MD SIMULATIONS: HOMEWORK QUESTIONS

Instructions:

These are all questions on logic; NO calculations; review lectures; work by yourself: due April 10, 2019

1. Describe and name interaction potentials needed to simulate (at atomistic level):
   - ideal gas
   - liquid of charged/uncharged spherical particles with excluded volume
   - biomolecular systems like solvated DNA/protein

2. Name the reasons (as many as you can) why .pdb structures from Protein Data Bank may be bad inputs for MD simulations? Consider X-ray crystal and solution NMR structures as examples. What approaches are typically used to make those structures usable for MD simulations ?

3. What are periodic boundary conditions (PBC) and why they are commonly used in all-atom MD simulations? When analyzing MD simulation trajectory produced with the use of PBC, what must be necessarily taken into account ?

4. What statistical ensembles can be simulated with MD ? Which of them naturally follows from the first principles of classical MD ? Does it matter what simulation ensemble you choose and why ?

5. What is ergodic hypothesis and what is the main assumption behind it? Why it is of primary importance in MD simulations ? Provide examples of systems for which ergodic hypothesis is not valid; how useful may be MD simulations of such systems?

6. Why free energy, rather than potential energy (interaction potentials), governs overall behavior of the system simulated with MD? Can free energy be measured in MD simulations and why?

7. Why Free Energy Perturbation (FEP) method can often NOT be straightforwardly used to compute even small free energy differences? Provide your thoughts.

8. What is Thermodynamic Integration method and what processes can be effectively studied with it ?

9. What is Umbrella Sampling and why it is often used in conjunction with Potential of Mean Force (PMF) calculations ?

10. When modeling biological systems at coarse-grain (CG) resolutions, what is the main motivation for choosing certain resolution ? What strategy is typically used to develop accurate CG models (interaction parameters governing MD simulations of such systems) ? What criteria used to determine maximum simulation time step ?

11. What is the minimum input for MD simulation ? (list the files and mention information provided by these files)