Coulomb interactions

The work required to bring to charges from infinite distance to distance r is given by:[1]

$$\Delta H_{coulomb} = k\frac{q_1 q_2}{\varepsilon r}$$

q_1 and q_2 are the charges on atoms one and two (numbers like -2, 0, $+1$); k is a constant that gives units $(1,389\ \text{Å} \cdot kJ \cdot mol^{-1})$; ε is the "dielectric constant" that describes how well the environment damps electric fields. For biomolecules, ε is a "fudge factor" that weakens coulomb interactions. Reasonable values are given below.

environment	ε
vacuum	1
protein interior	≈ 4
protein surface	≈ 20
water	78.5
insulator	∞

Task

- Load 1STN.pdb in pymol
- Zoom in on residue 121 (this should be a histidine).
- The histidine sidechain is forming an ion pair with another residue. What residue is this? What is the distance (in Å) between the polar atoms on histidine and its partner?
- Estimate how much this interaction stabilizes the folded state of the protein.
- Is this a lot or a little?

[1] Note that we continue to pretend that enthalpy and internal energy are equivalent. The thermodynamics police made me put this disclaimer here.

Conformational Entropy

The entropy of a state is given by:

$$S = Rln(N)$$

where R is the gas constant and N is the number of configurations (microstates, as we've constructed things). The change in entropy between two states is:

$$\Delta S_{A \to B} = Rln\left(\frac{N_B}{N_A}\right)$$

Task

- Load ala.pdb in pymol
- Use the "Wizard→Mutagenesis" tool and click on the alanine.
- Mutate it to your assigned amino acid.
- Estimate the entropy to immobilize the amino acid in a folded protein.
- What assumptions did you make in this estimate? Are they justified?

Hydrophobic effect

Download excel spreadsheet shows $\Delta\Delta G_{water \rightarrow octanol}$ for blocked Ala-X-Ala peptides at 25 $^{\circ}C$, where X is an amino acid. (The $\Delta\Delta$ arises because these energies are determined relative to the energy to transfer the amino acid glycine from water to octanol).

1. Which amino acids are *most* favorable to transfer? Does this make sense?
2. Which amino acids are *least* favorable to transfer? Does this make sense?
3. How might you predict/calculate amino acid transfer free energies from these structures?

Now we're going to try to understand where these transfer energies come from, and practice *PyMOL* on the way. Download ala-gln-ala.pdb.

1. Next, you will calculate the surface area of polar atoms (N and O) and nonpolar atoms (C and S). In the command line, type:
   (a) get_area (name N*,O*)
   (b) get_area (name C*,S*)
   (c) Record the values in Angstroms^2 that are returned.
2. Put these values into the "N/O" and "C/S" columns of the spreadsheet. (I pre-calculated these values for the rest of the amino acids). Then plot:
   (a) $\Delta\Delta G$ vs the N/O areas. Fit a line to the data. What do you observe?
   (b) $\Delta\Delta G$ vs the C/S areas. Fit a line to the data. What do you observe?
3. Justify these graphs in molecular/atomic terms.