For this analysis, use on the *neutral* sidechains, not the *ionized* sidechains.

1. Is the surface area of carbon, nitrogen, or oxygen a better predictor of the octanol transfer free energy? Can you explain why this might be?

2. Graph the octanol transfer free energy for the neutral amino acids against the surface area you identified above.

   (a) What points are outliers?
   (b) What do they have in common?
   (c) What molecular explanation might explain this?

3. Remove the weirdo data points you identified in #2.

   (a) How many $kJ \cdot mol^{-1}$ of free energy do you gain for transferring a square angstrom of carbon to octanol?
   (b) What is the R^2 for the linear fit?

4. Again, using the non-weirdo points from #2:

   (a) How well do the results correlate between octanol, NMA, EtOH, and hexane?
   (b) What aspects of the protein interior do these solvents model well? Poorly?
   (c) Can you learn anything about the intrinsic accuracy of these surface area/energy calculations for proteins from the difference between the models?

5. These surface areas were calculated using the structures in the "pdb" directory, using a single conformation for each sidechain.

   (a) Choose two (non-weirdo) amino acids of your choice. Load up the structures from the "pdb" directory in PyMOL. Use the mutagenesis wizard to put the sidechain in different conformations. Measure the solvent-accessible surface area of carbon for each conformation.
   (b) How big is the spread of SASA relative to the trend $\Delta G_{transfer}$ vs. SASA?

6. Finally: the "Calculating protein energetics" packet has a model carefully parameterized to reproduce the hydrophobic effect associated with protein folding.

   (a) Use the *nonpolar* portion of the model to estimate $\Delta G_{transfer}$ for each amino acid.
   (b) How well does this corrleaate with the octanol scale?

7. Combining what you observed in #4, #5, and #6: can you estimate the confidence you would have in an energy calculated using a surface area calculation? (You may not have the stats skills to do this rigorously. That's fine. The goal is to wrestle with it intellectually).