HW 3

1. The hydrophobic effect is driven by the increase of solvent entropy. It will increase the number of hydrogen bonds within water molecules, which are reoriented tangentially to fight against hydrophobic molecules' disruption.

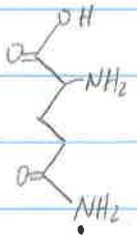
Solvation refers to interactions between solvent and solute molecule. The interaction can be hydrogen bonding, VdW and other types of interactions. When dissolving the solute, the solvent entropy increases.

A hydrogen bond is the electrostatic attraction between polar groups.

The hydrogen bond and solvent entropy are independent.

HW 3 Problem 2

a. the closest two heavy-chain pair:

Chain D Y102 / OG1  & Chain A Q384 / NE2 

b. Lennard-Jones potential → VdW (CHARMm param 19)

$$E_{vdW} = \varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - 2\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right]$$

from Table IV: (Neria et al, 1996)

for Y102/OG1: $r_i^{min} = 1.6\text{Å}$ $\varepsilon_i = 0.1591$ kcal/mol

for Q384/NE2: $r_j^{min} = 1.6\text{Å}$ $\varepsilon_j = 0.2384$ kcal/mol

from PyMol Measurement: $r_{ij} = 2.8\text{ Å}$

$\therefore \sigma_{ij} = r_i^{min} + r_j^{min} = 1.6 + 1.6 = 3.2\text{Å}$

$$\varepsilon_{ij} = \sqrt{\varepsilon_i \varepsilon_j} = \sqrt{0.1591 \times 0.2384} = 0.1948 \text{ kcal/mol}$$

$$\therefore E_{vdW} = 0.1948 \times \left[\left(\frac{3.2}{2.8}\right)^{12} - 2\times\left(\frac{3.2}{2.8}\right)^{6}\right] = 0.1948 \times 0.5084 = 0.0990 \frac{\text{kcal}}{\text{mol}}$$

c. Gaussian exclusion model of Lazaridis & Karplus E_{sdv}

for Atom i: Y102/OH

$R_i = \frac{1}{2}\sigma_{ij} = \frac{1}{2} \times 3.2 = 1.6\text{Å}$

→ $V_i = 10.8\text{Å}^3$ $\lambda_i = 3.5\text{Å}$ $r_i = \varepsilon_i = 0.1591$

$\Delta G_i^{ref} = -5.920$ kcal/mol $\Delta G_i^{free} = -6.70$ kcal/mol

$x_i = \frac{r_i - R_i}{\lambda_i} = -0.4117$ $d_i = \frac{2\Delta G_i^{free}}{\sqrt{\pi}\lambda_i} = -2.160$ kcal/mol

for Atom j: Q384/NH2

I don't know the value of r is → correct or not.

$R_j = 1.6\text{Å}$

$V_j = 11.2\text{Å}^3$ $\lambda_j = 3.5\text{Å}$ $r_j = \varepsilon_j = 0.2384$

$\Delta G_j^{ref} = -5.450$ kcal/mol $\Delta G_j^{free} = -7.80$ kcal/mol

$x_j = \frac{r_j - R_j}{\lambda_j} = -0.3890$ $d_j = \frac{2\Delta G_j^{free}}{\sqrt{\pi}\lambda_j} = -2.515$ kcal/mol

$\Delta G_{sdv,i} = \Delta G_i^{ref} - f_i(r_{ij})V_j$

$\Delta G_{sdv,j} = \Delta G_j^{ref} - f_j(r_{ij})V_i$

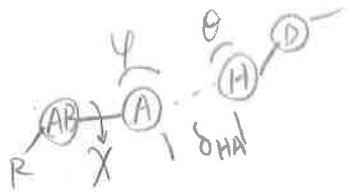
$E_{sdv} = \Delta G_{sdv,i} + \Delta G_{sdv,j}$

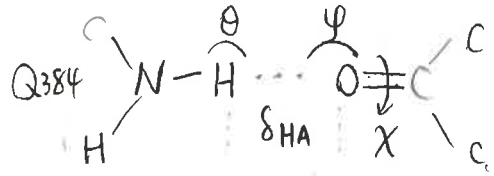
$= \Delta G_i^{ref} + \Delta G_j^{ref} - \frac{d_i e^{-x_i^2} + d_j e^{-x_j^2}}{4\pi r_{ij}^2}$

$= -5.920 - 5.450 + \frac{2.160\, e^{-0.4117^2} + 2.515\, e^{-0.3890^2}}{4\pi(2.8)^2}$

$= -11.3296$ kcal/mol < 0.

→ The solute is less soluble.





δHA = 2.0Å
θ = 127.6°
ψ = 108.4°
χ = 137.2°

χ: H-O-Cz-CE1

d. Hydrogen bond between Y102/OH & Q384/NH_2

$$E_{HB} = -kT \ln\left[\frac{P_{obs}(\delta_{HA}, \psi, \theta, \chi)}{P_{random}(\delta_{HA}, \psi, \theta, \chi)}\right] \overset{\text{independent}}{=} -kT \ln\left(\frac{P_\delta P_\psi P_\chi P_\theta}{P_{radius} P_{r,\psi} P_{r,\chi} P_{r,\theta}}\right)$$

$$= -kT(\ln P_\delta + \ln P_\psi + \ln P_\theta + \ln P_\chi)$$

$W_{HB} = kT$ $= W_{HB}[E(\delta HA) + E(\psi) + E(\theta) + E(\chi)]$

from Karxtemme's paper

$\delta_{HA} = 2.0Å$ $E_{\delta A} = -\ln \frac{f_{protein}(\delta_{HA})}{f_{random}(\delta HA)} \approx \frac{501/\text{total counts}}{\frac{1}{31}}$

I didn't see the frequency distribution, And I don't know the total counts.

$$E_\psi = -\ln \frac{f_{protein}(\psi)}{f_{random}(\psi)} =$$

etc

d.1: H placement will change the length δ_{HA}, and θ: O-H-A, and ψ: AB-A-H. Thus it can change the energy. Also, it can create new H Bond and breaks the old one.

d.2
- PyMol places H atoms in positions based upon the structure of the neighbor to which it will bound. If the position is ambiguous, PyMol will randomly choose a position without optimization.
- PyRosetta places Hydrogens based on its database, which provids correct placements of every atoms with an amino acid. I think it will calculate the bond length, bond angle and torsion angle of the H, and then place it into right place.

d.3: Based on the bond length, angle, torsion angles, place it and refine the placement by score comparison after some movements.

2. e.

Based on my calculation, the Solvation contributes most ΔG^{ref}: the two atoms are fully solvated

It's not a valid question.

		VdW	Solvation	Hbond
3. My Calculation :	Q-Y:	0.099 kcal/mol	-11.3296 kcal/mol	\
PyRosetta	fa_atr	fa_rep	1.310	-0.276
	-1.121	8.382		
	weighted: 2.791			

Q: Why do they differ?

A For VdW and Sol, I calculated two side chain atoms, but the PyRosetta energy contains all atoms in two residues. And Pyrosetta has a weight serie.

4. a. b see fig. 1 2 3, · b: CH-NI $\frac{1}{2}k_b = 422$ kcal/mol·Å² $b_0 = 1.45$Å

c. No, the Statistics don't match.

CHARMm: $b_0 = 1.45$Å ← average length.

$E = \frac{1}{2}k_b(b-b_0)^2$, $F = -\nabla E = -k_b b + k_b b_0$, $F = -K b + k_0 b_0$

· spring constant

$\therefore K_{CHARMm} = k_b = 2 \times \frac{1}{2}k_b = 844$ kcal/mol·Å²

∴ for CHARMm, $b_0 = 1.45$Å $K = 844$ kcal/mol·Å²

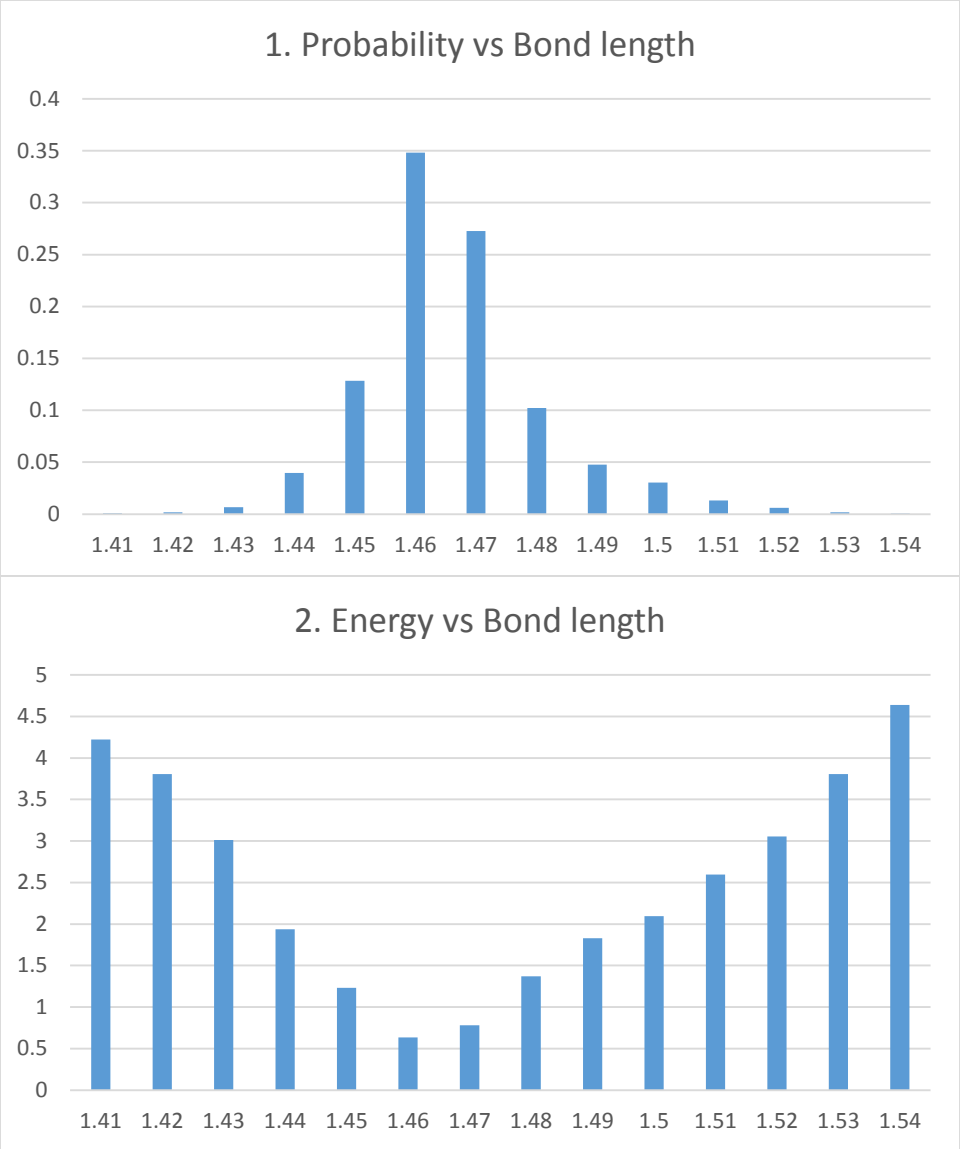
After I fit a parabola to my data

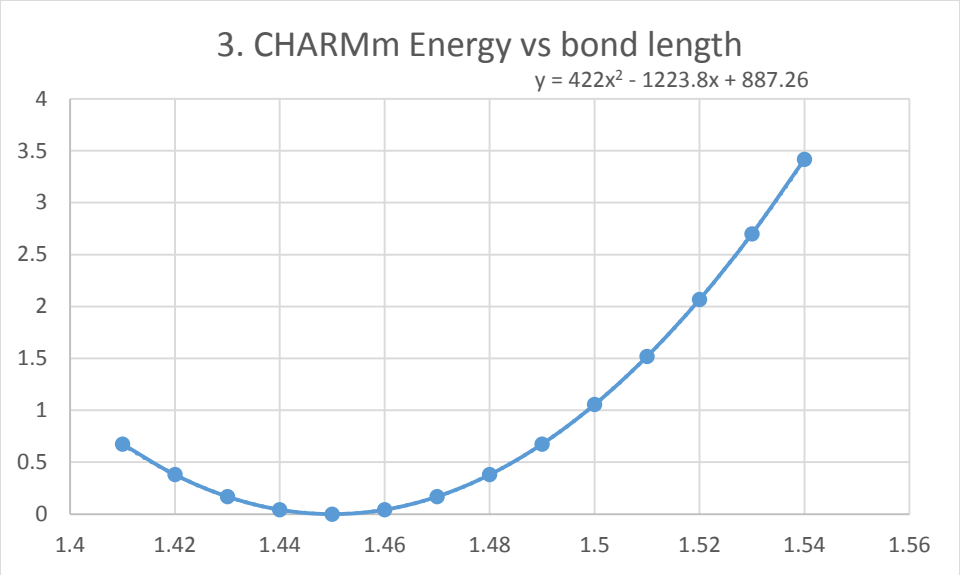
The equation of this parabola is: $E = 827.18\,b^2 - 2436\,b + 1794.7$

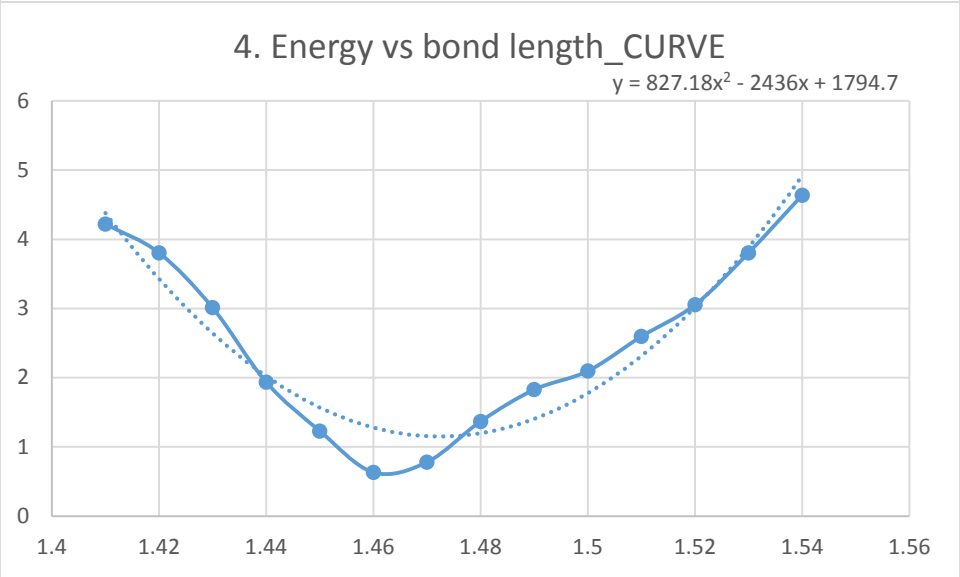
→ $b_0 = b_{min} = 1.4725$ Å ← average length.

$F = -\nabla E = -827.18 \times 2b - 2436 = -Kb + \text{Constant}$.

→ $\therefore K = 827.18 \times 2 = 1654.36$ kcal/mol·Å²


1. Probability vs Bond length
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
1.41 1.42 1.43 1.44 1.45 1.46 1.47 1.48 1.49 1.5 1.51 1.52 1.53 1.54
2. Energy vs Bond length
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
1.41 1.42 1.43 1.44 1.45 1.46 1.47 1.48 1.49 1.5 1.51 1.52 1.53 1.54


3. CHARMm Energy vs bond length
y = 422x² - 1223.8x + 887.26
4
3.5
3
2.5
2
1.5
1
0.5
0
1.4
1.42
1.44
1.46
1.48
1.5
1.52
1.54
1.56


4. Energy vs bond length_CURVE
y = 827.18x² - 2436x + 1794.7
6
5
4
3
2
1
0
1.4
1.42
1.44
1.46
1.48
1.5
1.52
1.54
1.56