Molecular Dynamics Calculations using NAMD

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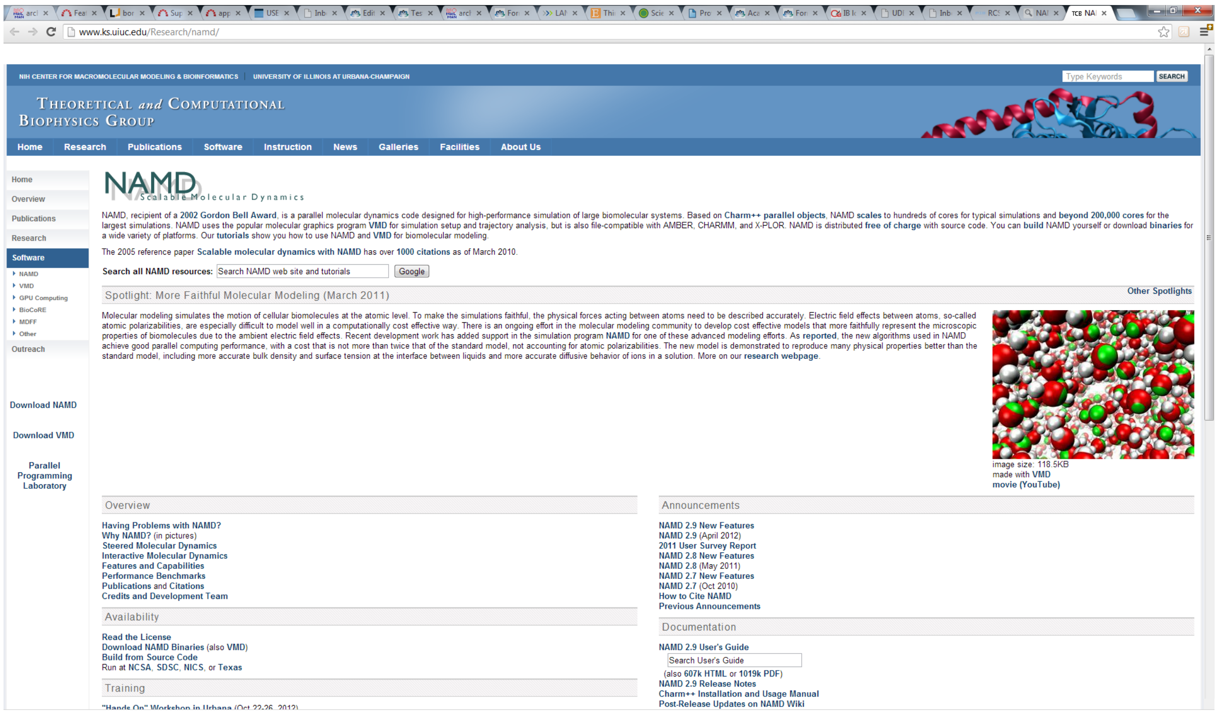
A.Introduction

NAMD (Fig.1), is a parallel molecular dynamics code designed for high-performance simulations of large biomolecular systems. Based on Charm++ parallel objects NAMD scales to hundreds of thousands of processors on high-end parallel platforms and tens of processors on commodity clusters using gigabit ethernet. NAMD uses the popular molecular graphics program VMD for simulation setup and trajectory analysis, but is also file-compatible with AMBER, CHARMM, and X-PLOR. NAMD is distributed free of charge with source code. Detailed description of NAMD may be found at http://www.ks.uiuc.edu/Research/namd/. The detailed guide and tutorial for NAMD may be downloaded from http://www.ks.uiuc.edu/Research/namd/2.7/ug/ and http://www.ks.uiuc.edu/Training/Tutorials/namd/namd-tutorial-win.pdf, respectively. The instructions below do not explain every detail, but it provides a simple guide on how to run basic simulations (protein in water box) instead.



www.ks.uiuc.edu/Research/namd/

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Download NAMD

Download VMD

Parallel Programming Laboratory

NAMD Scalable Molecular Dynamics

NAMD, recipient of a 2002 Gordon Bell Award, is a parallel molecular dynamics code designed for high-performance simulation of large biomolecular systems. Based on Charm++ parallel objects, NAMD scales to hundreds of cores for typical simulations and beyond 200,000 cores for the largest simulations. NAMD uses the popular molecular graphics program VMD for simulation setup and trajectory analysis, but is also file-compatible with AMBER, CHARMM, and X-PLOR. NAMD is distributed free of charge with source code. You can build NAMD yourself or download binaries for a wide variety of platforms. Our tutorials show you how to use NAMD and VMD for biomolecular modeling.

The 2005 reference paper Scalable molecular dynamics with NAMD has over 1000 citations as of March 2010.

Search all NAMD resources: Search NAMD web site and tutorials [Google]

Spotlight: More Faithful Molecular Modeling (March 2011) — Other Spotlights

Molecular modeling simulates the motion of cellular biomolecules at the atomic level. To make the simulations faithful, the physical forces acting between atoms need to be described accurately. Electric field effects between atoms, so-called atomic polarizabilities, are especially difficult to model well in a computationally cost effective way. There is an ongoing effort in the molecular modeling community to develop cost effective models that more faithfully represent the microscopic properties of biomolecules due to the ambient electric field effects. Recent development work has added support in the simulation program NAMD for one of these advanced modeling efforts. As reported, the new algorithms used in NAMD achieve good parallel computing performance, with a cost that is not more than twice that of the standard model, not accounting for atomic polarizabilities. The new model is demonstrated to reproduce many physical properties better than the standard model, including more accurate bulk density and surface tension at the interface between liquids and more accurate diffusive behavior of ions in a solution. More on our research webpage.

image size: 118.5KB
made with VMD
movie (YouTube)

Overview

Having Problems with NAMD?
Why NAMD? (in pictures)
Steered Molecular Dynamics
Interactive Molecular Dynamics
Features and Capabilities
Performance Benchmarks
Publications and Citations
Credits and Development Team

Availability

Read the License
Download NAMD Binaries (also VMD)
Build from Source Code
Run at NCSA, SDSC, NICS, or Texas

Training

"Hands On" Workshop in Urbana (Oct 22-26, 2012)

Announcements

NAMD 2.9 New Features
NAMD 2.9 (April 2012)
2011 User Survey Report
NAMD 2.8 New Features
NAMD 2.8 (May 2011)
NAMD 2.7 New Features
NAMD 2.7 (Oct 2010)
How to Cite NAMD
Previous Announcements

Documentation

NAMD 2.9 User's Guide
Search User's Guide
(also 607k HTML or 1019k PDF)
NAMD 2.9 Release Notes
Charm++ Installation and Usage Manual
Post-Release Updates on NAMD Wiki

Fig. 1. NAMD Web page

B. Standard simulations

Check the computer system to ensure all programs are installed. If you are working on ARCHIE-WeSt all example files can be found at the directory:

```
/users/cwb08102/NAMD_Training
```

Check what modules are loaded by typing:

```
module list
```

check what modules are available to load by typing:

```
module avail
```

load the modules by typing:

```
module load /apps/bin/vmd/1.9.1
module load /mpi/gcc/openmpi/1.4.5
module load /libs/gcc/fftw2/float-mpi/2.1.5
module load /apps/gcc/namd/mpi/2.8
```

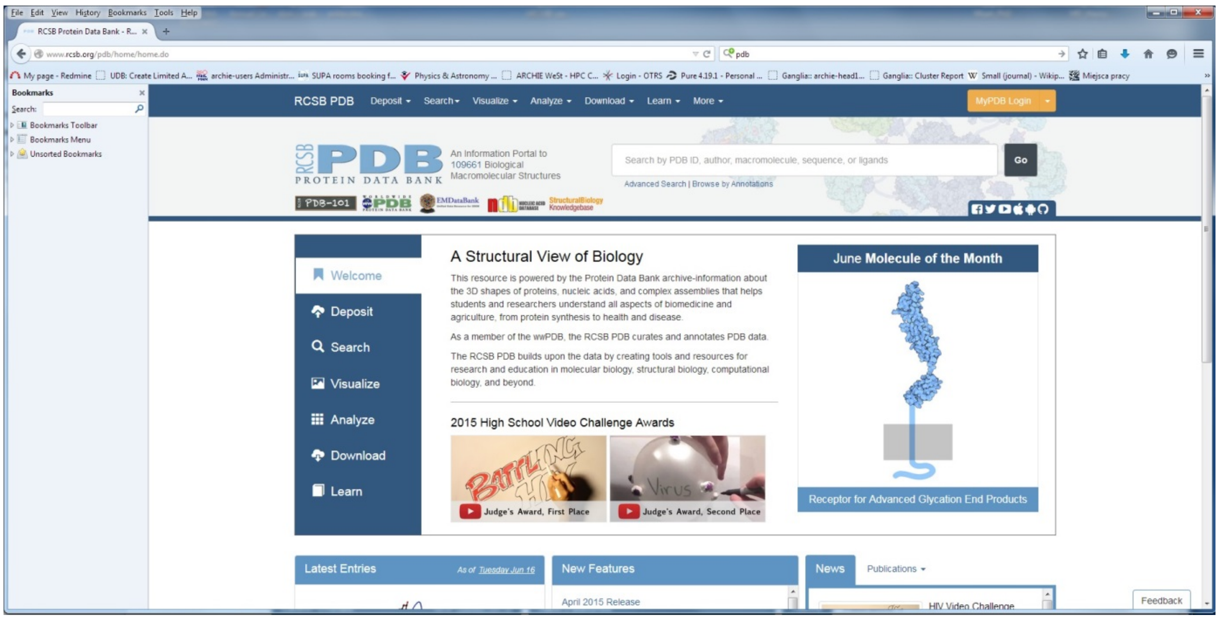
Note: The way you set up your account and environment depends on computer system you work on.

1. Protein structure

To simulate the protein first we need the *x,y,z* coordinates of each atom in the protein. Such information is deposited in the PDB (protein data bank) which consist of X-ray as well as NMR protein structures. Due to technical reasons, X-ray structures are available for large proteins only. The main difference between NMR and X-ray structures is that in NMR structures hydrogen atoms are included while there are no hydrogen atoms in X-ray structure (H atoms are too light to X-ray diffraction experiments). Usually we are interested in large proteins and that is why calculations using the X-ray structure as a first example are described.

a) Download the correct structure

Go to PDB (http://www.rcsb.org/pdb/home/home.do), and look for protein structure you are interested in (Fig.2). Let's say that you are looking for hen egg white lysozyme (HEWL). If you already know the PDB ID (1iee) you can type it in the first text window. Usually you don't know the ID, so give the protein name (e.g. hen egg white lysozyme) in the second text window and click search. You will see a lot of records. There is more than one structure deposited in PDB, so look for the protein obtained with the highest resolution, without ligands and protein engineering procedures. We need the native structure. Check the year when the structure was published, read carefully records provided about structure details and download the original paper describing the structure published (Fig. 3). Once you are sure it is the right structure, download it to your computer in the pdb format (Fig. 3). Let's call this file `protein_original.pdb`.


RCSB PDB
Deposit
Search
Visualize
Analyze
Download
Learn
More
MyPDB Login
RCSB PDB PROTEIN DATA BANK
An Information Portal to 109661 Biological Macromolecular Structures
Search by PDB ID, author, macromolecule, sequence, or ligands
Go
Advanced Search | Browse by Annotations
PDB-101
EMDataBank
StructuralBiology Knowledgebase
Welcome
June Molecule of the Month
Receptor for Advanced Glycation End Products
Judge's Award, First Place
Judge's Award, Second Place
Latest Entries
As of Tuesday Jun 16
New Features
April 2015 Release
News
Publications
HIV Video Challenge
Feedback

A Structural View of Biology

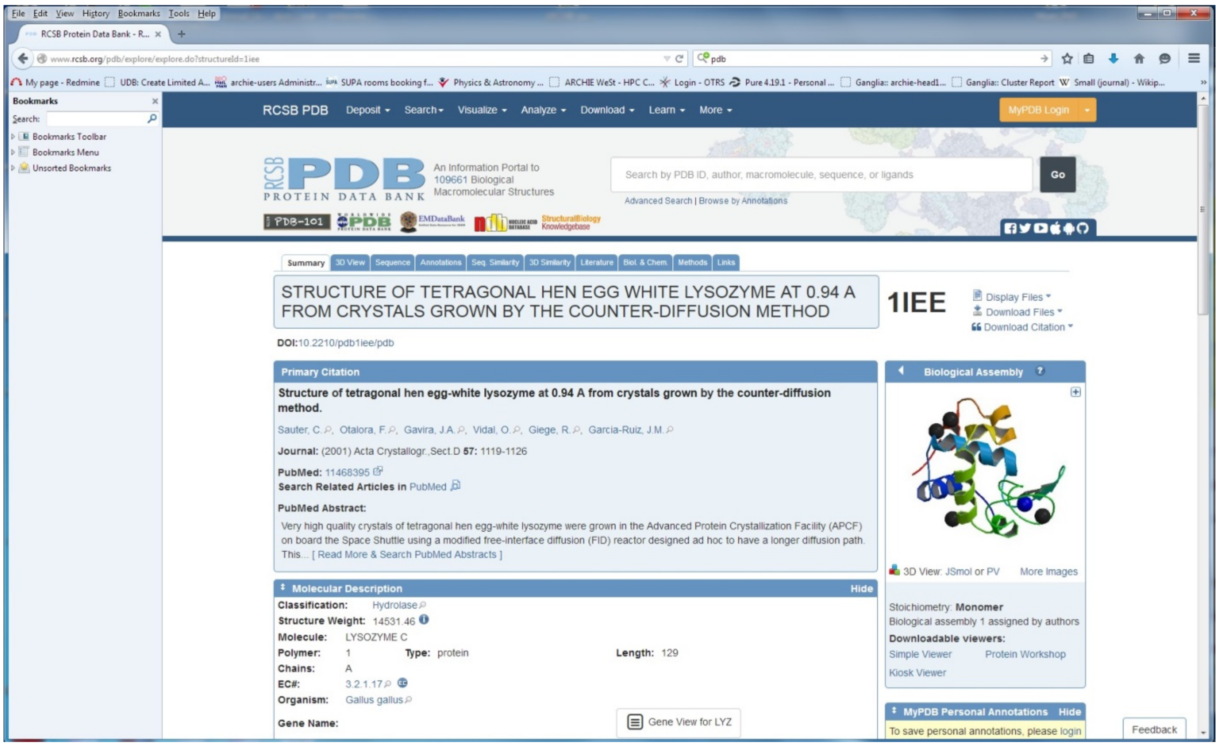
This resource is powered by the Protein Data Bank archive-information about the 3D shapes of proteins, nucleic acids, and complex assemblies that helps students and researchers understand all aspects of biomedicine and agriculture, from protein synthesis to health and disease.

As a member of the wwPDB, the RCSB PDB curates and annotates PDB data.

The RCSB PDB builds upon the data by creating tools and resources for research and education in molecular biology, structural biology, computational biology, and beyond.

2015 High School Video Challenge Awards

Fig.2. Protein Data Bank (pdb) starting page



RCSB PDB PROTEIN DATA BANK An Information Portal to 109661 Biological Macromolecular Structures

STRUCTURE OF TETRAGONAL HEN EGG WHITE LYSOZYME AT 0.94 A FROM CRYSTALS GROWN BY THE COUNTER-DIFFUSION METHOD

1IEE

DOI:10.2210/pdb1iee/pdb

Primary Citation

Structure of tetragonal hen egg-white lysozyme at 0.94 A from crystals grown by the counter-diffusion method.

Sauter, C., Otalora, F., Gavira, J.A., Vidal, O., Giege, R., Garcia-Ruiz, J.M.

Journal: (2001) Acta Crystallogr.,Sect.D **57:** 1119-1126

PubMed: 11468395
Search Related Articles in PubMed

PubMed Abstract:

Very high quality crystals of tetragonal hen egg-white lysozyme were grown in the Advanced Protein Crystallization Facility (APCF) on board the Space Shuttle using a modified free-interface diffusion (FID) reactor designed ad hoc to have a longer diffusion path. This... [Read More & Search PubMed Abstracts]

Biological Assembly

3D View: JSmol or PV   More Images

Stoichiometry: **Monomer**
Biological assembly 1 assigned by authors
Downloadable viewers:
Simple Viewer   Protein Workshop
Kiosk Viewer

Molecular Description

Classification:	Hydrolase		
Structure Weight:	14531.46		
Molecule:	LYSOZYME C		
Polymer:	1	**Type:** protein	**Length:** 129
Chains:	A		
EC#:	3.2.1.17		
Organism:	Gallus gallus		
Gene Name:		Gene View for LYZ	

MyPDB Personal Annotations
To save personal annotations, please login

Fig. 3. PDB – searching result and Download the structure

b) See the protein

Open the vmd program and then go to `Main menu → File → New molecule → protein_original.pdb`. The other way to see the protein is type in your terminal command line `vmd protein_original.pdb`, the result will be exactly the same. Now play in VMD: rotate the protein, change the representation (`Main menu → Graphics → Representations`), and view the protein structure. Read the VMD tutorial to learn how to visualize and present the protein, how to change colors, how to highlight only a chosen residue etc.

2. Prepare the simulations

The *.psf file together with *.pdb contain all information about our protein. The *.pdb file includes only initial coordinates of atoms, the *.psf file includes all other information (bond length, angles, force constants, charges, van der Waals parameters etc.). The psf file is created basing on the *.pdb file and the `top_all27_prot_na.inp` (the topology file). Since it is possible to change the topology file by adding new parameters it is better to use the file `top_all27_prot_surf.inp` created by myself.

a) Prepare the pdb file

Open the protein_original.pdb file using **vi** or any other editor. Read the file, check if there are missing residues where should be disulphide bonds (`SSBOND`) etc. Note that everything which is not a protein is called HETATM (hetero atom). First we need to have all segments (water, protein, ions) in a separate files. Copy the protein_original.pdb file with the name: only_protein.pdb (eg. we assume that we do not need water and ions coming from the pdb, if we would we will have to add more segments in psfgen.inp file) and delete everything what is not a protein.

b) Create a psfgen.inp file

We need to create a psfgen_HEWL.inp file:

```
psfgen << ENDMOL

topology top_all27_prot_surf_na.inp

alias residue HIS HSD
alias atom ILE CD1 CD
alias residue HOH TIP3
alias atom HOH O OH2
alias residue NA SOD
alias residue CL CLA

segment PRO {
pdb only_protein.pdb
}

patch DISU PRO:6 PRO:127
patch DISU PRO:30 PRO:115
patch DISU PRO:64 PRO:80
patch DISU PRO:76 PRO:94

coordpdb only_protein.pdb PRO

writepsf only_HEWL.psf

guesscoord

writepdb only_HEWL.pdb

ENDMOL
```

Then type in the command line type:

```
 ./psfgen_HEWL.inp > log
```

to run the psfgen module. To see details read the log file (note that psfgen_HEWL.inp should be an executable file).

In the psfgen_HEWL.inp file lines starting from "alias" are used to change names, in the pdb the histidine residue is called HIS, while NAMD uses HSD. Similarly the atom CD1 in ILE (isoleucine residue) in NAMD is called as CD, water is not HOH but TIP3 and oxygen in water molecule is not O (as in pdb) but OH2. Moreover, sodium and chlorine atoms are called SOD and CLA in NAMD.

The lines starting from a word "patch" are creating a disulphide bonds between chosen cysteines: CYS6-CYS127, CYS30-CYS115, CYS64-CYS80 and CYS76-CYS94. Note that only the residue number is given. The "patch DISU PRO:6 PRO:127" entry means that we want to connect protein (PRO) residue number 6 with protein residue number 127. Using VMD (or by reading the protein_oryginal.pdb file using any text editor) we can check which of those residues are cysteines. Note that not all proteins have disulphide bridges – that is why it is very important to read the information coming from the PDB. If disulphide bridges are not required simply delete lines starting with the word "patch".

The word "guesscoord" means that we want to guess coordinates of any missing atoms. So the program will guess coordinates of all missing hydrogens in the protein structure and water as well. Moreover, sometimes even if heavier atoms then hydrogen are missing in the pdb structure, the program will guess all of them. How does NAMD know which atoms should be guessed and where to put them? The information is in the `top_all27_prot_surf_na.inp` and `only_protein.pdb` files. In the second one there is a list of residues, atoms and positions. The residue is compared with the library (top file) and if something is missing, the program automatically adds the missing atoms using a geometrical information stated in the top file.

As the result of typing
./psfgen.inp > log

Three files are created: `only_HEWL.psf`, `only_HEWL.pdb` and the log file. Open them using any text editor (for example vi, nedit or joe) to see what they look like and what information they contain. Please note that in the log file you may see something like:

```
…
Warning: poorly guessed coordinates for 26 atoms (10 non-hydrogen):
Warning: poorly guessed coordinate for atom HT1  LYS:1    PRO
Warning: poorly guessed coordinate for atom HT2  LYS:1    PRO
Warning: poorly guessed coordinate for atom HT3  LYS:1    PRO
Warning: poorly guessed coordinate for atom HG   LEU:8    PRO
Warning: poorly guessed coordinate for atom HG   LEU:17   PRO
Warning: poorly guessed coordinate for atom HG   LEU:25   PRO
Warning: poorly guessed coordinate for atom HG   LEU:56   PRO
Warning: poorly guessed coordinate for atom HG2  PRO:70   PRO
Warning: poorly guessed coordinate for atom HG   LEU:75   PRO
Warning: poorly guessed coordinate for atom HG   LEU:83   PRO
Warning: poorly guessed coordinate for atom HG   LEU:84   PRO
Warning: poorly guessed coordinate for atom OT1  LEU:129    PRO
Warning: poorly guessed coordinate for atom OT1  LEU:129    PRO
Warning: poorly guessed coordinate for atom OT1  LEU:129    PRO
…
```

This warning only means that the guessed positions of above atoms probably are not perfect. NAMD will manage that later, at the minimization step.

View your files in VMD by typing

```
vmd only_HEWL.pdb only_HEWL.psf
```

(or type in the command line `vmd`, then go to `Main menu` → `File` → `New molecule` → `open` → `only_HEWL.pdb` highlight `only_HEWL.pdb,` right click and chose `Load data into molecule → only_HEWL.psf)`

Note that your files contain only the protein: there is no water, surface, or counter ions. To add counter ions first you have to solvate the protein.

c) Solvation

Now we need to add water to the system, we can do this with VMD. By the default the protein is solvated using the TIP3P water model.

Open your files in the VMD by typing `vmd only_HEWL.pdb only_HEWL.psf` and go to `Main menu → Tk Console.` To solvate type:

```
% solvate only_HEWL.psf only_HEWL.pdb +x 22 -x 22 +y 27 -y 28 +z 20 -z 8 -o
only_HEWL_S
```

(in the example `-t 9` option is used – see below)

The new, solvated structure will appear. Numbers +x 22, -x22, +y 27 etc. are the space in Å (10^{-10} m) between the protein and the end of the water box. You can change these numbers. Nevertheless, the surface used for HEWL was lying in the (*x,y*) plane and extend the protein by 22Å in +x and -x direction and by 27Å and 28Å in the +y and -y directions, respectively. The initial distance between the protein and the surface was 8Å and the end of the primary cell for HEWL on surface was 20Å away from the protein in the z direction. So the water box used to add ions was about the same as the water box used in the adsorption simulations. If you have different protein or a different surface first check the distances in all directions.

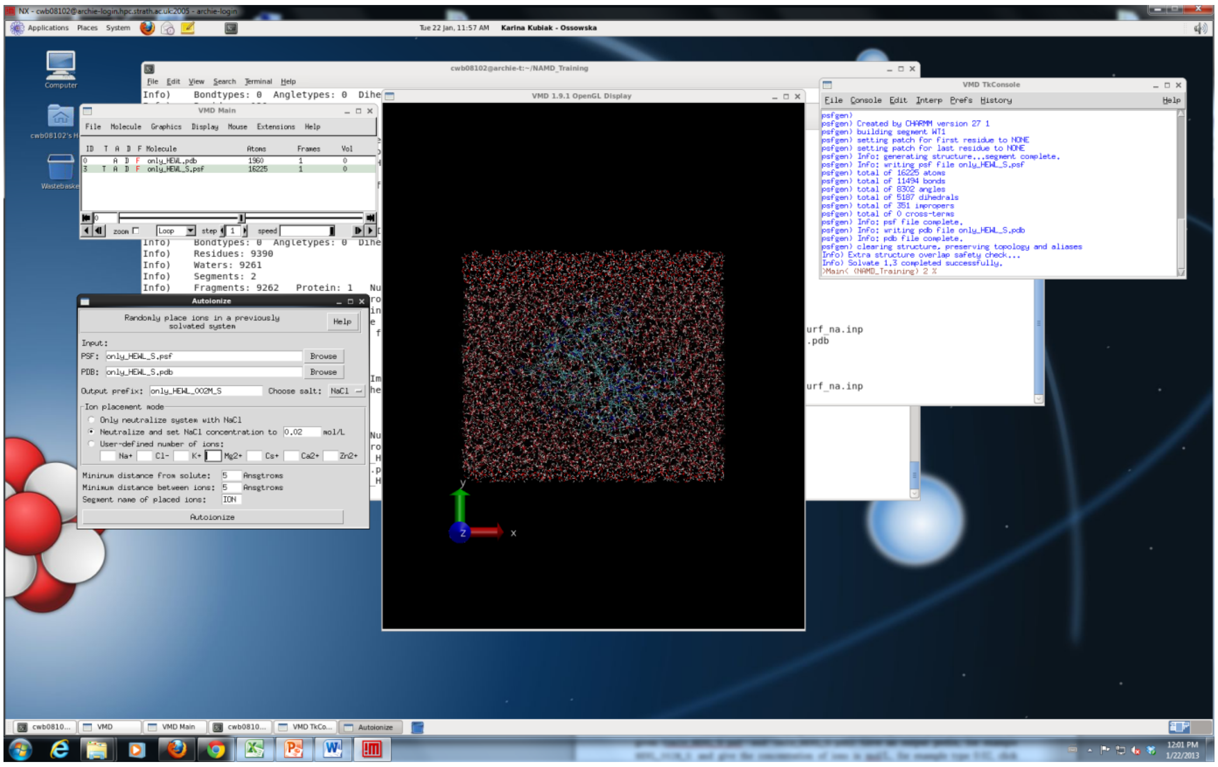
Note: If you are going to simulate the protein only in water you can use any margin, but the best choice is to use the same margin in each direction and not smaller than 9Å (at least three water molecules between the protein and the end of the water box). To do this you can type -t `9` instead of typing distances in the each direction (e.g. type: `% solvate only_HEWL.psf only_HEWL.pdb -t 9 -o only_HEWL_S).` We will use this structure for the next steps.

Note: Check carefully your final, solvated structure. This preparation step, together with adding ions is crucial in the following simulations. If your D0 or D1 simulation fails sometimes is necessary to come back to the solvation stage and change the parameters used.

Do not leave VMD yet – now you should add ions.

d) Add counter ions

Now we need to neutralize the protein by adding counter ions. We can do it under VMD but it is not possible to neutralize the system without water. So select new molecule in the main menu (highlight in yellow) and then add ions. Go to `Main menu → Extensions → Modeling → Add Ions.` A new window will open. Check if the input files your solvated files are given (`only_HEWL_S.psf` and `only_HEWL_S.pdb`). Give an output prefix, for example `HEWL_002M_S` and give the concentration of ions in mol/L, for example type 0.02, select neutralize and set NaCl concentration to 0.02mol/l, check if the Segment ID is ION and then click Autoionize button. (Fig. 4). Scroll up the VMD Tkconsole and check the protein charge before adding ions, how many atoms are added and what is the current charge of the system. If you will try to ionize the structure without water, VMD will show the error and it will close (because the volume is unknown). Check (visually) where ions are placed.



VMD Main
File Molecule Graphics Display Mouse Extensions Help
Autoionize
Help
Browse
Autoionize
VMD TkConsole
File Console Edit Interp Prefs History Help
VMD 1.9.1 OpenGL Display

ID	T	A	D	F	Molecule	Atoms	Frames	Vol
0		A	D	F	only_HEWL.pdb	1960	1	0
3	T	A	D	F	only_HEWL_S.psf	16225	1	0

```
Info)     Bondtypes: 0  Angletypes: 0  Dihe
Info)     Residues: 9390
Info)     Waters: 9261
Info)     Segments: 2
Info)     Fragments: 9262   Protein: 1   Nu
```

Randomly place ions in a previously solvated system

Input:
PSF: only_HEWL_S.psf
PDB: only_HEWL_S.pdb
Output prefix: only_HEWL_002M_S   Choose salt: NaCl
Ion placement mode
Only neutralize system with NaCl
[✓ Neutralize and set NaCl concentration to 0.02 mol/L]
User-defined number of ions: Na+ Cl- K+ Mg2+ Cs+ Ca2+ Zn2+
Minimum distance from solute: 5 Angstroms
Minimum distance between ions: 5 Angstroms
Segment name of placed ions: ION

```
psfgen)
psfgen) Created by CHARMM version 27 1
psfgen) building segment WT1
psfgen) setting patch for first residue to NONE
psfgen) setting patch for last residue to NONE
psfgen) Info: generating structure...segment complete.
psfgen) Info: writing psf file only_HEWL_S.psf
psfgen) total of 16225 atoms
psfgen) total of 11494 bonds
psfgen) total of 8302 angles
psfgen) total of 5187 dihedrals
psfgen) total of 351 impropers
psfgen) total of 0 cross-terms
psfgen) Info: psf file complete.
psfgen) Info: writing pdb file only_HEWL_S.pdb
psfgen) Info: pdb file complete.
psfgen) clearing structure, preserving topology and aliases
Info) Extra structure overlap safety check...
Info) Solvate 1.3 completed successfully.
>Main< (NAMD_Training) 2 %
```

Fig. 4. Adding ions under vmd.

To run protein simulation in water only (+ buffer of course) you shall use your two new files: `HEWL_002M_S.pdb and HEWL_002M_S.psf` as they are and run simulation D0 (water equilibration). First you have to center and fix the protein (using ctrbox.tcl, and fix.tcl, see below).

d) Center and Fix the protein

Now we need to center your water box and find atoms which have to be fixed in the D0 simulation (n only water minimization). To do that you need two scripts written by myself: ctrbox.tcl and fix_protein.tcl. Go to `to Main Menu → Extensions → TK Console` and in the Tk console type:

```
% play ctrbox.tcl
% ctrbox HEWL_002M_S.psf HEWL_002M_S.pdb HEWL_002M_SC
```

New files `HEWL_002M_SC.pdb` and `HEWL_002M_SC.psf` will appear. At the end of the `HEWL_002M_SC.pdb` file, the dimensions of the primary cell are given (open the file using **vi** to see them). Leave VMD and open again using the most recent structures:

```
vmd HEWL_002M_SC.pdb HEWL_002M_SC.psf
```

Go to `to Main Menu → extensions → TK Console` and in the Tk console type:

```
% play fix_protein.tcl
```

The new file fix_protein.pdb is created. Do not forget to change the name to `HEWL_002M_FIX.pdb`.

Now we can start the simulation.

3. Run the Simulations

The proper simulation contains three main steps: (i) water equilibration (D0 dynamics), (ii) heating of the system (D1 dynamics) and (iii) the simulation (D2 and further). The water equilibration step is necessary to get a proper water model in which water positions are randomized (note that before equilibration your water is well ordered which is not natural.

a) Water minimization and equilibration

Typical input to the water equilibration step (file `HEWL_002M_D0.inp`):

```
structure       HEWL_002M_SC.psf
coordinates     HEWL_002M_SC.pdb

paratypecharmm  on        #it is possible to use GROMACS or AMBER FF
parameters      par_all27_prot_surf_na.inp       #parameters file
exclude         scaled1-4 #what is not included in non bonding interactions
1-4scaling      1.0

switching       on       # "smooth" nonbonding interactions to 0
switchdist      8        # at 8Å we start to "smooth electrostatic
cutoff          12       # to 0, which should be obtained at 12Å
pairlistdist    14       # to which distance the atoms are treated as a pair
margin          4        # ideally the margin should be 0, sometimes
stepspercycle   20       # you need to increase that

wrapWater       on       #how to show water which left the simulation cell
rigidBonds      water    #water is treated as a rigid body to reduce no. of
                                                                # calculations
timestep 1.0             #in femto seconds

outputenergies  100
outputtiming    100
binaryoutput    yes
outputname      HEWL_002M_D0 #output files name
dcdfreq         100

temperature     300          # temperature in Kelvins
```

```
langevin            on       # using Langevin  dynamics
langevinDamping     5
langevinTemp        300
langevinHydrogen    no

useFlexibleCell         yes  # the water box can be flexible to keep the
useGroupPressure        yes  # constant pressure

LangevinPiston          on    # Langevin piston method to keep (scale)
LangevinPistonTarget    1.01325     # temperatures is used
LangevinPistonPeriod    200
LangevinPistonDecay     100
LangevinPistonTemp      300

cellBasisVector1 59.43600082397461       0.0      0.0          #primary cell
cellBasisVector2         0.0      52.60499572753906        0.0 # vector taken
cellBasisVector3         0.0      0.0      58.24599838256836   #from *SC.pdb
cellOrigin               0.0      0.0      0.0

fixedAtoms       on
fixedAtomsFile   HEWL_002M_FIX.pdb    #atoms which cannot move: - protein
fixedAtomsCol    O

minimize 1000                # water minimization for 1000 steps
run 100000                   # heating water only for 100 ps
```

In the above example, when margin was 0, in the output file (`HEWL_002M_D0.out`) the error has appeared:

```
…
WRITING COORDINATES TO DCD FILE AT STEP 20700
The last position output (seq=20700) takes 0.001 seconds, 308.133 MB of
memory in use
TIMING: 20800  CPU: 67.2482, 0.00324654/step  Wall: 67.2482,
0.00324654/step, 0.0723257 hours remaining, 308.132812 MB of memory in use.
ENERGY:   20800         0.0000         0.0000         0.0000         0.0000
-58172.7614      5297.1181         0.0000         0.0000      8448.0484
-44427.5948       298.7737    -52875.6432    -44424.0259       297.2008
72.7791        73.6412     155428.6534       -58.2830       -58.3755

WRITING COORDINATES TO DCD FILE AT STEP 20800
The last position output (seq=20800) takes 0.001 seconds, 308.133 MB of
memory in use
FATAL ERROR: Periodic cell has become too small for original patch grid!
Possible solutions are to restart from a recent checkpoint,
increase margin, or disable useFlexibleCell for liquid simulation.
FATAL ERROR: Periodic cell has become too small for original patch grid!
...
...
```

Calculations have stopped, the margin was increased to 2, then to 4 and finally the D0 stage was competed. Try to not increase margin more than it is required. The other option is restart the calculation without increasing the margin, and repeat that as long as the trajectory is fine. It is not possible to determine when it will happen.

If the calculations are correct, five new files should be created: `HEWL_002M_D0.out (you can call it the log file, HEWL_002M_D0.vel, HEWL_002M_D0.xsc, HEWL_002M_D0.coor, HEWL_002M_D0.dcd`

File type	contents	Format
out	The log file. Contains energies, temperature, pressure etc in each frame.	Text
vel	Final velocities	Binary
xsc	Final cell dimensions	Binary
coor	Final coordinates	Binary
dcd	Trajectory	Binary

The end of the correct output file should look as follows:

`HEWL_002M_D0.out`

```
WRITING COORDINATES TO DCD FILE AT STEP 101000
The last position output (seq=101000) takes 0.001 seconds, 308.012 MB of
memory in use
TIMING: 101000  CPU: 325.262, 0.0034132/step  Wall: 325.262,
0.0034132/step, 0 hours remaining, 308.011719 MB of memory in use.
ETITLE:      TS           BOND          ANGLE          DIHED          IMPRP
ELECT            VDW       BOUNDARY           MISC        KINETIC
TOTAL           TEMP      POTENTIAL         TOTAL3        TEMPAVG
PRESSURE      GPRESSURE         VOLUME       PRESSAVG      GPRESSAVG

ENERGY:  101000         0.0000         0.0000         0.0000         0.0000
-58042.8008      5127.2276         0.0000         0.0000      8339.4205
-44576.1526       294.9320    -52915.5731    -44570.9090       295.3623
-257.6267      -246.7263    155248.3516       -66.3426       -66.6349

WRITING EXTENDED SYSTEM TO OUTPUT FILE AT STEP 101000
WRITING COORDINATES TO OUTPUT FILE AT STEP 101000
CLOSING COORDINATE DCD FILE
The last position output (seq=-2) takes 0.016 seconds, 309.918 MB of memory
in use
WRITING VELOCITIES TO OUTPUT FILE AT STEP 101000
The last velocity output (seq=-2) takes 0.002 seconds, 309.129 MB of memory
in use
====================================================

WallClock: 326.861908  CPUTime: 326.861908  Memory: 309.128906 MB
End of program
```

Explanation of other parameters used can be found in the NAMD tutorial. Note that the protein is static, while water and ions are not. Observe that four files have been produced: `HEWL_002M_D0.out`, `HEWL_002M_D0.dcd`, `HEWL_002M_D0.coor` and `HEWL_002M_D0.xsc`. The first one contains the information about running the program, energies reached in each time and temperatures etc. The second one is the trajectory file (coordinates of atoms in the each time step), the third one contains coordinates of atoms in the last time step and the fourth one contains data describing parameters for periodic boundary conditions (PBC). Now you can watch your trajectory in VMD. Type in the commend line

```
vmd HEWL_002M_SC.pdb HEWL_002M_SC.psf
```

Go to `Main Menu → Load data into trajectory → HEWL_surf_002M_D0.dcd`

The Trajectory is not very exciting, since only water molecules are moving. Note that during first two steps they are moving quite slowly (the minimization stage) and then they suddenly start to speed up (the heating stage).

b) heating of the system

Now we need to heat the whole system to required temperature, let's say 300K. We will start from 0K, then we will set random initial velocities and heat the system.

Typical input to the whole system heating step (file `HEWL_002M_D1.inp`):

```
structure         HEWL_002M_SC.psf
coordinates       HEWL_002M_SC.pdb
bincoordinates    HEWL_002M_D0.coor  # the last structure from water
                                                  # equilibration stage
paratypecharmm    on
parameters        par_all27_prot_surf_na.inp
exclude           scaled1-4
1-4scaling        1.0

switching         on
switchdist        8
cutoff            12
pairlistdist      14
margin            0
stepspercycle     20

wrapWater         on
warpAll           on #nothing will disappear from the primary simulation cell
rigidBonds        water

timestep 1.0

outputenergies    100     # how frequently the information is written to *.out
outputtiming      100
binaryoutput      yes
outputname        HEWL_002M_D1
dcdfreq           100     # how frequently the dcd file is written

temperature       0       # initial temperature


reassignFreq       1000   # how frequently the temperature will be increased
reassignIncr       10      # what is the increment
reassignHold       300     # task temperature

extendedSystem    HEWL_002M_D0.xsc

minimize 10000        # number of minimization steps of the whole system
run 300000            # total simulation time (heating + equilibration)
```

Note that at this stage you are using the coordinates produced in the water equilibration. Once is finished watch the *.D1.dcd file and note that a *D1.vel file containing velocities of each atom at the last time stem was created. In the above example we will minimize protein, water and ions for 10,000 steps, then we will heat the system from 0K to 300K by increasing the temperature by 10K every 1000 steps, It means that we will heat for 30 x 1000steps =30000steps=30ps and then we will run the simulation in the constant temperature (equilibrations) 300K for 300ps-30ps=270ps.

c) The production simulation

Now you can run the production simulation, only trajectories D2 (and further) are usually analyzed in details, nevertheless always have a look on D0 and D1 trajectories to be sure that the preparation stage was fine.

The typical input for the production simulation (file `HEWL_002M_D2.inp`):

```
structure        HEWL_002M_SC.psf
coordinates      HEWL_002M_SC.pdb
bincoordinates   HEWL_002M_D1.coor

paratypecharmm   on
parameters       par_all27_prot_surf_na.inp
exclude          scaled1-4
1-4scaling       1.0

switching        on
switchdist       8
cutoff           12
pairlistdist     14
margin           0
stepspercycle    20

wrapWater        on
wrapAll          on
rigidBonds       water

timestep 2.0                   # note that 2fs time step is used

outputenergies   100
outputtiming     100
binaryoutput     yes
outputname       HEWL_002M_D2
dcdfreq          200
restartfreq      100000
restartname      rest_HEWL_002M_D2  # how frequently the restart files will
                                    # be saved
binvelocities    HEWL_002M_D1.vel   # in previous stages we haven't used the
                                    # velocity file - for D0 we haven't such
                                    # file, in D1 the initial temperature
                                    # was 0K so atoms haven't velocities.
langevin             on
langevinDamping      5
langevinTemp         300
langevinHydrogen     no

extendedSystem   HEWL_002M_D1.xsc

run 5000000
```

Note: now a 2fs time step is used. It is not always safe, it can be used only for a stable system (ensure that the system is stable before using 2fs time step!). A bigger timestep will produce a longer trajectory in the same wall-clock time, but the simulation can be unstable. When using 2fs, in principle the SHAKE algorithm should be used for all hydrogens, not only for water hydrogens. Using bigger time step can cause an "explosion" of your system. 1fs is usually safer but … slower ☹

If you want to run next 10 ns copy the above input file and change names D1 → D2 and D2 → D3.

Enjoy your simulations!

Note: in our example on ARCHIE the job length is 500,000 steps = 1ns (not 10ns as in the above input).

4. How to launch the job

If you want to run the simulation on the HPC you need one extra file to submit your job. The sample job script for ARCHIE-WeSt (`HEWL_D0.sh`):

```
#

export PROCS_ON_EACH_NODE=12

# ************* SGE qsub options ****************
#Export env variables and keep current working directory
#$ -V -cwd
#$ -P training.prj
#Select parallel environment and number of parallel queue slots (nodes)
#$ -pe mpi-verbose 10
#Combine STDOUT/STDERR
#$ -j y
#Specify output file
#$ -o out.$JOB_ID
#Request resource reservation (reserve slots on each scheduler run until
enough have been gathered to run the job
#$ -R y
#Request exclusivity of each node
# ************** END SGE qsub options ************

export NCORES=`expr $PROCS_ON_EACH_NODE \* $NSLOTS`

export OMPI_MCA_btl=openib,self

# Execute NAMD2 with configuration script with output to log file
charmrun +p$NCORES -v namd2 HEWL_002M_D0.inp > HEWL_002M_D0.out
```

It will run your job on 120 cores (10 nodes with 12 cores each). Up to 120 cores NAMD scales almost linear (9.8 speedup) on ARCHIE. To submit the job type:

```
qsub HEWL_D0.sh
```

to check the status type:

```
qstat
```

To check the calculation progress see the output file (`HEWL_002M_D0.out`)

To run trajectories D0, D1 and D2 one after other the end of the above use `HEWL_D0_D2.sh` script:

```
…
# Execute NAMD2 with configuration script with output to log file
charmrun +p$NCORES -v namd2 HEWL_002M_D0.inp > HEWL_002M_D0.out
charmrun +p$NCORES -v namd2 HEWL_002M_D1.inp > HEWL_002M_D1.out
charmrun +p$NCORES -v namd2 HEWL_002M_D2.inp > HEWL_002M_D2.out
```

Note: The job script is HPC-specific. To run NAMD on ARCHER or other HPC you would need to modify it.

If you want to run simulation on your local computer, you would need a file called `nodelist`:

```
group main
host localhost
```

To run the job type in the terminal:

```
./run_namd.bash HEWL_002M_D0
```

6. How to analyze the trajectory

1) visual analysis
2) calculate rmsd and rmsf using the tcl script provided (root mean square distance and fluctuations of particular residues, respectively)
3) measure distances during the trajectories (for details see vmd tutorial)
4) write your own tcl scripts

C.Advanced Simulations

1. PME

To see how to use Particle Mesh Ewald method for calculating electrostatic interactions in our case study see files: `HEWL_002M_PME_D0.inp`, `HEWL_002M_PME_D0.inp` and `HEWL_002M_PME_D0.inp`. Lines like the following have appeared:

```
PME                yes
PMEGridsizex       60
PMEGridsizey       53
PMEGridsizez       59
```

Note the numbers given should be not smaller than basic cell vectors (cellBasisVector). The PME grid size should be a number which can be produced by adding or multiplying (or both) numbers 2, 3 and 5. In our case `cellBasisVector1` was `59.43600082397461`, so we need to produce number ~60 (3x5x2x2=60), `cellBasisVector2` was `52.60499572753906` (2x3x2x2x2+5=53), `cellBasisVector3` was `58.24599838256836` (3x3x2x3+5=59)

2. SMD

a) Constant velocity pulling

In this case again we need a SMD file, which should be created basing on the original *SC*pdb file. Again we will pull only one atom `CZ` from residue `ARG128`

cp `HEWL_002M_SC.pdb HEWL_002M_SMD.pdb`

`HEWL_002M_SMD.pdb`:

```
…
ATOM   1930  NE  ARG P 128  -17.843  -1.453 -18.235  0.00  0.00       PRO  N
ATOM   1931  HE  ARG P 128  -18.195  -1.709 -19.143  0.00  0.00       PRO  H
ATOM   1932  CZ  ARG P 128  -18.593  -1.453 -17.171  1.00  0.00       PRO  C
ATOM   1933  NH1 ARG P 128  -18.147  -1.043 -15.996  0.00  0.00       PRO  N
ATOM   1934 HH11 ARG P 128  -18.730  -1.076 -15.196  0.00  0.00       PRO  H
…
```

In this file change the occupancy values for all normal atoms to 0.00. The occupancy value 1.00 indicates the SMD atom.

`HEWL_002M_D2_v0005Aps.inp`:

```
structure          HEWL_002M_SC.psf
coordinates        HEWL_002M_SC.pdb
bincoordinates     HEWL_002M_PME_D1.coor
```

```
paratypecharmm  on
parameters      par_all27_prot_surf_na.inp
exclude         scaled1-4
1-4scaling      1.0

switching       on
switchdist      8
cutoff          12
pairlistdist    14
margin          0
stepspercycle   20

wrapWater       on
wrapAll         on
rigidBonds      water

timestep 2.0

outputenergies  100
outputtiming    100
binaryoutput    yes
outputname      HEWL_002M_D2_v0005Aps
dcdfreq         200
restartfreq     100000
restartname     rest_HEWL_002M_D2_v0005Aps
binvelocities   HEWL_002M_PME_D1.vel

SMD             on
SMDFile         HEWL_002M_SMD.pdb
SMDk            4
SMDVel          0.00001
SMDDir          0.0 0.0 1.0
SMDOutputFreq   100

langevin            on
langevinDamping     5
langevinTemp        300
langevinHydrogen    no

extendedSystem  HEWL_002M_PME_D1.xsc

run 5000000
```

In this case the pulling velocity has to be specified in the input file – parameter `SMDVel`. Value 1x10^{-5} indicates that the pulling velocity is 10^{-5} A/step. The step is 2fs, so the velocity is 5x10^{-3} A/ps. The total trajectory length is 10ns, so the atom should move by 50 A during the trajectory. `SMDk` specifies the spring constant, from my experience 4 is the best value. Sample output:

`HEWL_002M_PME_D2_v0005Aps.out`

```
…
WRITING COORDINATES TO DCD FILE AT STEP 499800
The last position output (seq=499800) takes 0.001 seconds, 309.785 MB of
memory in use
TIMING: 499800  CPU: 2004.69, 0.0042082/step  Wall: 2004.69,
0.0042082/step, 0.000233789 hours remaining, 309.785156 MB of memory in
```

```
use.
ENERGY:   499800        813.0956       1119.8652        641.3451          66.5502
-58379.7599       4427.1856          0.0000          0.0000      10249.3769
-41062.3413        300.0943     -51311.7182     -40987.6851        299.7518
343.5534        311.7697     158153.2920        350.8725        349.1137
#   Timestep    Atom Coordinates            force
SMD  499900 -10.7265 -1.48513 -11.9009 -0 0 -75.3415
TIMING: 499900  CPU: 2005.09, 0.00398227/step  Wall: 2005.09,
0.00398227/step, 0.000110619 hours remaining, 309.785156 MB of memory in
use.
ENERGY:   499900        790.4483       1107.3516        645.1351          63.4061
-58390.6894       4438.7077          0.0000          0.0000      10272.2767
-41073.3640        300.7648     -51345.6407     -40992.6688        300.4989
291.3132        310.8214     158153.2920        335.7182        338.0513
…
```

b) Constant force pulling

In this example we will use the results from the adsorption trajectory. It means that initially the HEWL protein was placed in the system containing the mica surface model and 90ns trajectory was calculated. During that trajectory the protein adsorbed onto the surface (adsorption trajectory) and the last stage is treated as a starting structure for constant force pulling trajectory (desorption trajectory). It means that the structure after 90ns of adsorption trajectory was saved (under vmd) then water, surface and ions were again added and the system was centered. It means that files: `O1_90ns_002M_v0_SC.psf` and `O1_90ns_002M_v0_SC.pdb` were obtained. Then the trajectory D0 was run to minimize the water. Therefore we have files `O1_90ns_002M_v0_D0.coor`, `O1_90ns_002M_v0_D0.xsc`, `O1_90ns_002M_v0_D0.vel` and `O1_90ns_002M_v0_D0.dcd` (the last two files are not needed for the SMD simulation). Note – the preparation stages are not included in the example.

In general we can address the problem that we have: `O1_90ns_002M_v0_SC.psf`, `O1_90ns_002M_v0_SC.pdb`, `O1_90ns_002M_v0_D0.coor` and `O1_90ns_002M_v0_D0.xsc` files and we want to run SMD trajectory with constant force pulling. First we have to create the pdb file which will contain information about pulled atoms (the constant force file or SMD file). Copy your *SC*pdb file with other name:

```
cp O1_90ns_002M_v0_SC.pdb O1_90ns_002M_v0_force_f800pN.pdb
```

The new file requires some changes. Let's assume we want to pull ARG128 CZ atom in the z direction with the force 800pN (11.54 kcal/mol). The most interesting part of the `O1_90ns_002M_v0_force_f800pN.pdb` file:

`O1_90ns_002M_v0_force_f800pN.pdb`

```
…
ATOM   1929  HD2 ARG A 128   21.098  -6.897 -27.912  0.00  0.00       BIA  H
ATOM   1930  NE  ARG A 128   20.244  -8.259 -29.183  0.00  0.00       BIA  N
ATOM   1931  HE  ARG A 128   20.153  -9.222 -28.935  0.00  0.00       BIA  H
ATOM   1932  CZ  ARG A 128    0.000   0.000   1.000 11.54  1.00       BIA  C
ATOM   1933  NH1 ARG A 128   21.059  -7.038 -30.984  0.00  0.00       BIA  N
ATOM   1934 HH11 ARG A 128   21.195  -7.096 -32.010  0.00  0.00       BIA  H
ATOM    1935  HH12  ARG A 128    20.604  -6.238 -30.648  0.00   0.00         BIA   H
ATOM    1936   NH2  ARG A 128    21.276  -9.260 -30.989  0.00   0.00         BIA   N
…
```

In this file the information of which atom (atoms) has to be pulled, what is the force value and direction is stored. The last column (B column, green circle) value is equal to 0.00 for all normal atoms. Value 1.00 indicates that the force will be applied to the atom. The occupancy column (orange circle) value is 0.00 for all normal atoms. In the case of the SMD atom it specifies the force value (in kcal/mol, 1kcal/mol=69.479pN). The (*x,y,z*) columns (blue circle) stores x,y,z coordinates of normal atoms and (x_1,y_1,z_1) coordinates of the force vector in the case of the SMD atom. (x_0,y_0,z_0) coordinates of the force vector are = and (*x,y,z*) coordinates of the SMD atom (stored in `O1_90ns_002M_v0_SC.pdb` file, as coordinates of all other atoms). The program will read only rows with B value 1.00 and will omit all rows with B value 0.00.

The SMD sample input to the production trajectory D2:

`HEWL_002M_PME_D2_f100pN.inp`:

```
structure         O1_90ns_002M_v0_SC.psf
coordinates       O1_90ns_002M_v0_SC.pdb
bincoordinates    O1_90ns_002M_v0_D0.coor

paratypecharmm    on
parameters        par_all27_prot_surf_na.inp
exclude           scaled1-4
1-4scaling        1.0

switching         on
switchdist        8
cutoff            12
pairlistdist      14
margin            0
stepspercycle     20

wrapWater         on
rigidBonds        water

timestep 2.0

outputenergies    100
outputtiming      100
binaryoutput      yes
outputname        O1_90ns_002M_v0_sD2_f800pN
dcdfreq           100

restartfreq       100000
restartname       rest_O1_90ns_002M_v0_sD2_f800pN

binvelocities     O1_90ns_002M_v0_D0.vel

constantforce     yes
consforcefile     O1_90ns_002M_v0_force_f800pN.pdb
SMDOutputFreq     100

langevin              on
```

```
langevinDamping      5
langevinTemp         300
langevinHydrogen     no

extendedSystem  O1_90ns_002M_v0_D0.xsc

fixedAtoms      on
fixedAtomsFile  O1_90ns_002M_v0_FIX.pdb
fixedAtomsCol   O

minimize 100
run 1000000
```

Note that to use constant force pulling, 3 new lines, highlighted in red are added. Lines highlighted in purple are needed for the surface which is kept static during the simulation. Note that a short minimization stage is required. To see the result of pulling, watch the trajectory file `O1_90ns_002M_v0_sD2_f800pN.dcd`

FINAL REMARKS

All example files can be found at ARCHIE-WeSt, `/users/cwb08102/NAMD_Training`

Remember to load modules:

```
/mpi/gcc/openmpi/1.4.5
/libs/gcc/fftw2/float-mpi/2.1.5
/apps/gcc/namd/mpi/2.8
/apps/bin/vmd/1.9.1
```

How to load the module:

```
module load /apps/bin/vmd/1.9.1
```

Modules and job submission scripts slightly differs between HPCs.