2.3: C- Molecular Interactions - Electrostatic Interactions

Electrostatic interactions are between and among cations and anions, species with formal charge of \(-2, -1, +1, +2\)...

Electrostatic interactions can be either attractive or repulsive, depending on the signs of the charges. Like charges repel. Unlike charges attract.

Favorable electrostatic interactions cause the vapor pressure of sodium chloride and other salts to be very low. If you leave crystals of table salt (NaCl; \(\text{Na}^+\) = cation, \(\text{Cl}^-\) = anion) on a hot pan, how long does it take before they vaporize and sublime away? A very very long time; electrostatic interactions are very very strong. The electrostatic interactions within a sodium chloride crystal are called ionic bonds. But when a single cation and a single anion are close together, within a protein, or within a folded RNA, those interactions are considered to be non-covalent electrostatic interactions. Non-covalent electrostatic interactions can be strong, and act at long range. Electrostatic forces fall off gradually with distance \((1/r^2\text{, where } r \text{ is the distance between the ions})\).
**Figure 3** shows electrostatic interactions in a cross section of a NaCl crystal. Each sodium cation experiences strong electrostatic interactions with adjacent chloride anions. In reality, the ionic radius of a sodium cation is less than that of a chloride anion. The coordinates of sodium chloride are here [coordinates].

Electrostatic interactions are the primary stabilizing interaction between phosphate oxygens of RNA (charge = -1) and magnesium ions (charge = +2), as shown in the figure below. There are many magnesium ions associated with RNA and DNA *in vivo*. As explained later in this document, electrostatic interactions are highly attenuated (dampened) by water. In protein folding, RNA folding and DNA annealing, electrostatic interactions are dependent on salt concentration and pH.

**Figure 4** shows electrostatic interactions. In RNA (for example in the ribosome), anionic phosphate oxygens (formal charge = -1) engage in attractive electrostatic interactions with cationic magnesium ions (formal charge = +2). Two phosphate groups can 'clamp' onto the Mg$^{2+}$ ion. The O to Mg$^{2+}$ distance is 2.1 Å. The dashed lines represent favorable electrostatic interactions.

### C1. Ion Pairs in Proteins

Favorable electrostatic interactions between paired anionic and cationic *amino acid* sidechains are reasonably frequent in proteins. Ion Pairs, sometimes called Salt Bridges, are formed when the charged group of a cationic amino acid (like lysine or arginine) is around 3.0 to 5.0 Å from the charged group of an anionic amino acid (like aspartate or glutamate). The charged groups in an ion pair are generally linked by hydrogen bonds, in addition to electrostatic interactions.

**Figure 5** shows an ion pair within a folded protein. An anionic aspartic acid (charge = -1) engages in attractive electrostatic interactions with cationic arginine (charge = +1). The dashed lines represent hydrogen bonds.

The electrostatic force between two point formal charges is given by:

$$\text{Force} = k \frac{q_1 q_2}{\epsilon r^2}$$

where $k = 9.0 \times 10^9$ nt-meter$^2$/coul$^2$

$q = -1.6 \times 10^{-19}$ coulombs for an electron.
\[ r = \text{distance between the point charges (meters)} \]

\[ \varepsilon = \text{the dielectric constant of the medium (unitless).} \]

\( \varepsilon \) is the dielectric constant. It reflects the tendency of the medium to shield charged species from each other. \( \varepsilon \) is 1 in a vacuum, around 4 in the interior of a protein and 80 in water. Water is very efficient at shielding charges, reducing electrostatic forces between ions. The problem of calculating electrostatic effects in biological systems is complex in part because of non-uniformity of the dielectric environment. The dielectric micro-environments are complex and variable, with less shielding of charges in regions of hydrocarbon sidechains and greater shielding in regions of polar sidechains.

The electrostatic energy is given by:

\[ \Delta E = k a \frac{q_1 q_2}{\varepsilon r} \]

where \( a = \text{Avogadro's number}. \)

One can crudely estimate the energetics of a charge-charge interaction in a protein. The energy of an amine (charge +1) and a carboxylic acid (charge -1) separated by 4 Å in the interior of protein is given by:

\[ \Delta E = -(9.0 \times 10^9 \text{nt-m}^2/\text{coul}^2)(6.02 \times 10^{23})(1.6 \times 10^{-19} \text{coul})^2 / (4 \times 10^{-10} \text{m}) \]

\[ = 87 \text{ kJoules/mole} = 21 \text{ kcal/mole} \]

This rough approximation is around 10-fold greater than the values determined experimentally. An ion pair contributes favorable \( \Delta G \) of 1 to 4 kcal/mole (4.1 to 16.4 kJoule/mole) to the stability of a native protein.

**A note on nomenclature.** The attractive forces between a Mg\(^{2+}\) ion and phosphate groups (above) are called electrostatic interactions. Species with formal charge (2,1,-1,-2) engage in electrostatic interactions. We use other terms (dipole-dipole...) to describe interactions between partial charges. The naming scheme is confusing because ALL molecular interactions are between electrons and electrons and between electrons and nuclei, and are actually electrostatic in nature. It might have been better to use different names that make more sense. However, by convention we have to restrict the term electrostatic to interactions between formally charged species.