

## CHEM 436 / CHEM 630: Molecular Modelling of Proteins TUTORIAL #3b: Molecular dynamics: Simple systems

### INTRODUCTION

The goal of this tutorial is to learn how to set up and interpret simple molecular dynamics simulations of a solvated molecule.

The system will be prepared with VMD (<http://www.ks.uiuc.edu/Research/vmd/>), using the “Add Solvation Box” and “Add Ions” extensions, and molecular dynamics will be performed with NAMD (<http://www.ks.uiuc.edu/Research/namd/>).

### REQUIRED PRE-LAB READING

None

### PRE-LAB REPORT

None

### READING

Chapter 6 of Leach (“Computer Simulation Methods”): Sections 6.1, 6.2, 6.4, 6.5, and 6.6.

### REFERENCE MATERIAL

*VMD User's Guide*

<http://www.ks.uiuc.edu/Research/vmd/current/ug/>

*NAMD User's Guide*

<http://www.ks.uiuc.edu/Research/namd/current/ug/>

### PROCEDURE

#### STEP 8: Prepare the PDB and PSF files of hydrated acetate

Download the PSF file of acetate and the PDB structure of acetate corresponding to your sequence number:

```
$ wget http://faculty.concordia.ca/glamoure/files/acetate.psf
$ wget http://faculty.concordia.ca/glamoure/files/acetate??.pdb
```

(“??” stands for the sequence number you were assigned, e.g., “02”.) Load these files into VMD:

```
$ vmd acetate.psf acetate??.pdb
```

From the VMD Main window, select menu “Extensions > Modeling > Add Solvation Box” and fill out the “Solvate” form with the following values:

```
PSF: acetate.psf
PDB: acetate??.pdb
Waterbox Only: Unchecked
Boundary: 2.4
Use Molecule Dimensions: Checked
Box Padding: 10 Å in all six directions
```

The “solvate” script will create a water “box”, with no water molecules closer than 2.4 Å from the acetate solute. It will write files “solvate.psf” and “solvate.pdb”, containing the acetate molecule and the water molecules.

◆ How many water molecules have been created?

Select menu “Extensions > Tk Console” and type the following:

```
% measure minmax [atomselect top all]
```

◆ Report the X,Y,Z dimensions and the approximate volume of the water box.

### STEP 9: Prepare PDB and PSF files of acetate in an NaCl solution

Acetate has a net charge of  $-1$  and its presence in solution is most likely the result of the dissolution of an acetate salt (e.g., sodium acetate). To account for that—and because NAMD requires the total system (solute + water + ions) to be electrically neutral—it is necessary to add counter ions.

Select menu “Extensions > Modeling > Add Ions” and fill out the “Autoionize” form with the following values:

```
PSF: solvate.psf
PDB: solvate.pdb
Ionic Concentration (mol/L): 0.5
Neutralize: Checked
```

The “autoionize” script will write two more files: “ionized.psf” and “ionized.pdb”, containing the acetate molecule, the water molecules, and sodium and chloride counter ions.

◆ How many copies of  $\text{Na}^+$  and  $\text{Cl}^-$  ions have been created, and how many water molecules have been deleted? What approximate salt concentration does this correspond to?

#### Note:

An easy way to count the water molecules in a PDB file is to extract all lines containing “OH2” atoms using the `grep` command and to count them using the `wc` command:

```
$ grep OH2 solvate.pdb
$ grep OH2 solvate.pdb | wc -l
```

### STEP 10: Perform constant-temperature, constant-pressure molecular dynamics

Download the NAMD configuration file for a simple molecular dynamics simulation:

```
$ wget http://faculty.concordia.ca/glamoure/files/md.conf
```

◆ Examine the content of that file and, in the “Methods” section of your report, explain the purpose of each line from the following sections:

- Force field
- Periodic boundary conditions
- Thermodynamic ensemble

Refer to the NAMD User’s Guide and to Leach’s textbook, if necessary. This is an essential part of the simulation protocol, so *be specific*.

◆ Modify the configuration file so that vectors “cellBasisVector1”, “cellBasisVector2”, and “cellBasisVector3” correspond to the X,Y,Z dimensions of your system, **plus 2 Å**.

Run NAMD as a background process by typing “&” at the end of the line:

```
$ namd2 md.conf > md.log &
```

#### Note:

This calculation may take a while (~10 minutes). You can follow its progress by periodically looking at the end of the log file using the `tail` command:

```
$ tail md.log
```

The calculation is done when the last line says “Program finished.”

### STEP 11: View the resulting trajectory

Load the “dcd” trajectory file into VMD by typing:

```
$ vmd ionized.psf md.dcd
```

Select menu “Graphics > Representations...” and create a new representation (using the “Create Rep” button). Set the two representations as following:

Style	Color	Selection
VDW	Name	not water
Lines	Name	water

#### Note:

The “style” is selected from the pull-down list “Drawing Method” and the “selection” should be typed in the text box “Selected Atoms”. For a better rendering of VDW, increase the sphere resolution.

◆ Use the control buttons from the “VMD Main” window to play the “trajectory”. Report any observation about the pairing of the Na<sup>+</sup>/Cl<sup>-</sup> or Na<sup>+</sup>/CH<sub>3</sub>COO<sup>-</sup>.

#### Help on VMD:

To view the properties of an atom:	type “0” and click on the atom
To label an atom:	type “1” and click on the atom
To measure a bond length:	type “2” and click on the two atoms
To measure an angle:	type “3” and click on the three atoms
To measure a dihedral angle:	type “4” and click on the four atoms
To rotate:	type “r”
To zoom in/out:	type “s”
To translate:	type “t”

### STEP 12: Extract the time-series of various thermodynamic properties

Extract the energies, temperature, pressure, and volume from the log file:

```
$ grep “ENERGY: ” md.log > md.ener
```

- ◆ Produce graphs of the following properties as a function of time (in picoseconds):
  - total energy (TOTAL)
  - total kinetic energy (KINETIC)
  - total potential energy (TOTAL – KINETIC)
  - instantaneous temperature (TEMP)
  - instantaneous pressure (PRESSURE)
  - volume of the simulation box (VOLUME)
- ◆ According to the time-series of these properties, how much time was needed for the system to reach equilibrium?
- ◆ Calculate the average value at equilibrium of each of the properties. What density (in g/cm<sup>3</sup>) does the equilibrium volume correspond to?

**Note:**

The easiest way to produce plots on Linux OS is to open the file in OpenOffice (Calc). The more adventurous ones can also try the command-line driven `gnuplot`. The following sequence of commands fits the average value of the total energy (TOTAL, column #12 of file "md.ener") starting from timestep #5000, stores the value in variable "A" and plots the total energy as a function of time along with the average value "A", then saves the graph in an image file called "plot\_md\_TOTAL.png":

```
$ gnuplot
gnuplot> fit [5000:] A 'md.ener' using 2:12 via A
gnuplot> plot 'md.ener' using 2:12 with linespoints notitle, A notitle
gnuplot> set terminal png
gnuplot> set output 'plot_md_TOTAL.png'
gnuplot> replot
gnuplot> quit
```

Alternatively, you can write all these commands in a text file (called, say, "plots.gnu") and load it:

```
$ gnuplot
gnuplot> load 'plots.gnu'
gnuplot> quit
```

**STEP 13: Calculate radial distribution functions (RDFs) of solvated ions**

Select menu "Extensions > Analysis > Radial Pair Distribution Function" and calculate the RDFs of the following eight "pairs" of selections:

Na <sup>+</sup> /water:	"name SOD"	"name OH2"
	"name SOD"	"water and name H1 H2"
Cl <sup>-</sup> /water:	"name CLA"	"name OH2"
	"name CLA"	"water and name H1 H2"
CH <sub>3</sub> COO <sup>-</sup> /water:	"name O1 O2"	"name OH2"
	"name O1 O2"	"water and name H1 H2"
	"name C1"	"name OH2"
	"name C1"	"water and name H1 H2"

Always check "Use PBC", "Display g(r)", and "Display Int(g(r))". For more accuracy, change the values of "delta r" and "max. r".

- ◆ What is the value of the water first coordination number for Na<sup>+</sup>, as described by the sodium-oxygen RDF? What is the value for Cl<sup>-</sup>?
- ◆ Based on the acetate RDFs and on your visual inspection of the molecular dynamics trajectory, describe the solvation structure of the acetate ion, as predicted by the force field.