Assignment 11: A Global Optimization Contest!

Our goal is to compute the lowest energy structure for the pentapeptide met-enkephalin, whose sequence is **Tyr–Gly–Gly–Phe–Met**. Many local minima exist for this molecule, so it is a challenge to reach the global minimum. *The student who finds the structure of the lowest energy will receive a prize from the instructor.*

The rules of this contest are:

1. use a molecule with *charged* COO^- and NH_3^+ ends
2. use the AMBER force field
3. use the distance dependent dielectric constant (**Discover** module, Parameters/Set command, Dist_Dependent button on)
4. use $1/2$ as the scale factor for 1–4 nonbonded interactions (i.e., Parameters/Scale_Terms command, p1_4 button on, and specify 0.5)

You can use *any* technique mentioned in this course (energy minimization, molecular dynamics, Monte Carlo sampling), as well as any other resources (e.g., web and literature), to find the global minimum of the pentapeptide.

Be Creative.

Hand in a detailed report describing how you reached the minimum for met-enkephalin and any particular difficulties, or interesting observations, you encountered along the way. Attach the Cartesian coordinate file and the energy value reached.

Also submit a three-dimensional picture of the configuration of lowest energy along with a table specifying all associated bond lengths and bond angle values, and the $\{\phi, \psi\}$ and χ dihedral-angle values per residue.

To qualify for consideration of the prize, send electronically the coordinate file with the minimized structure to the instructor and TA.

Good Luck!

Background Reading from Coursepack

- K. A. Dill and H. S. Chan, "From Levinthal to Pathways to Funnels", *Nature Struc. Biol.* **4**, 10–19 (1997).
- T. Lazaridis and M. Karplus, " 'New View' of Protein Folding Reconciled with the Old Through Multiple Unfolding Simulations", *Science* **278**, 1928–1931 (1997).