Chemistry 430 — Simulation in Chemistry & Biochemistry

Laboratory #3 — Properties of Pure Liquids via Molecular Dynamics Simulation

In this lab you will prepare a cubic periodic box containing a pure organic liquid, and then generate a molecular dynamics trajectory for the liquid. Post-processing analysis of the trajectory will then give estimates of the density, heat of vaporization, radial distribution, diffusion constant, *etc.* for your chosen liquid.

Protocol

(1) Below is a table containing the molecular weight, density, melting point and boiling point for several simple liquids. Your goal in this lab is to pick one of these molecules, perform a molecular dynamics simulation on a liquid sample of your chosen substance, and then compute values for the density, heat of vaporization, diffusion constant and radial distribution functions. For the molecules that exist in multiple conformations, you can also monitor the approach to conformational equilibrium.

Molecule	**MW**	**Density**	**MP**	**BP**
Acetic Acid	60.05	1.049	46	118
Acetone	58.08	0.791	-94	56
Acetonitrile	41.05	0.786	-48	82
Ammonia	17.03	0.682	-78	-33
Aniline	93.13	1.022	-6	184
Benzene	78.11	0.874	6	80
Chlorobenzene	112.56	1.107	-45	132
Cyclohexane	84.16	0.779	7	81
Cyclopentene	68.12	0.774	-135	44
Dimethyl Formamide	73.10	0.944	-98	153
Dimethyl Sulfoxide	78.13	1.101	18	189
Ethanol	46.07	0.794	-114	78
Ethane Thiol	62.13	0.839	-145	35
Ethyl Acetate	88.11	0.902	-84	77
Ethyl Iodide	155.97	1.950	-108	71
Ethylene Glycol	62.07	1.113	-13	197
Formamide	45.04	1.134	3	210
Methanol	32.04	0.791	-98	65
Methyl Disulfide	94.20	1.046	-85	109
Methyl t-Butyl Ether	88.15	0.740	-109	52
Nitromethane	61.04	1.127	-29	101
Pentane	72.15	0.626	-130	36
Phenol	94.11	1.017	41	182
Tetrahydrofuran	72.11	0.889	-108	66
Trifluoroethanol	100.01	1.373	-44	79
Trimethyl Amine	59.11	0.636	-117	4
Water	18.02	1.000	0	100

(2) First, obtain a TINKER **`.xyz`** file with a single molecule of your chosen substance. Files for isolated molecules, set up to use the OPLS-AA force field, are provided on the course website for this lab. You will need to use the special version of the **`oplsaa.prm`** file also provided on the lab site. This version of the parameter file has extra parameters for some molecules in the list. In addition, copy the **`tinker.key`** file from the lab website, which initially contains just a single line pointing to the OPLS-AA parameters. Place all of these files into a new directory that you create and where you will perform this lab.

(3) Examine the **`.xyz`** file and compare the atom types in the column just to the right of the x,y,z-coordinates against the OPLS-AA parameter file obtained in the previous step to verify that the correct atom types are used for your molecule.

(4) Minimize your molecule using the Tinker **`minimize`** program to clean up any distortions in the original geometry. Copy your molecule to a second file with some different name, edit this second file to translate the molecule to some new set of coordinates using any text editor, and then use the Tinker **`xyzedit`** program to merge your two molecule files into a single file containing a dimer. Run the **`minimize`** program to find the optimal structure and energy for the dimer. What is the energy of interaction of the two molecules in the dimer, *i.e.*, the energy of the dimer minus twice the energy of the monomer? Are you sure that you have found the best dimer structure?

(5) Run the Tinker **`xyzedit`** program on the minimized monomer (not the dimer from step 4!). Use the **`xyzedit`** option to create a cubic periodic box filled with multiple copies of your molecule. You should construct a box of about 25-30 Angstroms on a side, and you will need to calculate the number of molecules to place into the box based on the molecular weight and density of your chosen liquid. Note that 1 Angstrom is equal to 10^{-10} meters or 0.1 nanometers, and Avogadro's number is $6.02214076 \times 10^{23}$.

(6) Make sure the box size in Angstroms is set via the appropriate keyword (for example, **`X-AXIS 25.0`**, or whatever box size you chose in step 5) in your **`tinker.key`** keyfile. In that same keyfile, you should also set the cutoff distance for the van der Waals interactions. This value must be somewhat less than half the box dimension – a value of 9 Angstroms is typical for OPLS simulations. For example, you could add the keyword **`VDW-CUTOFF 9.0`**. We will use Ewald summation for electrostatics by adding the **`EWALD`** keyword to the keyfile. And set the real-space Ewald cutoff to 7 Angstroms via **`EWALD-CUTOFF 7.0`** keyword. Then enable use of pair neighbor lists for both VDW and electrostatic interactions by adding the **`NEIGHBOR-LIST`** keyword. Finally, add the **`RATTLE`** keyword to fix all bonds to hydrogen atoms at their ideal lengths.

(7) Next you will minimize the energy of the solvent box to remove any bad or high energy contacts. To complete this step, run the Tinker **`minimize`** program to perform the minimization of your liquid box. You should use a moderate convergence criterion for the minimization of about 1.0 kcal/mol/Ang instead of the tighter default of 0.01. If your initial attempt at minimization fails, you may need to first perform the minimization with the **`CHARGETERM NONE`** keyword line added to the **`tinker.key`** file. It may also be necessary to remove the **`RATTLE`** keyword to get the minimization to start correctly. If you make these changes to get the minimization to run initially, then rerun the minimization after removing the **`CHARGETERM NONE`** keyword, and adding back the **`RATTLE`** keyword.

(8) Start an MD simulation using the Tinker **`dynamic`** program and performed in the isothermal-isobaric ensemble (constant temperature and pressure, also referred to as NPT). We will use a standard integration method due to Beeman, and add a thermostat and barostat to maintain temperature and pressure, respectively. First, put the keyword **`INTEGRATOR BEEMAN`** into the **`tinker.key`** file. Then, when running the calculation, use room temperature (298K = 25°C) for the target temperature, as long as your substance is a liquid at that temperature. Otherwise use a target temperature midway between the melting and boiling points. The target pressure should be 1 Atm.

(9) As input to the **`dynamic`**, you will be asked for values related to collection of your MD trajectory. Use a 2 fs (fs = femtosecond = 10^{-15} seconds) time step for integration, and save coordinate snapshots every 1.0 ps (ps = picosecond = 10^{-12} seconds). Ideally, your production period should be run for at least a nanosecond (10^{-9} seconds) or longer. You will generally need to discard the first portion of the trajectory (perhaps 200 ps) as an "equilibration period". Following equilibration, you can use the remaining "production period" of the trajectory in your analysis to determine the density, heat of vaporization, and radial distributions for the OPLS-AA model of your liquid. The full trajectory produced by **`dynamic`** will be written to a single Tinker archive (**`.arc`**) file.

(10) In order to actually run your MD calculation, you should submit the job in the "background" on your computer inside a terminal window. This can be done with a command similar to the one below, which incorporates the suggested options from steps 8 and 9 above:

```
dynamic mol.xyz 500000 2.0 1.0 4 298.0 1.0 >& mol.log &
```

where you should replace "mol" in this command with the file name you have chosen for your system. Make sure you understand all the parts of this command. Issuing such a command will start the MD job running, send any output that would have displayed on the screen to a file named "mol.log", and return a command line prompt in your terminal window. The MD job will run from some time (perhaps an hour), so you will probably want to continue with the rest of the lab at some later time.

(11) Average properties from your MD run can be determined by using the Tinker **`mdavg`** script (in the /bin directory of the Tinker distribution) on the log file from the molecular dynamics calculation. This will provide the average temperature, pressure, density, potential energy, *etc*. The instantaneous values of these same quantities can be found by inspecting and using **`grep`** on the log file. In particular, you should compare your computed density with the experimental value. What is the percentage error in the simulated density?

(12) You should figure out how to compute the heat of vaporization from your MD results. See the Leach textbook, or other recommended course books for further information on how to determine the heat of vaporization.

(13) Radial distribution functions can be computed from your saved MD coordinates using the Tinker **`radial`** program. For example, try computing the distribution function between pairs of like polar atoms, if your liquid contains a polar functional group. The theory and form of radial distributions is described in section 6.2.5 of Leach, and will be covered in a later course lecture. Provide a plot of the radial distribution function with your lab report.

(14) Use the Tinker `diffuse` program to compute the diffusion constant for individual molecules within your sample of liquid. Provide your best estimate of the diffusion constant of your liquid in your lab report, and compare to a values reported in the literature, if you can find one.

(15) Finally, if your liquid can exhibit alternative conformations, such as the "chair" and "boat" conformations of cyclohexane, determine the relative percentage of each conformation as a function of the simulation time. Does it look like your system has reached its conformational equilibrium state?

Questions

(1) Why is it necessary to minimize your liquid box before starting the MD run? What would likely happen if you skipped this step?

(2) Diffusion constants are typically computed via the Einstein relationship. What is this relationship, and how is it used to derive the diffusion constant?

(3) What methods can be used to determine whether an MD simulation is "equilibrated"? Not all properties equilibrate and/or convergence at the same rate. Which kinds of properties tend to converge more slowly?

(4) It is also possible to use an MD simulation to compute an estimate of the heat capacity of your liquid. Find the statistical mechanical fluctuation formula for the heat capacity and apply it to your simulation data (see Leach or a similar book). The value you derive will probably be rather uncertain, at best. Why?