Electrostatics in the cytoplasm

\[ \Phi = \int_{\partial V} \mathbf{E}(\mathbf{r}) \cdot d\mathbf{A} = \frac{Q}{D\epsilon_0} \]

\[ \nabla \cdot \mathbf{E} = \frac{\rho}{D\epsilon_0} \]

Figure 9.7 Physical Biology of the Cell, 2ed. (© Garland Science 2013)
Virus packing energy

\[ W = (7000 \text{ nm}) \times (0.5 \times 60 \text{pN}) \sim 2 \times 10^5 \text{ pN*nm} \]

\( \phi 29 \) model

\( R = 20 \text{ nm} \)

\( q = 2e/bp \times 20 \text{ kbp (base pairs)} = 40,000 \text{ e} \)

**build up energy in successive shells**

\[
U_{el} = \int dU = \int_0^R V(r) dq \quad \rightarrow \quad U_{el} = \frac{1}{4\pi \varepsilon_0 D} \frac{3}{5} \frac{Q^2}{R}
\]

\( U = 1.38 \times 10^8 \text{ pN*nm}!!! \)
Polarization

Charges, dipoles move and reorient in the presence of an electric field

Water has a permanent dipole, meaning it also responds to electric fields
Polarization of the media is what gives rise to the dielectric constant, $D$

$D$ diminishes the force between two charged objects

$D = 1$ (vacuum)  \hspace{1cm}  D = 80$ (water)  \hspace{1cm}  D \sim 2$ (membrane)  \hspace{1cm}  D \sim 4$ (protein)
In the chaotic environment of water, how far apart, $l_B$, can two attracting monovalent ions drift before thermal forces take over?

\[ U = qV = \frac{e^2}{4\pi\varepsilon_0 D l_B} = k_B T \]

\[ l_B = 0.7 \text{ nm!} \]

Electrostatic interactions are short range in water.
Polarization in an ionic solution

Ions in solution are attracted to charged objects, concentrate near them (e.g., DNA)

Water is a conductor $\rightarrow$ ions move to cancel field, forming a “skin” that screens the protein from the outside environment
Combining electrostatics and stat. mech.

**BAD** assumption

**GOOD** - Boltzmann distribution

\[ c_{\pm}(x) = c_\infty e^{\mp zqV(x)/kT} \]

\[ \rho(x) = zqc_+(x) - zqc_-(x) \]
Poisson-Boltzmann Equation

\[
\frac{d^2 V(x)}{dx^2} = \frac{zc_\infty}{D\epsilon_0} \left( e^{zqV(x)/kT} - e^{-zqV(x)/kT} \right)
\]

Non-linear differential equation for potential around an object in an ionic solution

- assume \( V \ll kT/zq \) (~25 mV or less)

\[
e^{zqV(x)/kT} \approx 1 + zqV(x)/kT
\]

electrostatic surface potential solved by PB methods (APBS)

Debye-Hückel equation

\[
\frac{d^2 V(x)}{dx^2} = \frac{2z^2q^2c_\infty}{D\epsilon_0 kT} V(x)
\]

PBoC 9.3.4
Solving Debye-Hückel equation

\[
\frac{d^2 V(x)}{dx^2} = \frac{2z^2 q^2 c_\infty}{D \epsilon_0 kT} V(x)
\]

\[
V(x) = Ae^{-x/\lambda_D} \quad \lambda_D = \sqrt{\frac{D \epsilon_0 kT}{2z^2 q^2 c_\infty}} \quad \text{Debye length}
\]

A can be solved by boundary condition at \( x = 0 \)

for infinite plane, \( E(0) = -\frac{dV(x)}{dx} \bigg|_{x=0} = \frac{\sigma}{2\epsilon_0 D} \)

\[
V(x) = \frac{\sigma \lambda_D}{2D \epsilon_0} e^{-x/\lambda_D}
\]
Typical Debye length

\[ \lambda_D = \sqrt{\frac{D \epsilon_0 kT}{2z^2 q^2 c_\infty}} \]

Debye length is effectively distance at which electric field is no longer felt (\( \mathcal{V} \) drops to \( \mathcal{V}(0)/e \))

\( c = 150 \text{ mM}, \ z = 1 \ (\text{KCl}), \ D = 80, \ T = 300 \ K \)

\[ \lambda_D = 8 \ \text{Å} \]

electrostatic interactions are very short range in the cell!
Virus packing energy (take two)

φ29 model

\[ W = (7000 \text{ nm}) \times (0.5 \times 60 \text{ pN}) \sim 2 \times 10^5 \text{ pN} \times \text{nm} \]

\[ r = 20 \text{ nm} \]

\[ q = 40,000 \text{ e (now # ions)} \]

ion concentration \( c_\infty = 100 \text{ mM} \)

pack the ions into the capsid:

\[ W = NkT \ln\left( \frac{V_{\text{cloud}}}{V_{\text{capsid}}} \right) \]

\[ \lambda_D = 0.98 \text{ nm} \]

\[ V_{\text{cloud}} = L\pi\left[ (R_{\text{DNA}} + \lambda_D)^2 - R_{\text{DNA}}^2 \right] \approx 64,000 \text{ nm}^3 \]

\[ V_{\text{capsid}} = \frac{4\pi}{3} R_{\text{capsid}}^3 - L\pi R_{\text{DNA}}^2 \approx 12,000 \text{ nm}^3 \]

\[ W \sim 65,000 \text{ kT} \sim 2.71 \times 10^5 \text{ pN} \times \text{nm} \]
Barstar-Barnase complex - extremely strong (~21 kcal/mol binding free energy!)

Example from simulations

- protein–solvent (all, vdw+elect.)
- protein–protein (elect.)
- protein–solvent (all) + protein–protein (elect.)

Total PMF

Decomposition of potential of mean force

Nucleosomes

$R_{\text{DNA}} = 4.5 \text{ nm}$ \hspace{1cm} $L_p = 50 \text{ nm}$

$G_{\text{bend}} = 2(\pi L_p kT/R_{\text{DNA}})$ (2 turns)

$G_{\text{bend}} = 70 \text{ kT}$

$G_{\text{int.}} = 2(2\pi R_{\text{DNA}} \gamma_{\text{ad}})$

(from electrostatics)

Experiment to measure $\gamma_{\text{ad}}$ based on probability of site accessibility

$\gamma_{\text{ad}} = 1.67 \text{ kT/nm}$ \hspace{1cm} $G_{\text{int.}} = 94 \text{ kT}$
How DNA is packaged

https://www.youtube.com/watch?v=gbSIBhFwQ4s
DNA packing scales
Electric field acts on a particle (could be a protein or microscopic grain)

the field **also** acts on the surrounding ions (which have opposite charge of the core particle), causing a drag on the particle

**electrophoretic mobility** (from Smoluchowski, 1903)

\[
\mu = \frac{v}{E} = \frac{\epsilon_0 D \zeta}{\eta}
\]
Zeta (ζ) potential

The zeta potential is defined by the effective boundary between the ions “attached” to the particle and the bulk solution (the slipping plane). This boundary is also the Debye length!

Zeta potential notoriously difficult to calculate in simulations, instead use “effective” charge

\[ F = Q_{\text{eff}} E = \nu \gamma \rightarrow \mu = \frac{Q_{\text{eff}}}{\gamma} \]