Project 2. MD Simulations of a Protein/Ligand System

1. **Select a protein system** (Thrombin was used as an example in class)

Protein Class	PDB Code	-logk_d	Resolution
Neuraminidase	2QWG	8.4	1.8
DHFR	1DHF	7.4	2.3
L-arabinose	1ABE	6.52	1.7
Thrombin	1A5G	10.15	2.06
Human oxresin receptor 1	4ZJ8	~10	2.75

2. **Select top hits from autodock-vina screening**
   Top 2 and bottom 1

3. **Prepare ligand structures and residue topologies**
   - Add hydrogen with adt
   - Generate Gaussian gcrt file with antechamber
   - Run G09 to calculate electrostatic potentials (ESP)
   - Run Antechamber to assign RESP charges
   - An alternative is run antechamber to assign am1-bcc charge

4. Prepare topology files for minimization and MD simulations
   - xleap
   - tleap

5. Run Minimization and MD simulations using a delicate scheme
   - Minimization with main chain restrained using a set of gradually reduced restraint force constants

- MD simulation with main chain restrained using a set of gradually reduced restraint force constants
- Heat systems up using a set of temperatures
- Equilibrium phase
- Sampling phase

6. Analyze MD snapshots
    - Average structure
    - RMSD ~ simulation time plots
    - Quasi-harmonic analysis
    - MD movie

Suggestion: copy the command scripts, input files from the 1A5G subdirectories (/home/mmms/project2/1A5G).