BBSI Lab Assignment for 6/9/03

Today’s assignment will consist of using MOE to perform force field minimization calculations. We will do several types of analysis to determine which force fields are the best in reproducing experimental/ high level \textit{ab initio} results. Minimizations will be done using 2 different force fields, the Amber94 and MMFF94 force fields.

The molecules that will be used in the minimizations are a blocked alanine dipeptide, BPTI (Bovine Pancreatic Trypsin Inhibitor), and Crambin (a plant protein). The minimizations will be done with and with out solvation effects included. For analysis, you will plot a $\phi/\psi$ map for the blocked alanine dipeptide and evaluate force field energies for the 2 proteins as well as calculate a root mean square deviation (rmsd) value from the original structures.

1.) Download the necessary PDB files (BPTI and Crambin) from \url{www.rcsb.org} (instructions available in the Molecular Visualization lab available online at the BBSI website).

2.) To change the force field parameters in MOE, click on the \textit{Window} $\rightarrow$ \textit{Potential Control} tab at the top of the main MOE window. In the pop up window you will be able to change the force field (at the top) and last row in the first column will allow you to change the solvation.
   A.) For no solvation, set the solvation value to zero.
   B.) To add solvation, check the box and set the value to 1.

To calculate a rmsd for two structure (you will be doing this later for the Crambin and BPTI), open the Sequence Editor. In the Sequence Editor go to \textit{Homology} $\rightarrow$ \textit{Superpose}. Click the box at the bottom of the screen to print out the rmsd. This will print the rmsd value to the Command screen (you can open this in the main MOE window).

3.) Blocked alanine dipeptide can be built in MOE by using the \textit{Edit} $\rightarrow$ \textit{Protein Builder} tab. The just click on alanine (ALA) and select both the Acetylate N-Term and Amidate C-term tabs at the top of the screen.

Make a $\phi/\psi$ Plot for the blocked alanine dipeptide. Use the \textit{Compute} $\rightarrow$ \textit{Mechanics} $\rightarrow$ \textit{Dihedral Contour Plot} option. Select the $\phi$ angle (C$_O$-N-C$_\alpha$-C$_O$ ) first by clicking on the four atoms and then the $\psi$ angle (N-C$_\alpha$-C$_O$-N) the same way. Do this for the different force fields.

Go to the Pitt library website and get the following reference:

Compare your $\phi/\psi$ Plot to the plot found in the paper. See which force field gives the best results.

Try other amino acids and compare the $\phi/\psi$ maps. What features are the same; what features are different?

4.) Perform energy minimizations on both Crambin and BPTI with the Amber94 and MMFF94 force fields. Run the minimizations with and without solvent term(described above). This will be a total of 8 minimizations.

Overlay the minimized structure with the original structures in each case (outlined in the Molecular Visualization lab) and calculated the rmsd of the structures. See which force field is the “best” in reproducing the original structures. Also see how the solvent in the minimizations plays apart in the variance of the original structure.