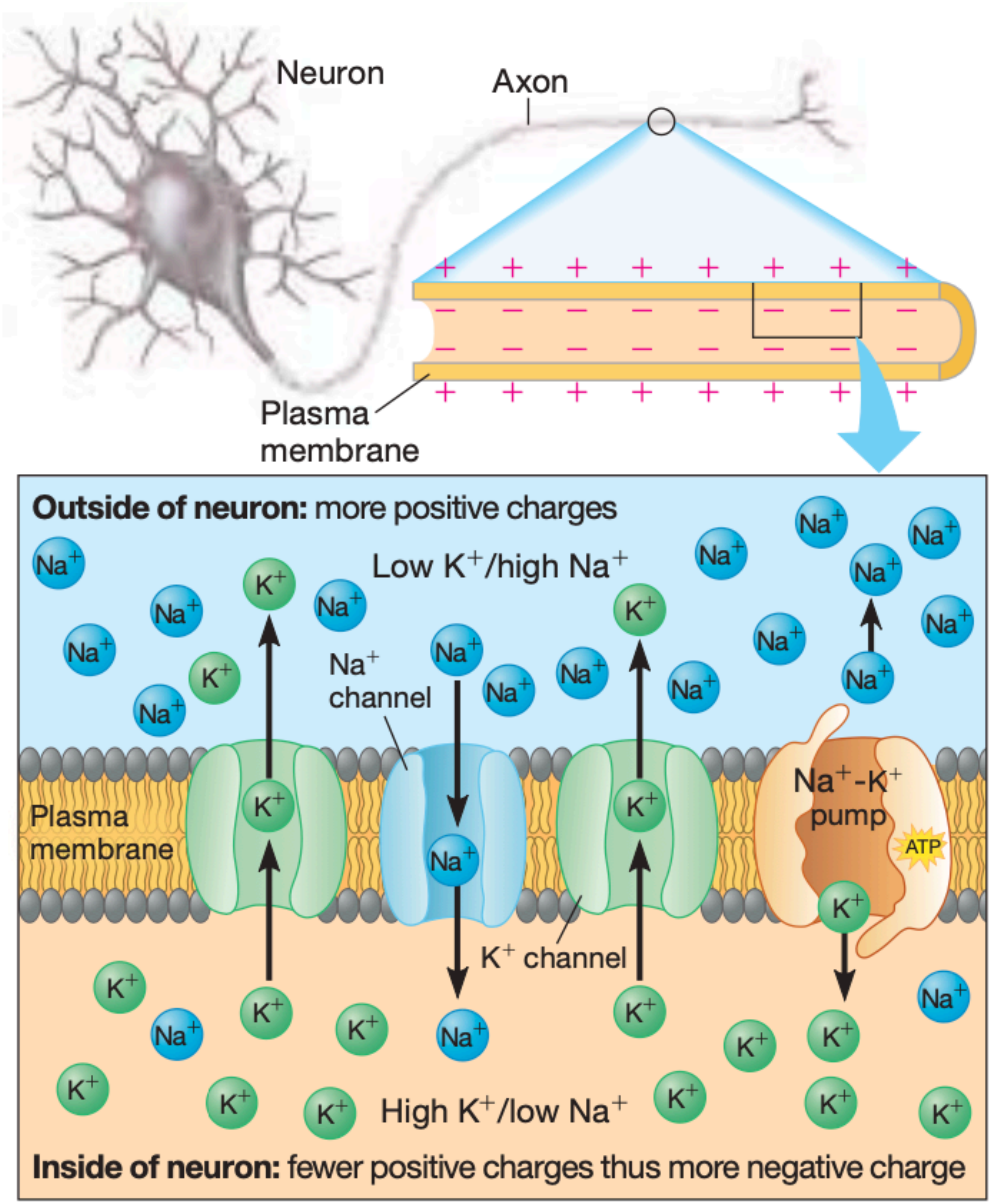
Nernst equation

"Resting" potential

Nernst equation gives the potential difference across a semi-permeable cell membrane, at equilibrium ("Resting" potential)

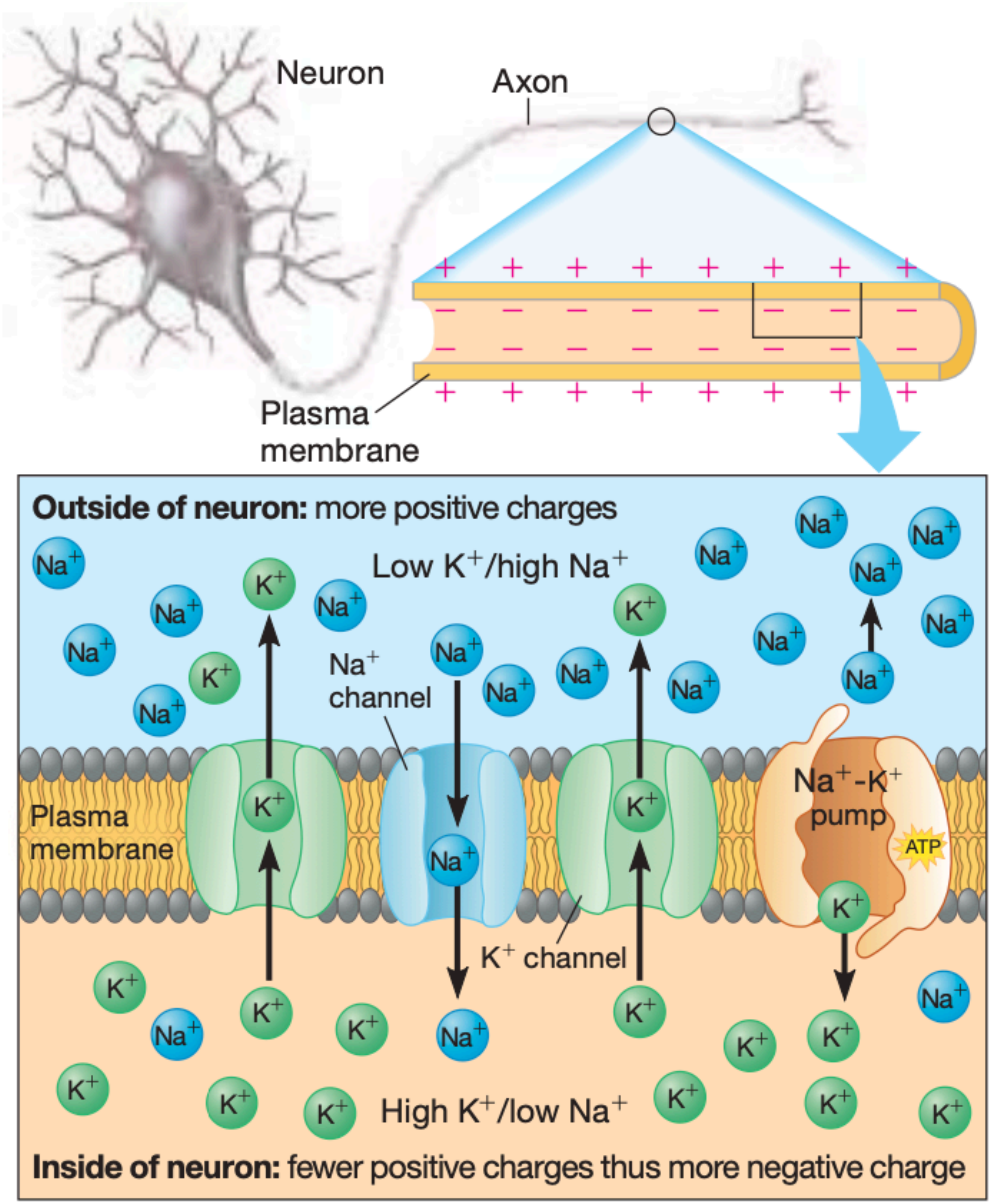
$$V_1 - V_2 = \Delta V = \frac{k_B T}{q} \ln \frac{C_1^{eq}}{C_2^{eq}}$$





▲ **Figure 28.3** How the resting potential is generated

Electrostatic potential difference across neuronal cell membrane



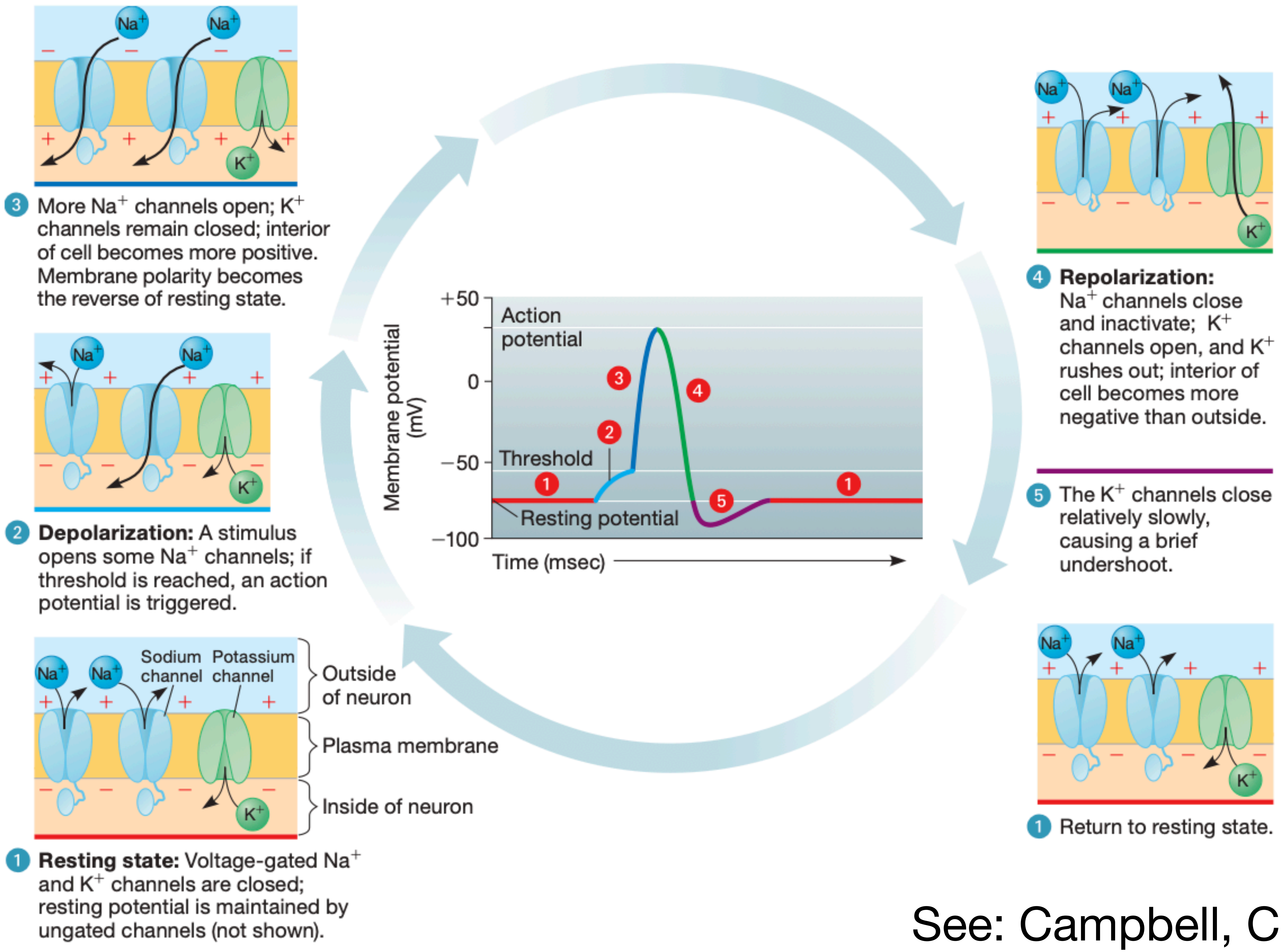
▲ **Figure 28.3** How the resting potential is generated

Change in this potential is the "nerve signal"

Any stimulus — a sound, tap on the knee—can act as a stimulus.

They can open the ion gates and change the potential!

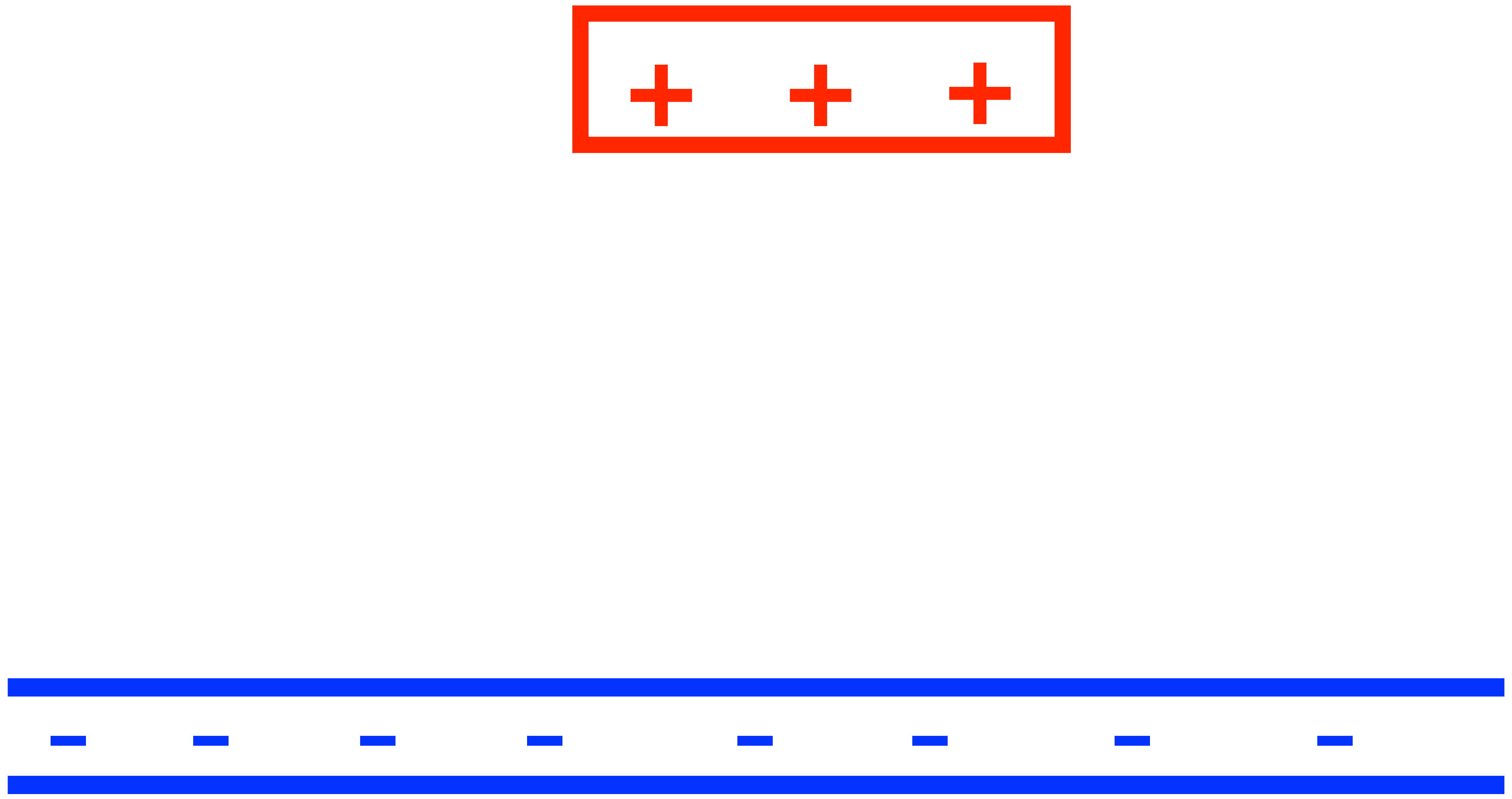
“Action potential” in neurons



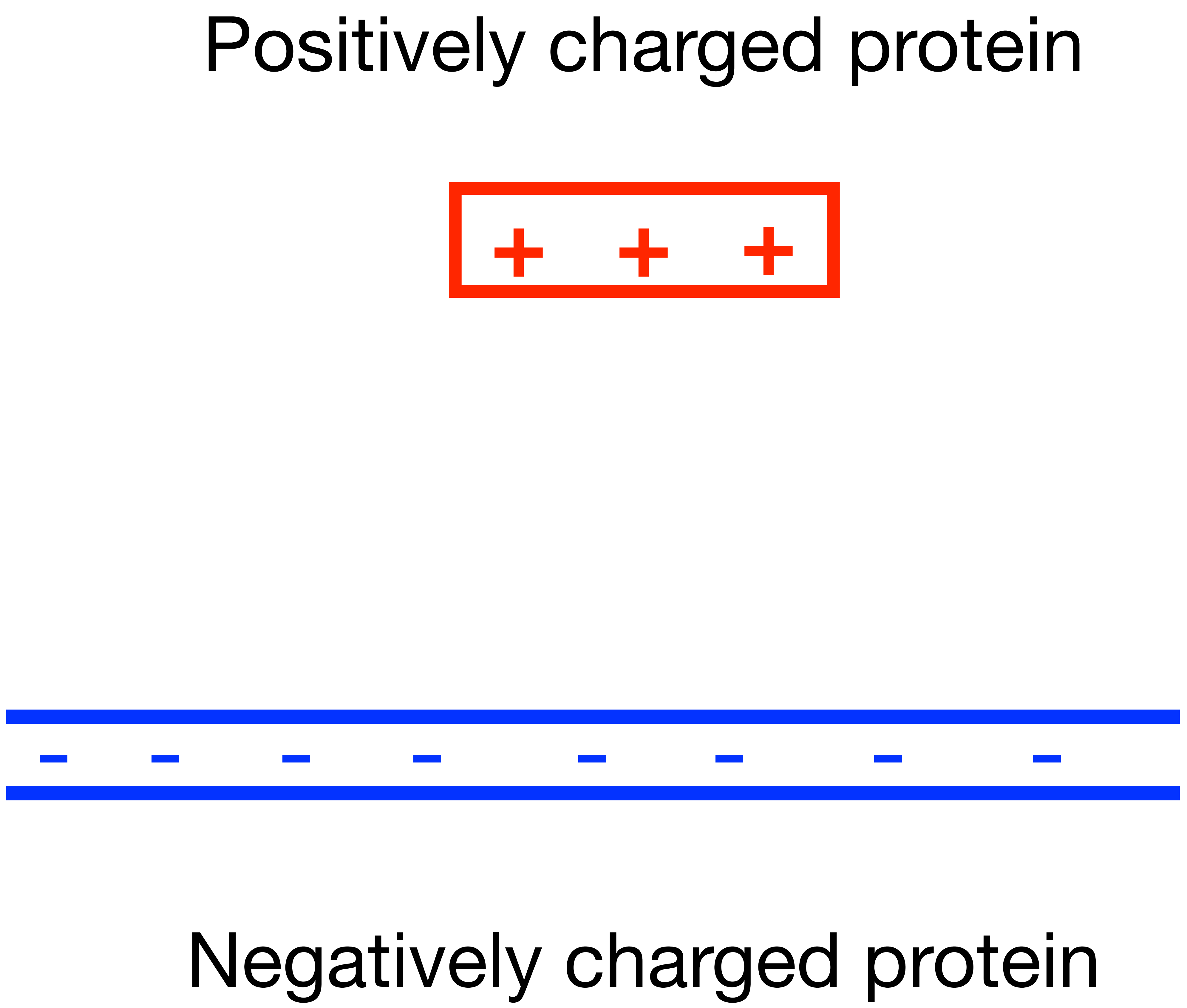
See: Campbell, Chapter 28

The salty water consequence: Coulomb’s law is nor more the same!

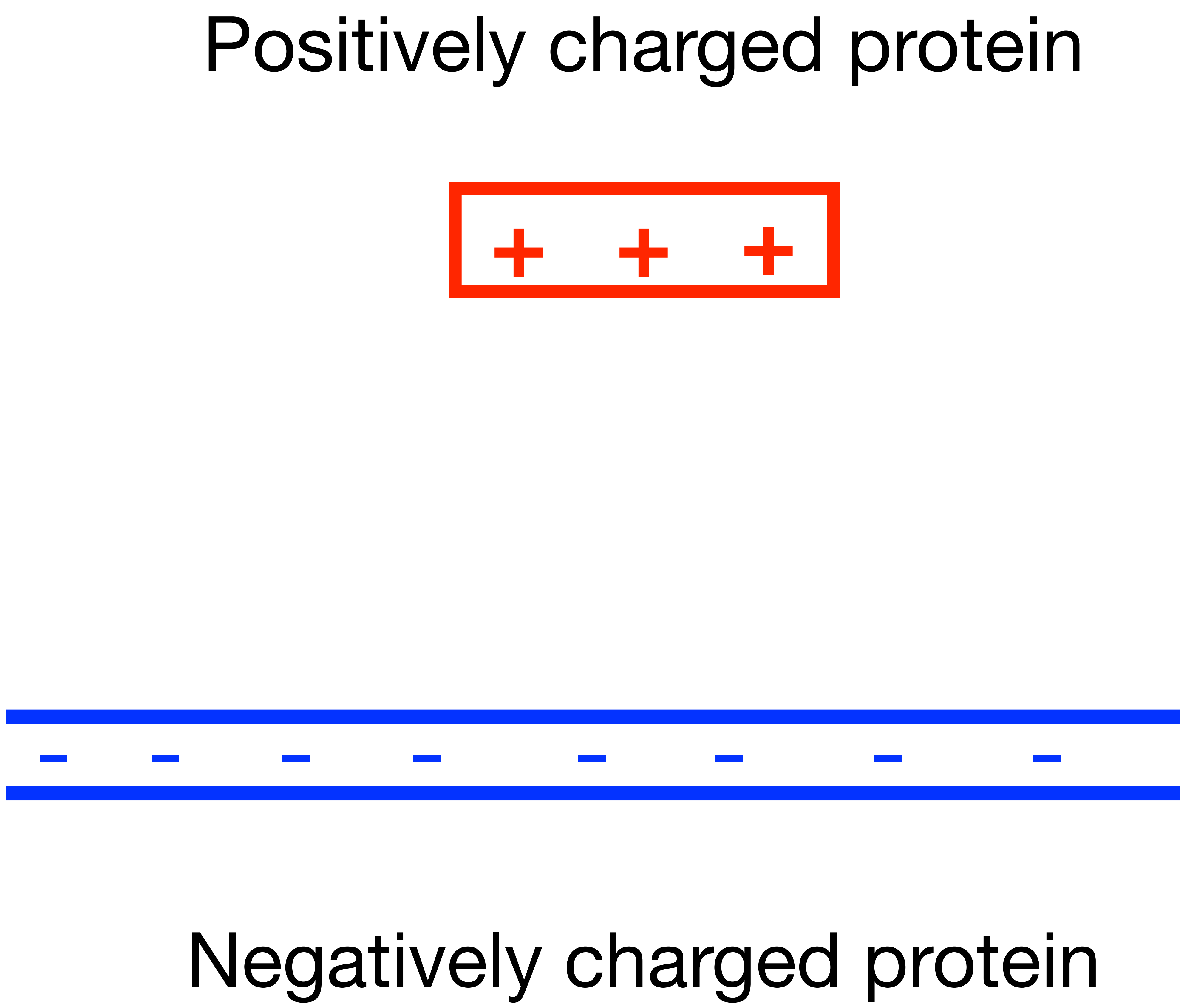
Positively charged protein



Negatively charged protein

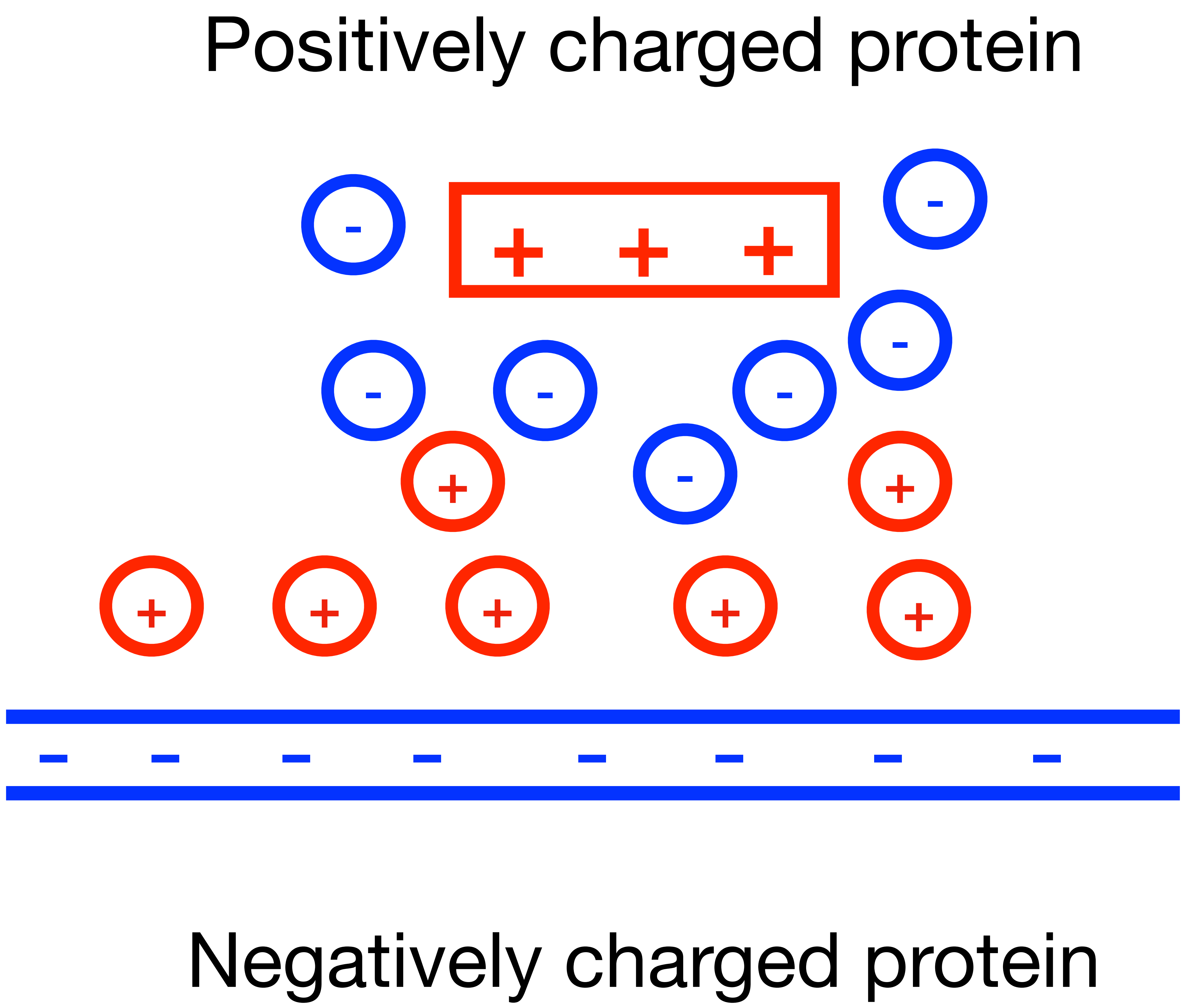


What is the interaction energy?

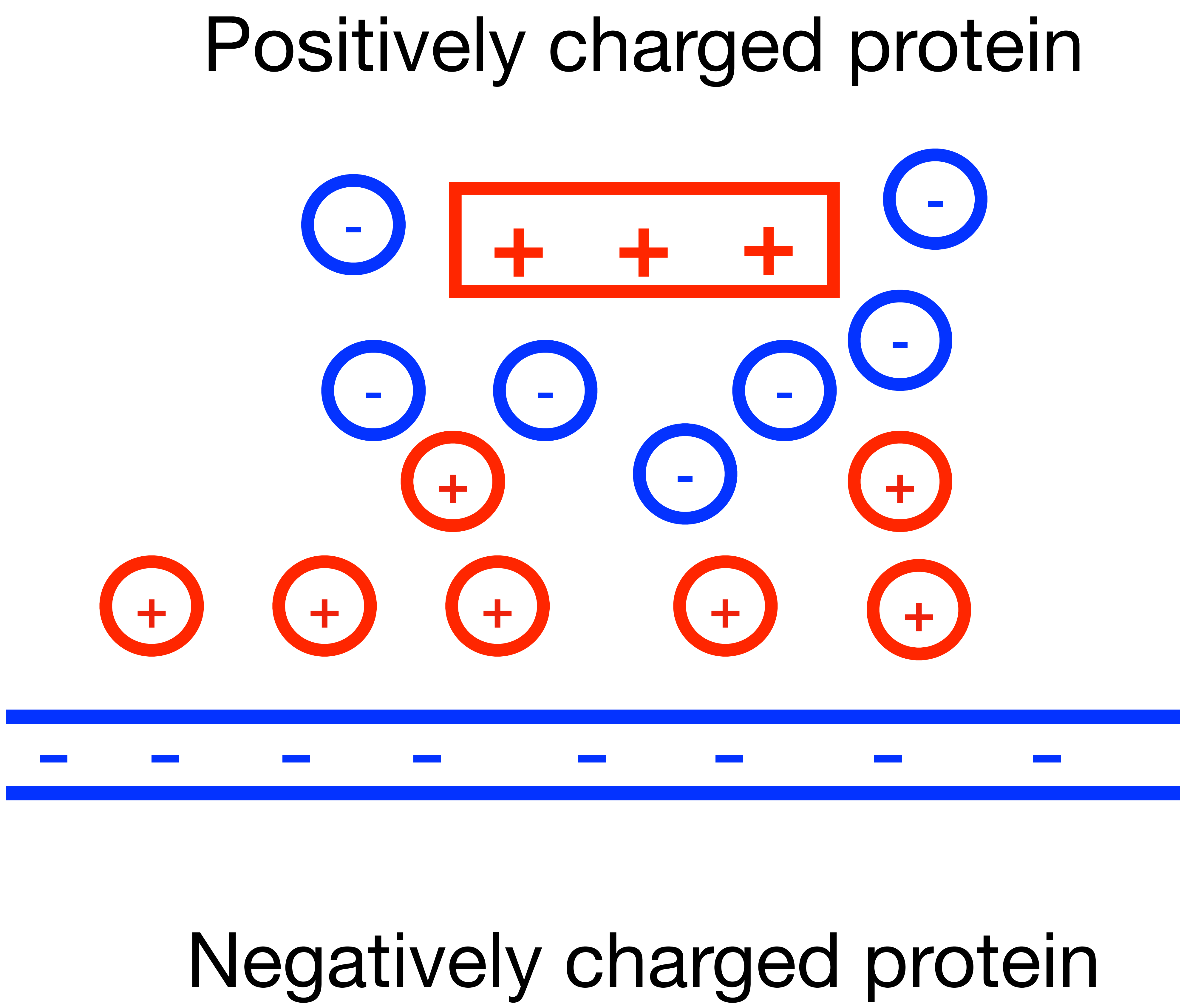


What is the interaction energy?

$$E = \frac{kQ_DQ_P}{r}$$



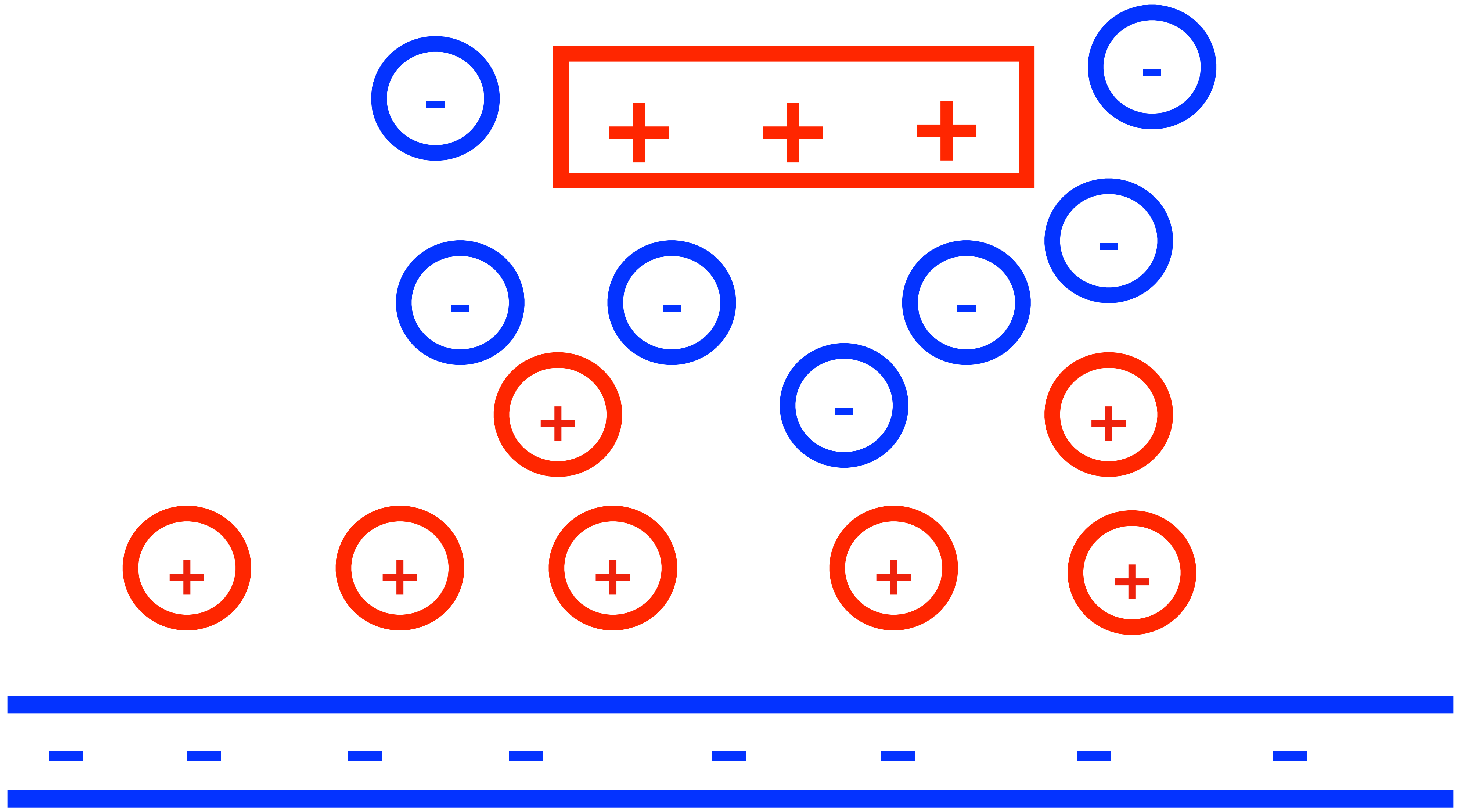
BUT, molecular biology is in salty water!



The ions "screen" the effective interaction between DNA and protein

Computing screened electrostatic potential

Positively charged protein



Negatively charged protein

$$\vec{\nabla} \cdot \vec{E} = \frac{-\rho}{\epsilon_0 \epsilon_r}$$

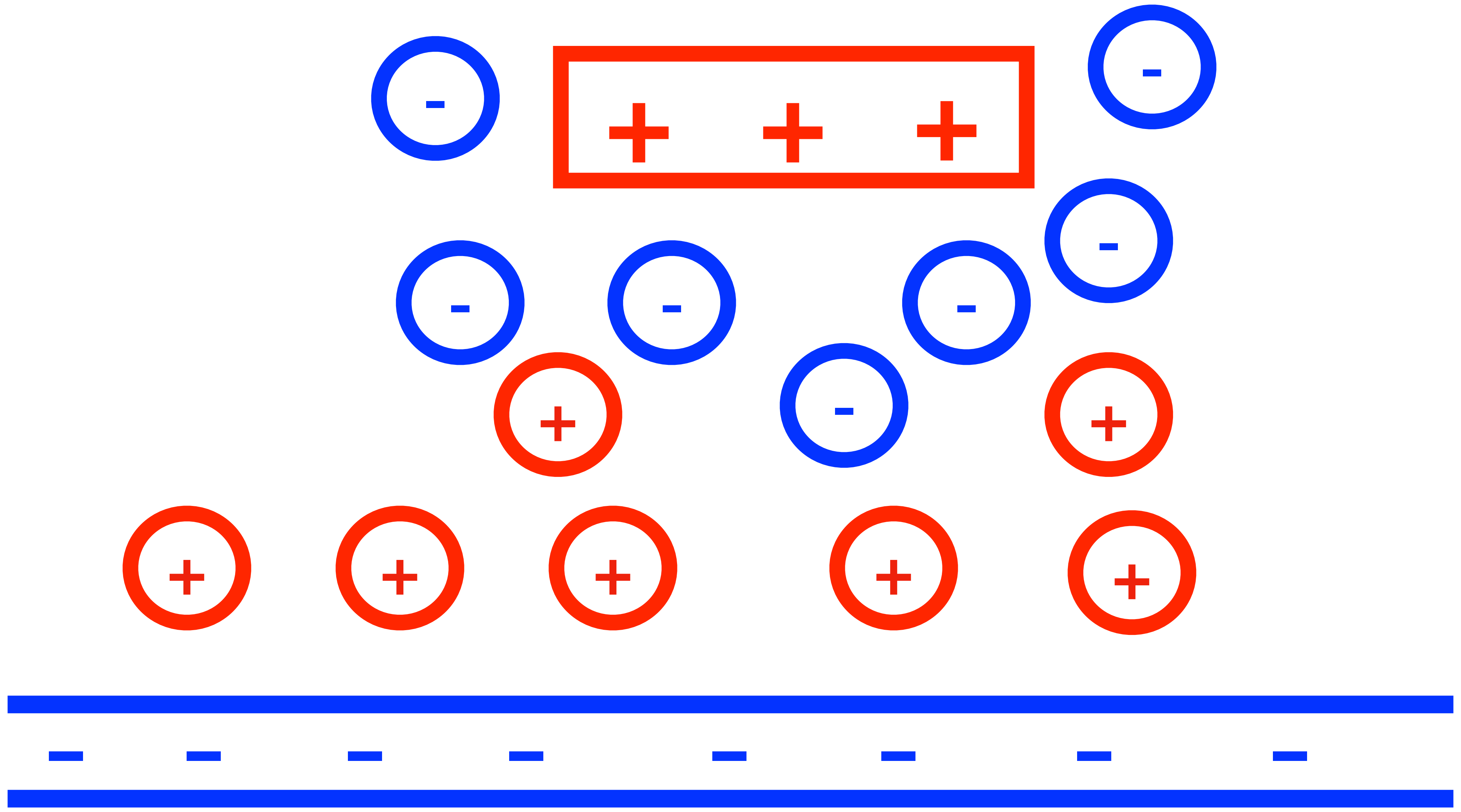
$$\vec{E} = -\vec{\nabla} V$$

$$\nabla^2 V = \frac{\rho}{\epsilon_0 \epsilon_r}$$

ρ = density of charged particles = probability of finding charged particles

Computing screened electrostatic potential

Positively charged protein



Negatively charged protein

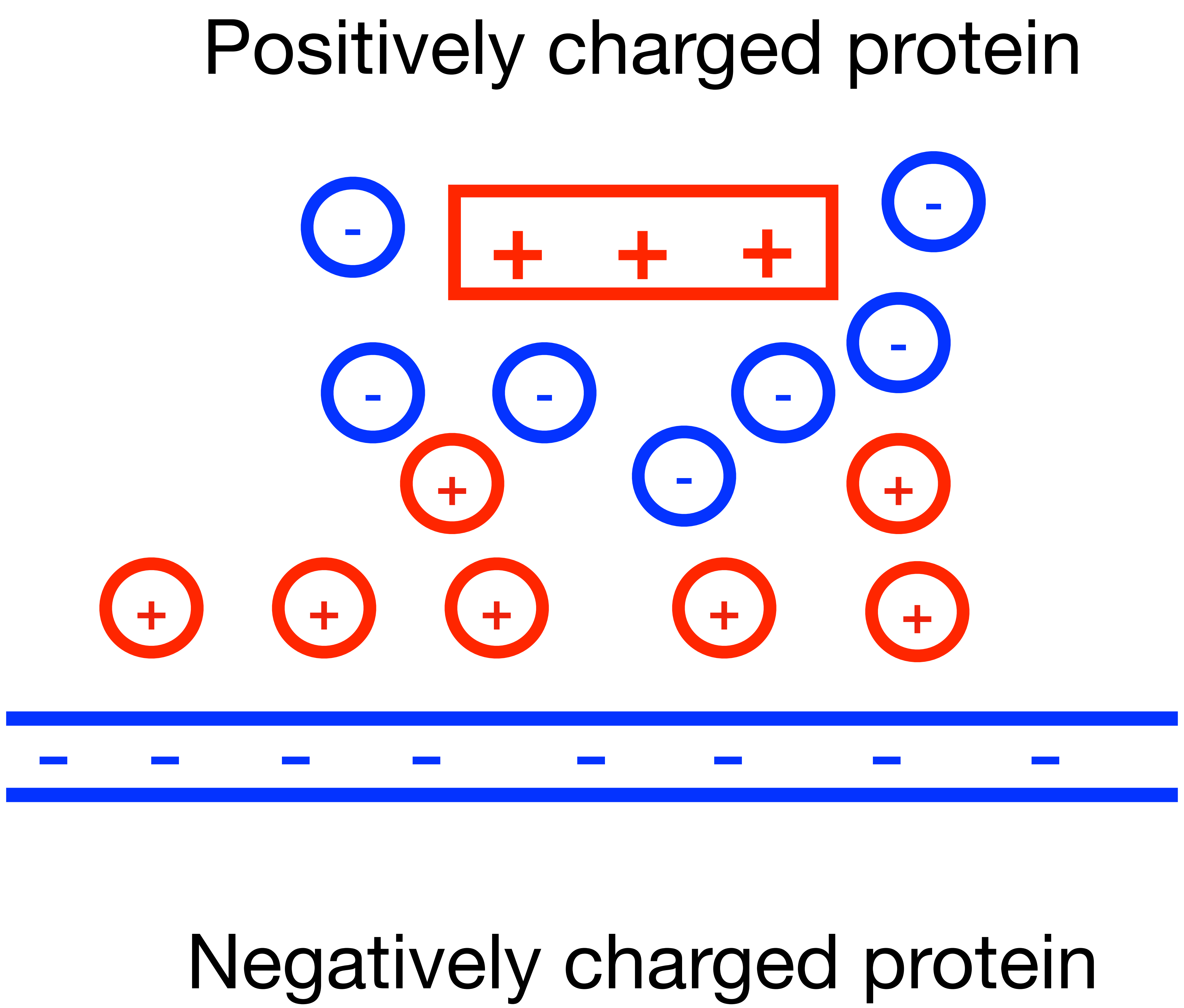
$$\vec{\nabla} \cdot \vec{E} = \frac{\rho}{\epsilon_0 \epsilon_r}$$

$$\vec{E} = -\vec{\nabla} V$$

$$\nabla^2 V = \frac{-\rho}{\epsilon_0 \epsilon_r}$$

$$\rho = \text{density or concentration of charged particles} = \sum_i q_i P_i$$

Computing screened electrostatic potential



$$\nabla^2 V = \frac{-\rho}{\epsilon_0 \epsilon_r}$$

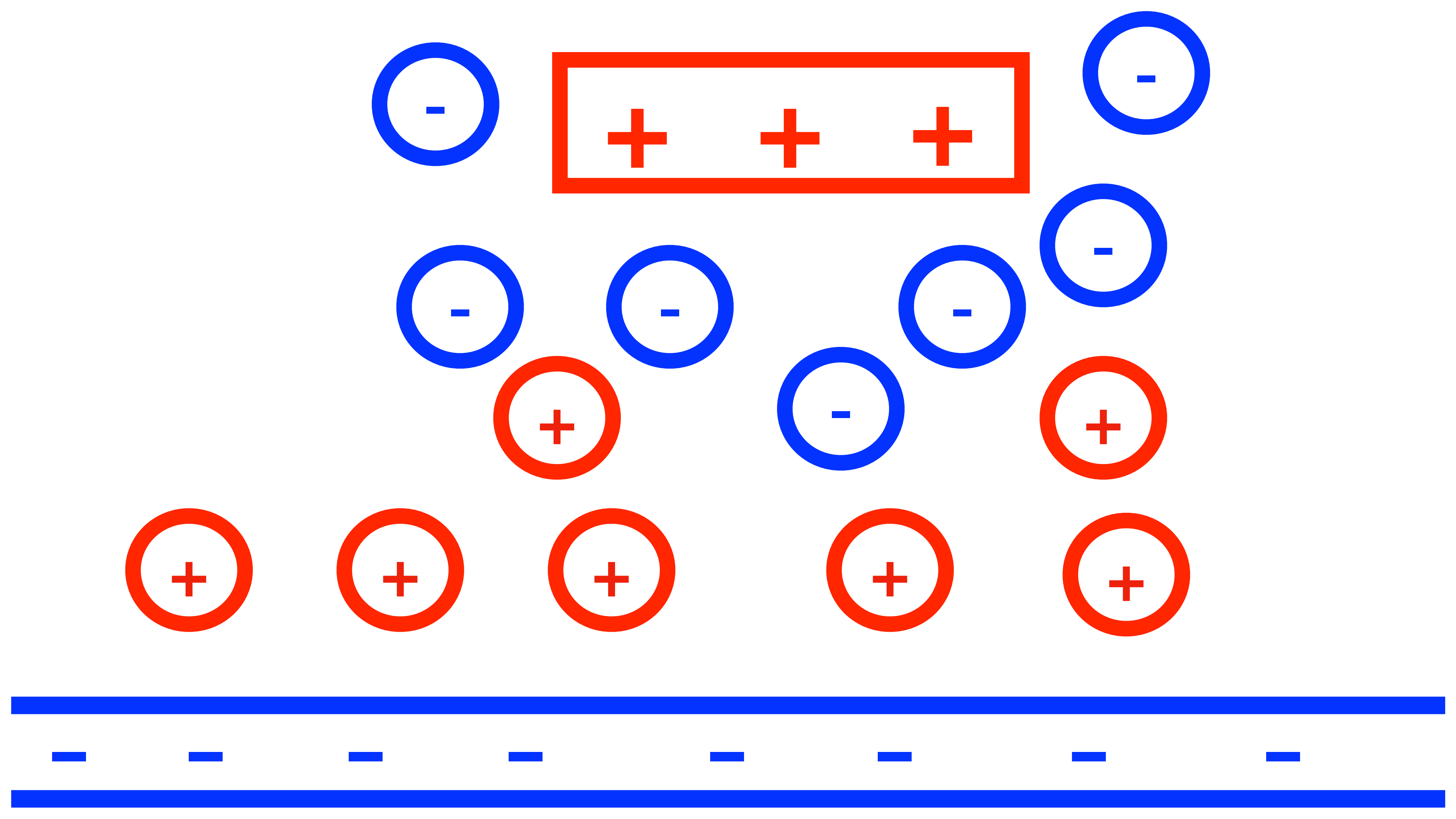
$$\rho = \sum_i q_i P_i$$

$$P_i = A \exp\left(\frac{-q_i V}{k_B T}\right)$$

$$\exp\left(-\frac{q_i V}{k_B T}\right) \approx 1 - \frac{q_i V}{k_B T}$$

Computing screened electrostatic potential

Positively charged protein



Negatively charged protein

$$\nabla^2 V = \frac{-\rho}{\epsilon_0 \epsilon_r}$$

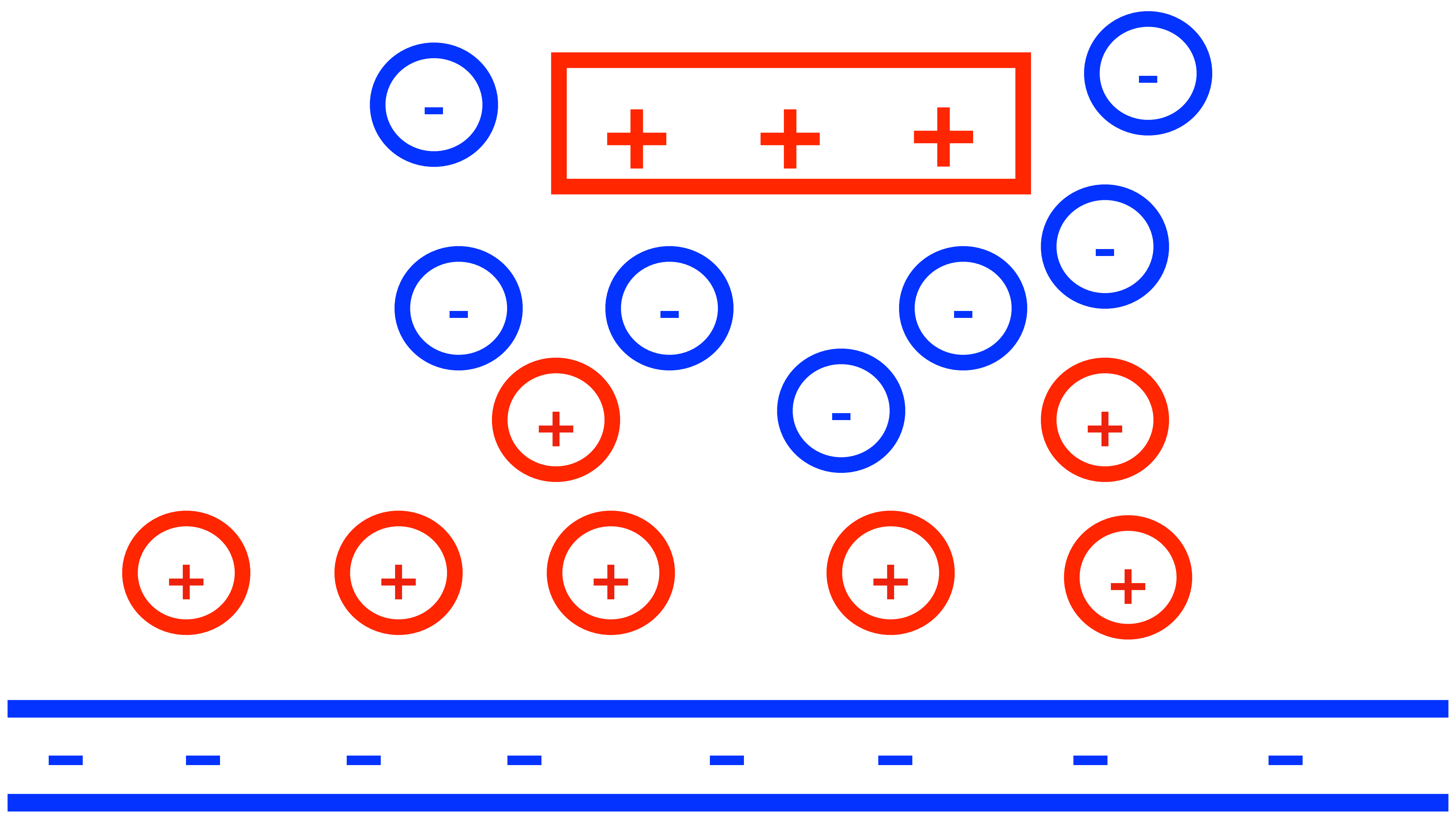
$$\rho = \sum_i q_i P_i$$

$$\nabla^2 V = \frac{-A}{\epsilon_0 \epsilon_r} \sum_i q_i \left(1 - \frac{q_i V}{k_B T}\right)$$

Overall system is charge neutral $\Rightarrow \sum_i q_i = 0$

Computing screened electrostatic potential

Positively charged protein



Negatively charged protein

$$\lambda_D = \sqrt{\sum_i \frac{\epsilon_0 \epsilon_r}{A} \frac{k_B T}{q_i^2}}$$

$$\nabla^2 V = \frac{-A}{\epsilon_0 \epsilon_r} \sum_i q_i \left(1 - \frac{q_i V}{k_B T}\right)$$

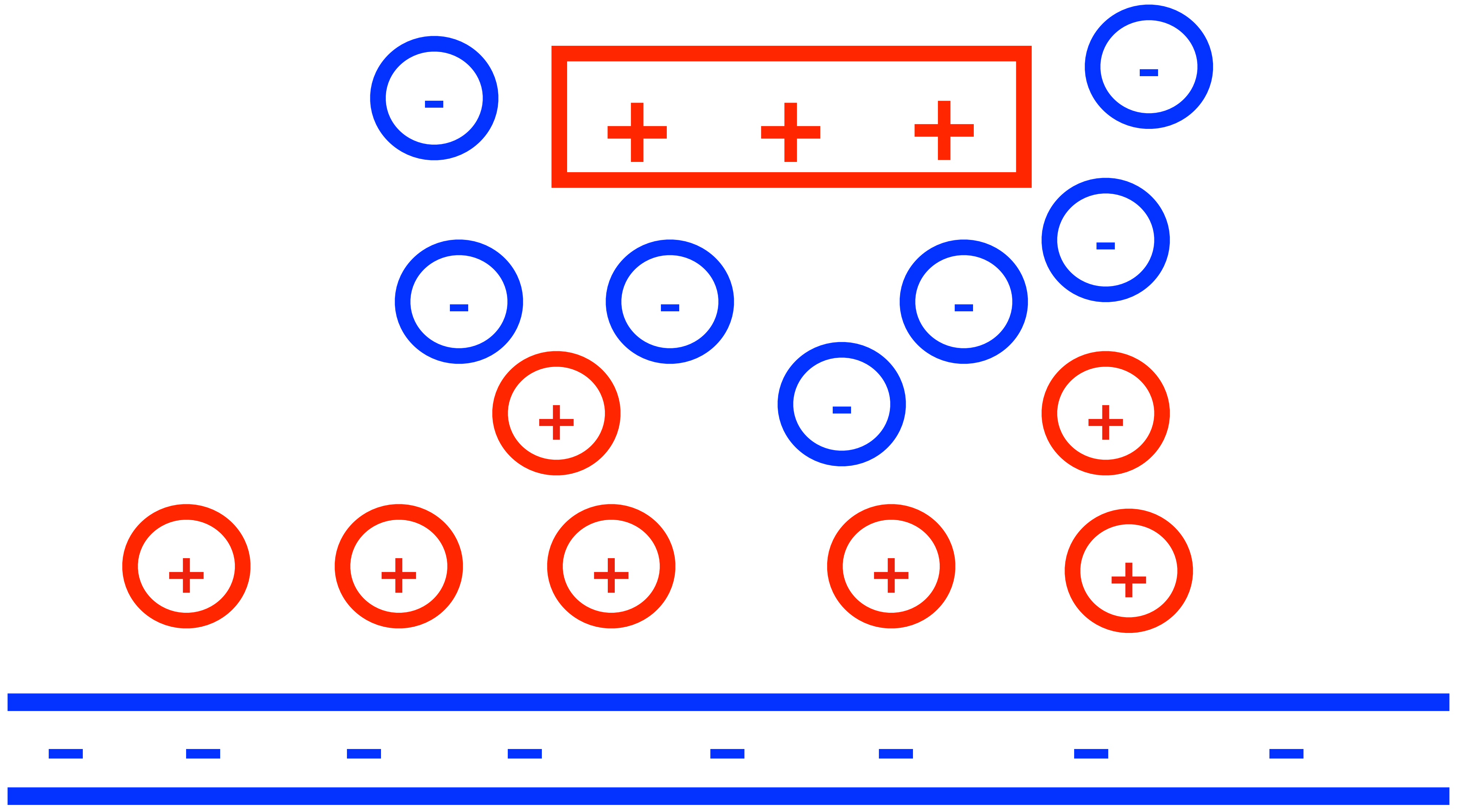
Overall system is charge neutral $\Rightarrow \sum_i q_i = 0$

$$\boxed{\nabla^2 V = \frac{A}{\epsilon_0 \epsilon_r} \sum_i \left(\frac{q_i^2 V}{k_B T}\right)}$$

$$\nabla^2 V = \left(\frac{1}{{\lambda_D}^2}\right) V$$

Screened electrostatic potential

Positively charged protein



Negatively charged protein

$$\nabla^2 V = \left(\frac{1}{{\lambda_D}^2}\right) V$$

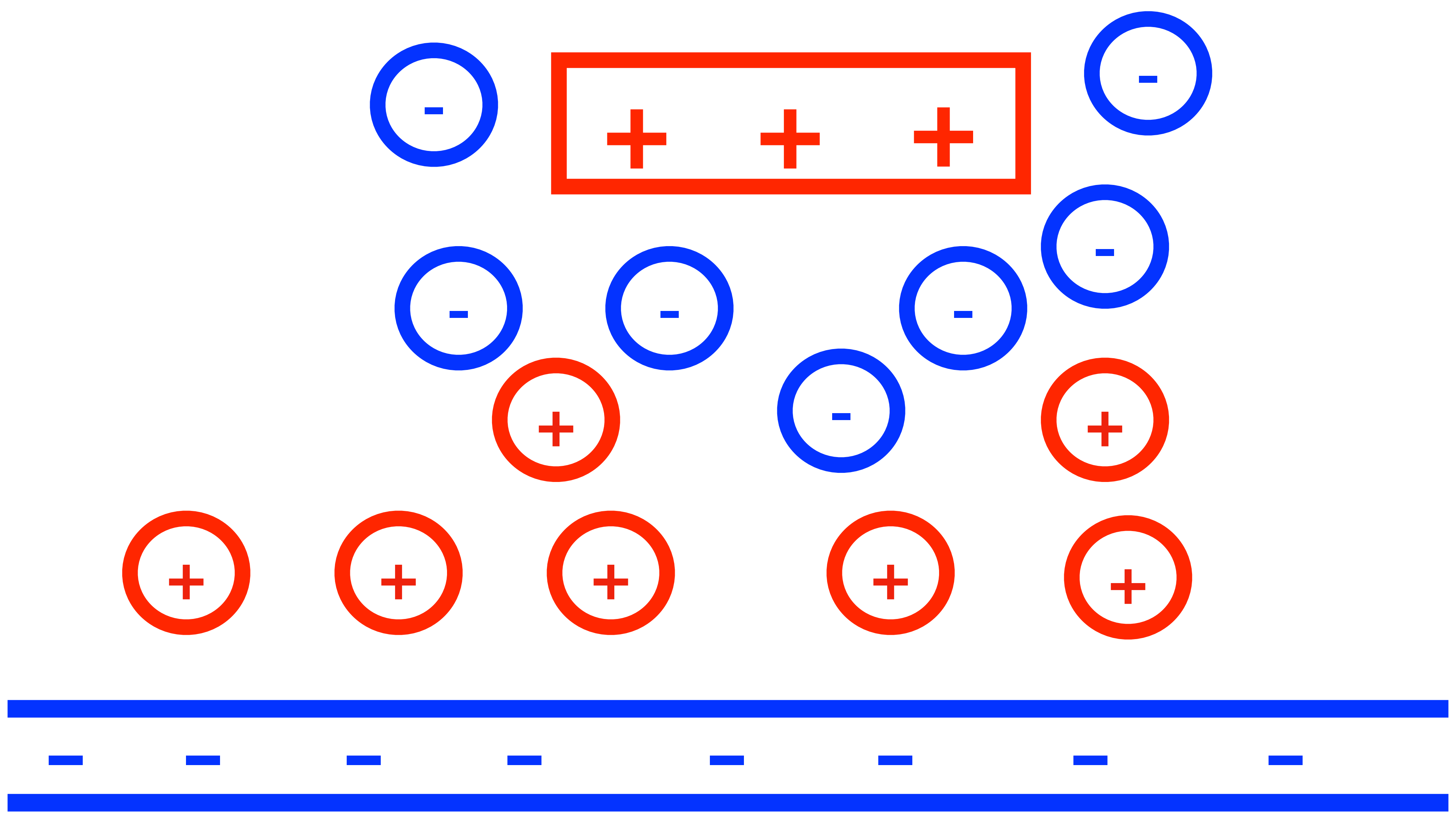
$$V = V_0 \exp\left(\frac{-r}{\lambda_D}\right)$$

$$\lambda_D = \sqrt{\sum_i \frac{\epsilon_0 \epsilon_r}{A} \frac{k_B T}{q_i^2}}$$

Boundary condition etc gives, $V_0 \propto \dfrac{1}{r}$

Screened electrostatic potential or screened-Coulomb potential

Positively charged protein



Negatively charged protein

$$V = \frac{B}{r} \exp\left(\frac{-r}{\lambda_D}\right)$$

$$\lambda_D = \sqrt{\sum_i \frac{\epsilon_0 \epsilon_r}{A} \frac{k_B T}{q_i^2}}$$

$$\lambda_D = \text{Debye length} \approx 1\text{nm}$$

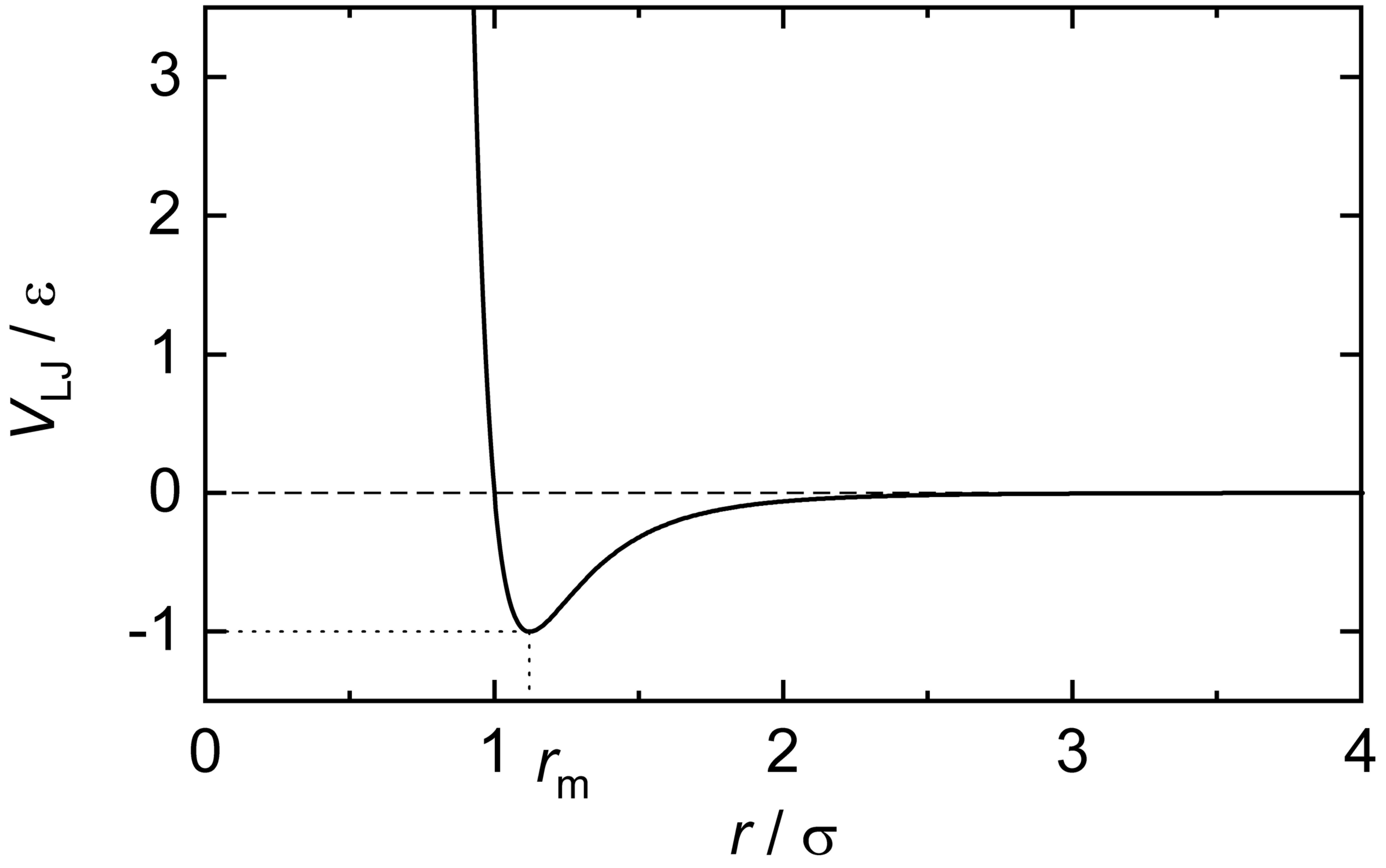
Negligible electrostatic interaction when distance >> 1nm

Other interaction energies

Inter-molecular effective potential

Lennard-Jones energy

$$V_{\mathrm{LJ}}(r) = 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right],$$



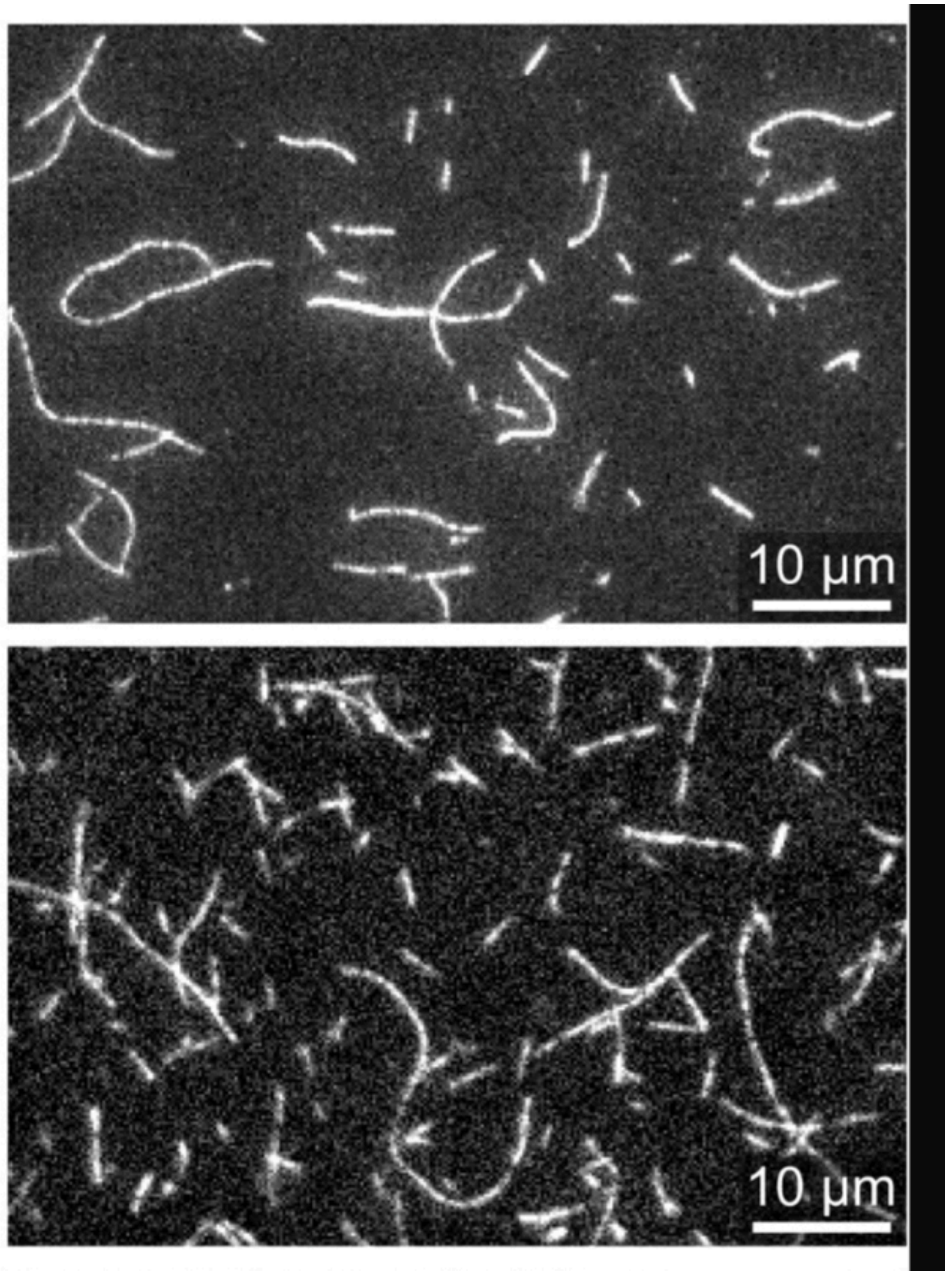
Short-range attraction; steric repulsion

3-body, 4-body potentials

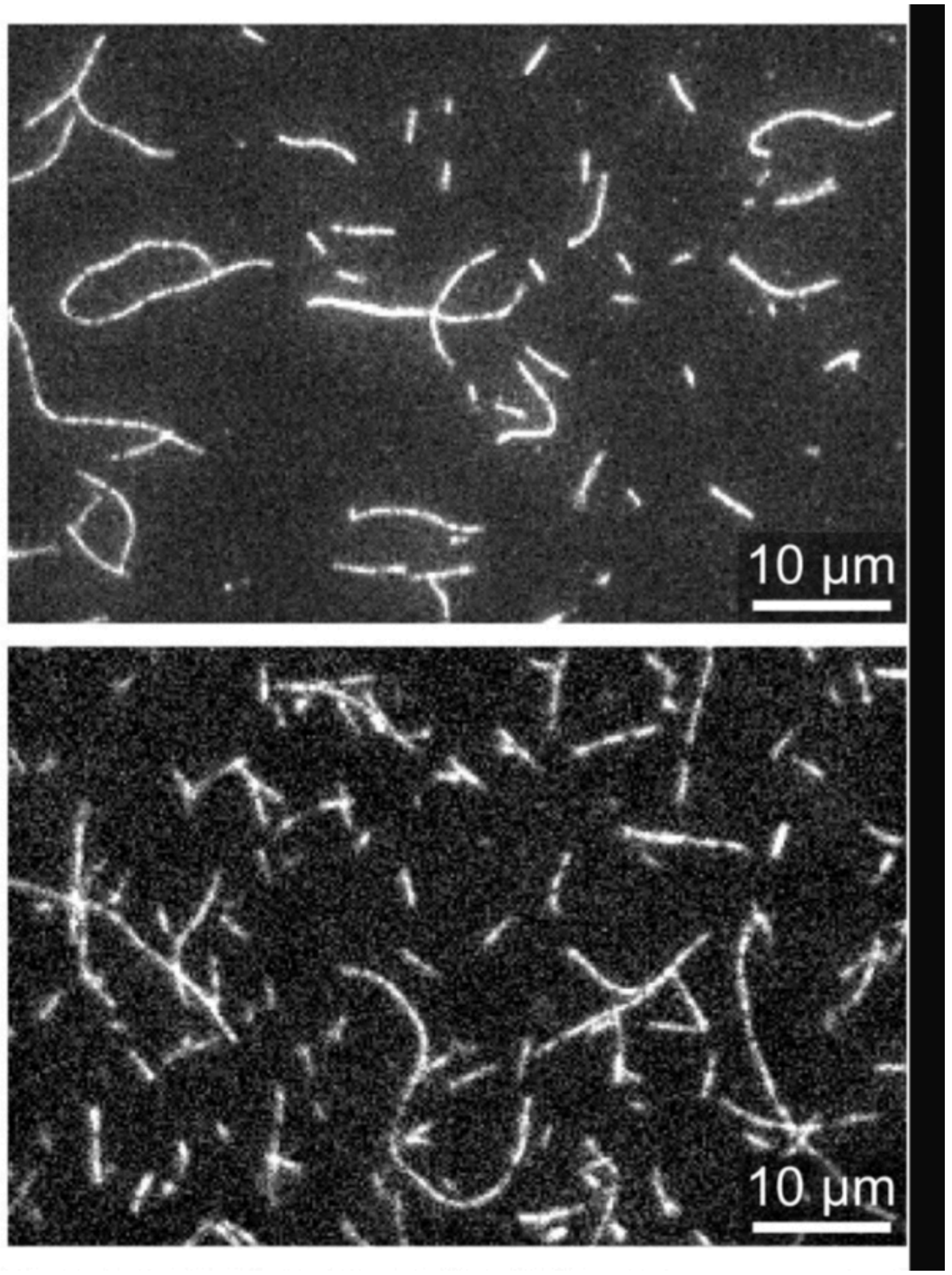
Curvature

Twist

By looking at microscopic images of bio-filaments (like actin or even DNA), can we say something about their properties?

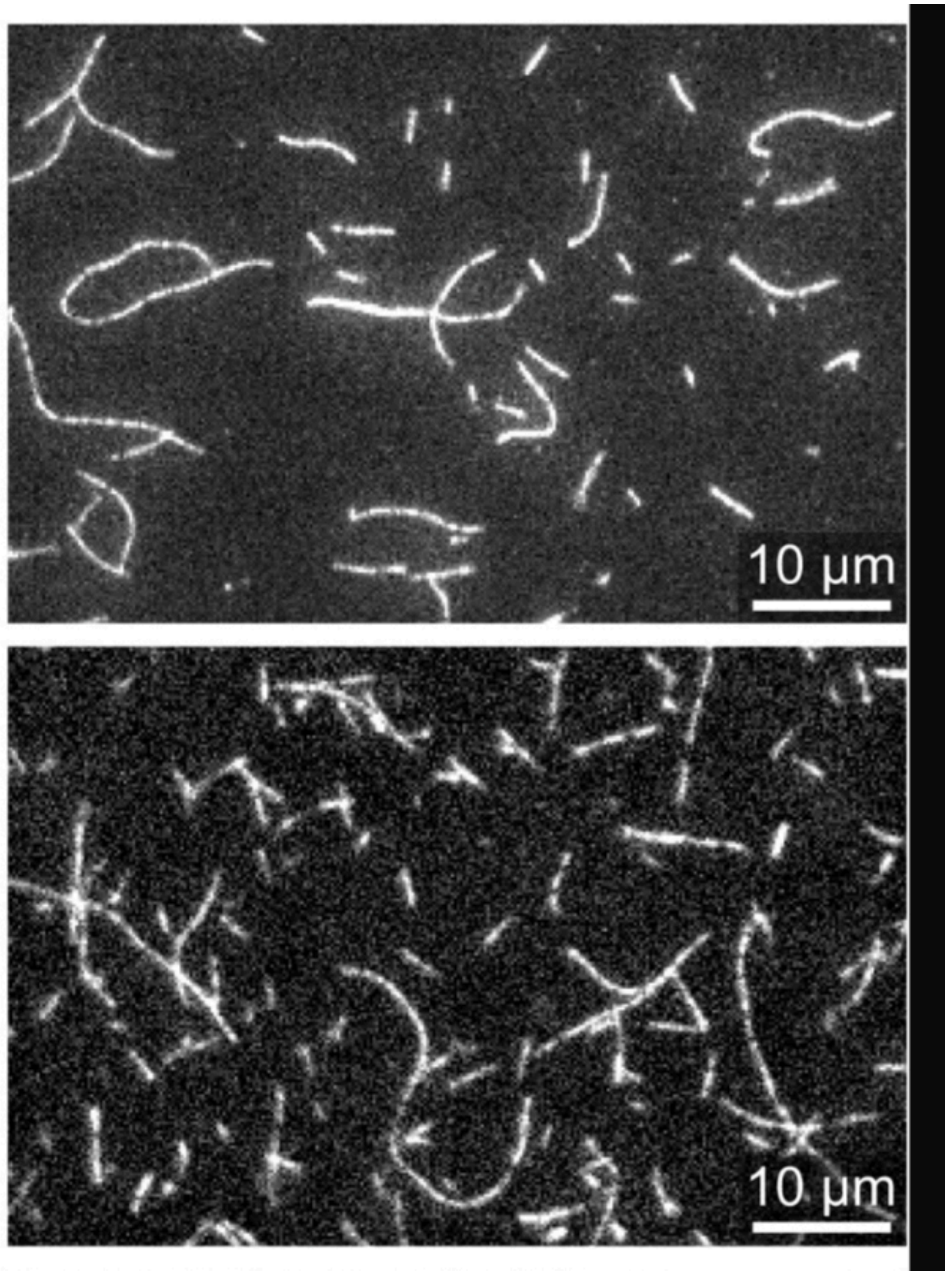


By looking at microscopic images of bio-filaments (like actin or even DNA), can we say something about their properties?



Can the thermal fluctuations make them bend?

By looking at microscopic images of bio-filaments (like actin or even DNA), can we say something about their properties?



Can the thermal fluctuations make them bend?

Elasticity Bendability, rigidity

Will affect force generation

Summary

- Ions channels across membranes lead to electrostatic potential difference
- Nernst equation
- Neurons: propagation of signal. Action potential
- Interaction between two charged macro-molecules like DNA and protein
- Screened due to the presence of ions
- Screened electrostatic potential falls exponential. Negligible beyond 1nm
- Other interaction energies in biology