Nanoscale Science and Engineering, 2016-II
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Assignment #5

Objective
In this problem set we will use a molecular dynamics code (black box for now) called LAMMPS to optimize the structure and compute the vibrational frequencies of a tripeptide from molecular dynamics at room T.

Motivation
First, you should know that tripeptides are essential proteins in cell communication, blood pressure regulation, thyroid function, and it is believed they also help to reverse skin damage (cosmetics) so understanding how the work dynamically is important. The specific function of a tripeptide is determined by the three amino-acids involved (linked by peptide bonds), and by how the molecule changes conformation under different conditions and in time.

As you know, energy minimization is used to determine stable states for a molecular structure. So we'll try to confirm if a given potential is good enough to model the tripeptide case attached, from our molecular mechanics (minimization) and molecular dynamics runs.

Procedures and questions

1. (10%) Identify the tripeptide, i.e. what is the amino acid sequence?
2. (20%) Prepare and include in your response, scripts to minimize the tripeptide molecule to an RMS force of 0.01 and an energy difference of 0.001 kcal/mol with:
   i. Steepest descent
   ii. Conjugate Gradient
   iii. FIRE method (read paper "Structural Relaxation Made Simple" by Bitzek etal)
   iv. Annealed Dynamics: 1 annealing cycle using standard micro canonical (NVT) dynamics per cycle, and a temperature profile starting at 100 K and ending at 0 K. Minimize after annealed dynamics.

Use LAMMPS with the Dreiding potential (read the attached paper from Mayo etal, dreiding.pdf to understand the potential forms). Since Dreiding is not explicitly supported in LAMMPS, I am attaching the corresponding input files to setup LAMMPS (data.tripeptide and in.tripeptide_singlepoint) for running potential interactions available in LAMMPS that would be equivalent to Dreiding. For the annealed dynamics case you'll need to understand and add the appropriate LAMMPS commands (hint, see "fix not" at http://lammps.sandia.gov/doc/fix_nh.html).

If you want to visualize your results on the actual molecular structure, you can download a molecular viewer, such as VMD http://www.ks.uiuc.edu/Research/vmd/

   a. Report in tabular form the number of minimization steps and the converged energy value (if it converges) for each case, 2i-iv. Please print the individual energy terms for bond, angle, torsion, vdw, and Coulomb (see the "thermo_style" command at http://lammps.sandia.gov/doc/thermo_style.html).

b. Conclude on which method performs better based on your analytical understanding of the method. After performing annealing dynamics, then minimize the structure. Explain and analyze your results.
c. Change the value of RMS force convergence to 0.001 (leave energy difference the same). How much does your structure change in RMS and energy after applying another cycle of minimization to the already minimized structures from part A. Plot the energy versus number of steps. What behavior do you see? Explain.

3. (20%) Now, equilibrate the molecule at room temperature (i.e. 298K) and run nvt dynamics for 5ns, dumping positions and velocities every 100fs (only after the system has equilibrated). Choose an appropriate integration timestep (e.g. 1fs) and temperature damping constant.
    a. Justify your choice of damping coefficient based on total energy and velocity distribution.
    b. Explain any changes in the tripeptide's conformation during the 5ns. For example, do you see any kinking? any drifting?
    c. Plot the conformational energy surfaces using a Ramachandran plot (which relates the 2 backbone torsion angles present in the molecule, see http://en.wikipedia.org/wiki/Ramachandran_plot for more info). Read the attached paper on "Conformational Search on the Tripeptides Structure by Molecular Dynamics", by Khebichat et al (2013) for details about what you should look for and provide additional insights.
4. (10%) Increase the temperature a bit, say to 310 and then 315K (i.e. the first is a physiologically normal body temperature and the second a high fever temperature).
    a. Is this a rigid or non-rigid tripeptide?
    b. Compute, plot and report the RDF (radial distribution function) between carbons, and between oxygens and nitrogens at each temperature (298,310,315K). See http://lammps.sandia.gov/doc/compute_rdf.html for more info on how to do this within your lammps script.
5. (20%) Build the velocity autocorrelation function (VACF) from the dumped file then compute a Fourier transform of the VAC results; plot the power spectrum and compare to experiment. As an alternative to step 8 and 9, you can use the "compute VACF" in LAMMPS (see http://lammps.sandia.gov/doc/compute_vacf.html) to calculate the VAC. You may want to do 8+9 to compute the VAC and then compare to the results obtained from a LAMMPS run.
    a. Describe your findings, i.e. can you point out the frequencies for the different vibrational modes in your tripeptide (bonds, angles, torsions, etc.)?
    b. How can you relate these calculations to experimental IR spectra data?

NOTE: The vibrational spectrum (or vibrational density of states) can be computed from atomic velocities obtained at fixed time intervals over the duration of an equilibrated simulation, you can then load the data into Matlab (or any of your favorite numerical software, e.g. Scipy with correlate and fftpack), take its discrete FFT and then absolute-square it. According to the Wiener-Khinchin theorem, this would be equivalent to taking the Fourier transform of the velocity auto-correlation function.

6. (20%) Conclude qualitatively on your findings. Be as thorough as possible. How do you think a tripeptide works? do you think modeling it's dynamics in solution, e.g. in water, will have a big effect on conformational changes?

Feel free to send me an email if you have any questions.