NAMD User's Guide

Version 2.6

M. Bhandarkar, R. Brunner, C. Chipot, A. Dalke, S. Dixit, P. Grayson, J. Gullingsrud, A. Gursoy, D. Hardy, J. Hénin, W. Humphrey, D. Hurwitz, N. Krawetz, S. Kumar, M. Nelson, J. Phillips, A. Shinozaki, G. Zheng, F. Zhu

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Description

The NAMD *User's Guide* describes how to run and use the various features of the molecular dynamics program NAMD. This guide includes the capabilities of the program, how to use these capabilities, the necessary input files and formats, and how to run the program both on uniprocessor machines and in parallel.

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> James C. Phillips, Rosemary Braun, Wei Wang, James Gumbart, Emad Tajkhorshid, Elizabeth Villa, Christophe Chipot, Robert D. Skeel, Laxmikant Kale, and Klaus Schulten. Scalable molecular dynamics with NAMD. *Journal of Computational Chemistry*, 26:1781-1802, 2005.

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1 Introduction

NAMD is a parallel molecular dynamics program for UNIX platforms designed for high-performance simulations in structural biology. This document describes how to use NAMD, its features, and the platforms on which it runs. The document is divided into several sections:

Section 1 gives an overview of NAMD.

Section 2 lists the basics for getting started.

Section 3 describes NAMD file formats.

Section 4 explains PSF file generation with psfgen.

Section 5 lists basic simulation options.

Section 6 lists additional simulation options.

Section 7 provides hints for X-PLOR users.

Section 8 provides sample configuration files.

Section 9 gives details on running NAMD.

Section 10 gives details on installing NAMD.

We have attempted to make this document complete and easy to understand and to make NAMD itself easy to install and run. We welcome your suggestions for improving the documentation or code at `namd@ks.uiuc.edu`.

1.1 New features in version 2.6

Ports to Itanium, Altix, and Opteron/Athlon64/EMT64

NAMD runs very fast on the Itanium processor under Linux, including the SGI Altix. Native binaries for 64-bit x86 processors such as AMD Opteron and Intel EMT64 are 25% faster than 32-bit binaries.

Port to Mac OS X for Intel Processors

NAMD has been ported to the new Intel-based Macintosh platform. Binaries are only 32-bit, but should run on newer 64-bit machines.

Ports to Cray XT3 and IBM BlueGene/L (source code only)

These two large, scalable, but immature platforms are now supported. Neither platform supports dynamic linking and our experience shows that binaries would be quickly out of date, so only source code is released. Also, BlueGene/L requires the latest development version of Charm++, rather than charm-5.9 as shipped with the NAMD source code.

Improved Serial Performance, Especially on POWER and PowerPC

Tuning of the NAMD inner loop has provided a 30% performance boost with the IBM XL compiler. New Mac OS X binaries are up to 70% faster, but users must download the IBM XL runtime library from `http://ftp.software.ibm.com/aix/products/ccpp/vacpp-rte-macos/`

Adaptive Biasing Force Free Energy Calculations

A new method, implemented in Tcl, efficiently calculates the potential of mean force along a reaction coordinate by applying adaptive biasing forces to provide uniform sampling.

Customizable Replica Exchange Simulations

The replica exchange method is implemented as a set of Tcl scripts that use socket connections to drive a set of NAMD jobs, exchanging temperatures (or any other scriptable parameter) based on energy.

Tcl-Based Boundary Potentials

Tcl-scripted forces may be efficiently applied individually to large numbers of atoms to implement boundaries and similar forces.

Reduced Memory Usage for Unusual Simulations

Memory usage for simulations of large, highly bonded structures such as covalent crystals and for sparse simulations such as coarse-grained models has been greatly reduced without affecting the performance of typical biopolymer simulations.

Support for CHARMM 31 Stream Files and CMAP Crossterms

Both NAMD and psfgen (standalone or VMD plug) read and interpret the new CHARMM 31 stream files (combining topology and parameters) and the new CMAP crossterm (dihedral-dihedral) potential function.

Support for OPLS Force Field

Geometric combining of Lennard-Jones σ (radius) parameters ($\sigma_{ij} = \sqrt{\sigma_i \sigma_j}$), as required by the OPLS force field, is available with the option `vdwGeometricSigma`.

1.2 NAMD and molecular dynamics simulations

Molecular dynamics (MD) simulations compute atomic trajectories by solving equations of motion numerically using empirical force fields, such as the CHARMM force field, that approximate the actual atomic force in biopolymer systems. Detailed information about MD simulations can be found in several books such as [1, 22]. In order to conduct MD simulations, various computer programs have been developed including X-PLOR [7] and CHARMM [6]. These programs were originally developed for serial machines. Simulation of large molecules, however, require enormous computing power. One way to achieve such simulations is to utilize parallel computers. In recent years, distributed memory parallel computers have been offering cost-effective computational power.

NAMD was designed to run efficiently on such parallel machines for simulating large molecules. NAMD is particularly well suited to the increasingly popular Beowulf-class PC clusters, which are quite similar to the workstation clusters for which is was originally designed. Future versions of NAMD will also make efficient use of clusters of multi-processor workstations or PCs.

NAMD has several important features:

- **Force Field Compatibility**
  The force field used by NAMD is the same as that used by the programs CHARMM [6] and X-PLOR [7]. This force field includes local interaction terms consisting of bonded interactions between 2, 3, and 4 atoms and pairwise interactions including electrostatic and van der Waals forces. This commonality allows simulations to migrate between these three programs.

- **Efficient Full Electrostatics Algorithms**
  NAMD incorporates the Particle Mesh Ewald (PME) algorithm, which takes the full electrostatic interactions into account. This algorithm reduces the computational complexity of electrostatic force evaluation from $O(N^2)$ to $O(N \log N)$.

- **Multiple Time Stepping**
  The velocity Verlet integration method [1] is used to advance the positions and velocities of the atoms in time. To further reduce the cost of the evaluation of long-range electrostatic forces, a multiple time step scheme is employed. The local interactions (bonded, van der Waals and electrostatic interactions within a specified distance) are calculated at each time step. The longer range interactions (electrostatic interactions beyond the specified distance) are only computed less often. This amortizes the cost of computing the electrostatic forces over several timesteps. A smooth splitting function is used to separate a quickly varying short-range portion of the electrostatic interaction from a more slowly varying long-range component. It is also possible to employ an intermediate timestep for the short-range non-bonded interactions, performing only bonded interactions every timestep.

- **Input and Output Compatibility**
  The input and output file formats used by NAMD are identical to those used by CHARMM and X-PLOR. Input formats include coordinate files in PDB format [3], structure files in X-PLOR PSF format, and energy parameter files in either CHARMM or X-PLOR formats. Output formats include PDB coordinate files and binary DCD trajectory files. These similarities assure that the molecular dynamics trajectories from NAMD can be read by CHARMM or X-PLOR and that the user can exploit the many analysis algorithms of the latter packages.

- **Dynamics Simulation Options**
  MD simulations may be carried out using several options, including
  - Constant energy dynamics,
  - Constant temperature dynamics via
    - Velocity rescaling,
    - Velocity reassignment,
    - Langevin dynamics,
  - Periodic boundary conditions,
  - Constant pressure dynamics via

    - Berendsen pressure coupling,
    - Nosé-Hoover Langevin piston,
  - Energy minimization,
  - Fixed atoms,
  - Rigid waters,
  - Rigid bonds to hydrogen,
  - Harmonic restraints,
  - Spherical or cylindrical boundary restraints.

- **Easy to Modify and Extend**
  Another primary design objective for NAMD is extensibility and maintainability. In order to achieve this, it is designed in an object-oriented style with C++. Since molecular dynamics is a new field, new algorithms and techniques are continually being developed. NAMD's modular design allows one to integrate and test new algorithms easily. If you are contemplating a particular modification to NAMD you are encouraged to contact the developers at `namd@ks.uiuc.edu` for guidance.

- **Interactive MD simulations**
  A system undergoing simulation in NAMD may be viewed and altered with VMD; for instance, forces can be applied to a set of atoms to alter or rearrange part of the molecular structure. For more information on VMD, see `http://www.ks.uiuc.edu/Research/vmd/`.

- **Load Balancing**
  An important factor in parallel applications is the equal distribution of computational load among the processors. In parallel molecular simulation, a spatial decomposition that evenly distributes the computational load causes the region of space mapped to each processor to become very irregular, hard to compute and difficult to generalize to the evaluation of many different types of forces. NAMD addresses this problem by using a simple uniform spatial decomposition where the entire model is split into uniform cubes of space called *patches*. An initial load balancer assigns patches and the calculation of interactions among the atoms within them to processors such that the computational load is balanced as much as possible. During the simulation, an incremental load balancer monitors the load and performs necessary adjustments.

1.3 User feedback

If you have problems installing or running NAMD after reading this document, please send a complete description of the problem by email to `namd@ks.uiuc.edu`. If you discover and fix a problem not described in this manual we would appreciate if you would tell us about this as well, so we can alert other users and incorporate the fix into the public distribution.

We are interested in making NAMD more useful to the molecular modeling community. Your suggestions are welcome at `namd@ks.uiuc.edu`. We also appreciate hearing about how you are using NAMD in your work.

1.4 Acknowledgments

This work is supported by grants from the National Science Foundation (BIR-9318159) and the National Institute of Health (PHS 5 P41 RR05969-04).

The authors would particularly like to thank the members of the Theoretical Biophysics Group, past and present, who have helped tremendously in making suggestions, pushing for new features, and testing bug-ridden code.

2 Getting Started

2.1 What is needed

Before running NAMD, explained in section 9, the following are be needed:

- A CHARMM force field in either CHARMM or X-PLOR format.
- An X-PLOR format PSF file describing the molecular structure.
- The initial coordinates of the molecular system in the form of a PDB file.
- A NAMD configuration file.

NAMD provides the `psfgen` utility, documented in Section 4, which is capable of generating the required PSF and PDB files by merging PDB files and guessing coordinates for missing atoms. If `psfgen` is insufficient for your system, we recommend that you obtain access to either CHARMM or X-PLOR, both of which are capable of generating the required files.

2.2 NAMD configuration file

Besides these input and output files, NAMD also uses a file referred to as the *configuration file*. This file specifies what dynamics options and values that NAMD should use, such as the number of timesteps to perform, initial temperature, etc. The options and values in this file control how the system will be simulated.

A NAMD configuration file contains a set of options and values. The options and values specified determine the exact behavior of NAMD, what features are active or inactive, how long the simulation should continue, etc. Section 2.2.1 describes how options are specified within a NAMD configuration file. Section 2.2.3 lists the parameters which are required to run a basic simulation. Section 7 describes the relation between specific NAMD and X-PLOR dynamics options. Several sample NAMD configuration files are shown in section 8.

2.2.1 Configuration parameter syntax

Each line in the configuration files consists of a *keyword* identifying the option being specified, and a *value* which is a parameter to be used for this option. The keyword and value can be separated by only white space:

```
keyword            value
```

or the keyword and value can be separated by an equal sign and white space:

```
keyword      =     value
```

Blank lines in the configuration file are ignored. Comments are prefaced by a `#` and may appear on the end of a line with actual values:

```
keyword            value          #  This is a comment
```

or may be at the beginning of a line:

```
#  This entire line is a comment . . .
```

Some keywords require several lines of data. These are generally implemented to either allow the data to be read from a file:

```
keyword             filename
```

or to be included inline using Tcl-style braces:

```
keyword {
  lots of data
}
```

The specification of the keywords is case insensitive so that any combination of upper and lower case letters will have the same meaning. Hence, `DCDfile` and `dcdfile` are equivalent. The capitalization in the values, however, may be important. Some values indicate file names, in which capitalization is critical. Other values such as `on` or `off` are case insensitive.

2.2.2 Tcl scripting interface and features

When compiled with Tcl (all released binaries) the config file is parsed by Tcl in a fully backwards compatible manner with the added bonus that any Tcl command may also be used. This alone allows:

- the "source" command to include other files (works w/o Tcl too!),
- the "print" command to display messages ("puts" is broken, sorry),
- environment variables through the env array ("$env(USER)"), and
- user-defined variables ("set base sim23", "dcdfile $base.dcd").

Additional features include:

- The "callback" command takes a 2-parameter Tcl procedure which is then called with a list of labels and a list of values during every timestep, allowing analysis, formatting, whatever.
- The "run" command takes a number of steps to run (overriding the now optional numsteps parameter, which defaults to 0) and can be called repeatedly. You can "run 0" just to get energies.
- The "minimize" command is similar to "run" and performs minimization for the specified number of force evaluations.
- The "output" command takes an output file basename and causes .coor, .vel, and .xsc files to be written with that name.
- Between "run" commands the reassignTemp, rescaleTemp, and langevinTemp parameters can be changed to allow simulated annealing protocols within a single config file. The useGroupPressure, useFlexibleCell, useConstantArea, useConstantRatio, LangevinPiston, LangevinPistonTarget, LangevinPistonPeriod, LangevinPistonDecay, LangevinPistonTemp, SurfaceTensionTarget, BerendsenPressure, BerendsenPressureTarget, BerendsenPressureCompressibility, and BerendsenPressureRelaxationTime parameters may be changed to allow pressure equilibration. The fixedAtoms, constraintScaling, and nonbondedScaling parameters may

be changed to preserve macromolecular conformation during minimization and equilibration (fixedAtoms may only be disabled, and requires that fixedAtomsForces is enabled to do this). The consForceScaling parameter may be changed to vary steering forces or to implement a time-varying electric field that affects specific atoms.

- The "checkpoint" and "revert" commands (no arguments) allow a scripted simulation to save and restore to a prior state.
- The "reinitvels" command reinitializes velocities to a random distribution based on the given temperature.
- The "rescalevels" command rescales velocities by the given factor.
- The "reloadCharges" command reads new atomic charges from the given file, which should contain one number for each atom, separated by spaces and/or line breaks.
- The "measure" command allows user-programmed calculations to be executed in order to facilitate automated methods. (For example, to revert or change a parameter.) A number of measure commands are included in the NAMD binary; the module has been designed to make it easy for users to add additional measure commands.
- The "coorfile" command allows NAMD to perform force and energy analysis on trajectory files. "coorfile open dcd `filename`" opens the specified DCD file for reading. "coorfile read" reads the next frame in the opened DCD file, replacing NAMD's atom coordinates with the coordinates in the frame, and returns 0 if successful or -1 if end-of-file was reached. "coorfile skip" skips past one frame in the DCD file; this is significantly faster than reading coordinates and throwing them away. "coorfile close" closes the file. The "coorfile" command is not available on the Cray T3E.

  Force and energy analysis are especially useful in the context of pair interaction calculations; see Sec. 6.11 for details, as well as the example scripts in Sec. 8.

Please note that while NAMD has traditionally allowed comments to be started by a # appearing anywhere on a line, Tcl only allows comments to appear where a new statement could begin. With Tcl config file parsing enabled (all shipped binaries) both NAMD and Tcl comments are allowed before the first "run" command. At this point only pure Tcl syntax is allowed. In addition, the ";#" idiom for Tcl comments will only work with Tcl enabled. NAMD has also traditionally allowed parameters to be specified as "param=value". This is supported, but only before the first "run" command. Some examples:

```
# this is my config file                          <- OK
reassignFreq 100 ; # how often to reset velocities  <- only w/ Tcl
reassignTemp 20 # temp to reset velocities to       <- OK before "run"
run 1000                                          <- now Tcl only
reassignTemp 40 ; # temp to reset velocities to     <- ";" is required
```

NAMD has also traditionally allowed parameters to be specified as "param=value" as well as "param value". This is supported, but only before the first "run" command. For an easy life, use "param value".

2.2.3 Required NAMD configuration parameters

The following parameters are *required* for every NAMD simulation:

- `numsteps` (page 45),
- `coordinates` (page 20),
- `structure` (page 20),
- `parameters` (page 20),
- `exclude` (page 48),
- `outputname` (page 21),
- one of the following three:
  - `temperature` (page 48),
  - `velocities` (page 20),
  - `binvelocities` (page 21).

These required parameters specify the most basic properties of the simulation. In addition, it is highly recommended that `pairlistdist` be specified with a value at least one greater than `cutoff`.

3 Input and Output Files

NAMD was developed to be compatible with existing molecular dynamics packages, especially the packages X-PLOR [7] and CHARMM [6]. To achieve this compatibility, the set of input files which NAMD uses to define a molecular system are identical to the input files used by X-PLOR and CHARMM. Thus it is trivial to move an existing simulation from X-PLOR or CHARMM to NAMD. A description of these molecular system definition files is given in Section 3.1.

In addition, the output file formats used by NAMD were chosen to be compatible with X-PLOR and CHARMM. In this way the output from NAMD can be analyzed using X-PLOR, CHARMM, or a variety of the other tools that have been developed for the existing output file formats. Descriptions of the output files formats are also given in Section 3.1.

3.1 File formats

3.1.1 PDB files

The PDB (Protein Data Bank) format is used to store coordinate or velocity data being input or output from NAMD. This is the standard format for coordinate data for most other molecular dynamics programs as well, including X-PLOR and CHARMM. A full description of this file format can be obtained from the PDB web site at `http://www.rcsb.org/pdb/`.

3.1.2 X-PLOR format PSF files

NAMD uses the same protein structure files that X-PLOR does. At this time, the easiest way to generate these files is using X-PLOR or CHARMM, although it is possible to build them by hand. CHARMM can generate an X-PLOR format PSF file with the command "`write psf card xplor`".

3.1.3 CHARMM19, CHARMM22, and CHARMM27 parameter files

NAMD supports CHARMM19, CHARMM22, and CHARMM27 parameter files in both X-PLOR and CHARMM formats. (X-PLOR format is the default, CHARMM format parameter files may be used given the parameter "`paraTypeCharmm on`".) For a full description of the format of commands used in these files, see the X-PLOR and CHARMM User's Manual [7].

3.1.4 DCD trajectory files

NAMD produces DCD trajectory files in the same format as X-PLOR and CHARMM. The DCD files are single precision binary FORTRAN files, so are transportable between computer architectures. They are not, unfortunately, transportable between big-endian (most workstations) and little endian (Intel) architectures. (This same caveat applies to binary velocity and coordinate files. The utility programs `flipdcd` and `flipbinpdb` are provided with the Linux/Intel version to reformat these files.) The exact format of these files is very ugly but supported by a wide range of analysis and display programs.

3.2 NAMD configuration parameters

3.2.1 Input files

- `coordinates` < coordinate PDB file >
  Acceptable Values: UNIX filename
  Description: The PDB file containing initial position coordinate data. Note that path names can be either absolute or relative. Only one value may be specified.

- `structure` < PSF file >
  Acceptable Values: UNIX filename
  Description: The X-PLOR format PSF file describing the molecular system to be simulated. Only one value may be specified.

- `parameters` < parameter file >
  Acceptable Values: UNIX filename
  Description: A CHARMM19, CHARMM22, or CHARMM27 parameter file that defines all or part of the parameters necessary for the molecular system to be simulated. At least one parameter file must be specified for each simulation. Multiple definitions (but only one file per definition) are allowed for systems that require more than one parameter file. The files will be read in the order that they appear in the configuration file. If duplicate parameters are read, a warning message is printed and the last parameter value read is used. Thus, the order that files are read can be important in cases where duplicate values appear in separate files.

- `paraTypeXplor` < Is the parameter file in X-PLOR format? >
  Acceptable Values: `on` or `off`
  Default Value: `on`
  Description: Specifies whether or not the parameter file(s) are in X-PLOR format. X-PLOR format is the default for parameter files! Caveat: The PSF file should be also constructed with X-PLOR in case of an X-PLOR parameter file because X-PLOR stores information about the multiplicity of dihedrals in the PSF file. See the X-PLOR manual for details.

- `paraTypeCharmm` < Is the parameter file in CHARMM format? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not the parameter file(s) are in CHARMM format. X-PLOR format is the default for parameter files! Caveat: The information about multiplicity of dihedrals will be obtained directly from the parameter file, and the full multiplicity will be used (same behavior as in CHARMM). If the PSF file originates from X-PLOR, consecutive multiple entries for the same dihedral (indicating the dihedral multiplicity for X-PLOR) will be ignored.

- `velocities` < velocity PDB file >
  Acceptable Values: UNIX filename
  Description: The PDB file containing the initial velocities for all atoms in the simulation. This is typically a restart file or final velocity file written by NAMD during a previous simulation. Either the `temperature` or the `velocities/binvelocities` option must be defined to determine an initial set of velocities. Both options cannot be used together.

- `binvelocities` < binary velocity file >
  Acceptable Values: UNIX filename
  Description: The binary file containing initial velocities for all atoms in the simulation. A binary velocity file is created as output from NAMD by activating the `binaryrestart` or `binaryoutput` options. The `binvelocities` option should be used as an alternative to `velocities`. Either the `temperature` or the `velocities`/`binvelocities` option must be defined to determine an initial set of velocities. Both options cannot be used together.

- `bincoordinates` < binary coordinate restart file >
  Acceptable Values: UNIX filename
  Description: The binary restart file containing initial position coordinate data. A binary coordinate restart file is created as output from NAMD by activating the `binaryrestart` or `binaryoutput` options. Note that, in the current implementation at least, the `bincoordinates` option must be used in addition to the `coordinates` option, but the positions specified by `coordinates` will then be ignored.

- `cwd` < default directory >
  Acceptable Values: UNIX directory name
  Description: The default directory for input and output files. If a value is given, all filenames that do not begin with a / are assumed to be in this directory. For example, if `cwd` is set to `/scr`, then a filename of `outfile` would be modified to `/scr/outfile` while a filename of `/tmp/outfile` would remain unchanged. If no value for `cwd` is specified, than all filenames are left unchanged *but are assumed to be relative to the directory which contains the configuration file given on the command line.*

3.2.2 Output files

- `outputname` < output PDB file >
  Acceptable Values: UNIX filename prefix
  Description: At the end of every simulation, NAMD writes two PDB files, one containing the final coordinates and another containing the final velocities of all atoms in the simulation. This option specifies the file prefix for these two files. The position coordinates will be saved to a file named as this prefix with `.coor` appended. The velocities will be saved to a file named as this prefix with `.vel` appended. For example, if the prefix specified using this option was `/tmp/output`, then the two files would be `/tmp/output.coor` and `/tmp/output.vel`.

- `binaryoutput` < use binary output files? >
  Acceptable Values: `yes` or `no`
  Default Value: `yes`
  Description: Activates the use of binary output files. If this option is set to `yes`, then the final output files will be written in binary rather than PDB format. Binary files preserve more accuracy between NAMD restarts than ASCII PDB files, but the binary files are not guaranteed to be transportable between computer architectures. (The utility program `flipbinpdb` is provided with the Linux/Intel version to reformat these files.)

- `restartname` < restart files >
  Acceptable Values: UNIX filename prefix
  Description: The prefix to use for restart filenames. NAMD produces PDB restart files

that store the current positions and velocities of all atoms at some step of the simulation. This option specifies the prefix to use for restart files in the same way that `outputname` specifies a filename prefix for the final positions and velocities. If `restartname` is defined then the parameter `restartfreq` must also be defined.

- `restartfreq` < frequency of restart file generation >
  Acceptable Values: positive integer
  Description: The number of timesteps between the generation of restart files. If `restartfreq` is defined, then `restartname` must also be defined.

- `restartsave` < use timestep in restart filenames? >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: Appends the current timestep to the restart filename prefix, producing a sequence of restart files rather than only the last version written.

- `binaryrestart` < use binary restart files? >
  Acceptable Values: `yes` or `no`
  Default Value: `yes`
  Description: Activates the use of binary restart files. If this option is set to `yes`, then the restart files will be written in binary rather than PDB format. Binary files preserve more accuracy between NAMD restarts than ASCII PDB files, but the binary files are not guaranteed to be transportable between computer architectures. (The utility program `flipbinpdb` is provided with the Linux/Intel version to reformat these files.)

- `DCDfile` < coordinate trajectory output file >
  Acceptable Values: UNIX filename
  Description: The binary DCD position coordinate trajectory filename. This file stores the trajectory of all atom position coordinates using the same format (binary DCD) as X-PLOR. If `DCDfile` is defined, then `DCDfreq` must also be defined.

- `DCDfreq` < timesteps between writing coordinates to trajectory file >
  Acceptable Values: positive integer
  Description: The number of timesteps between the writing of position coordinates to the trajectory file. The initial positions will not be included in the trajectory file.

- `DCDUnitCell` < write unit cell data to dcd file? >
  Acceptable Values: `yes` or `no`
  Default Value: `yes` if periodic cell
  Description: If this option is set to `yes`, then DCD files will contain unit cell information in the style of Charmm DCD files. By default this option is enabled if the simulation cell is periodic in all three dimensions and disabled otherwise.

- `velDCDfile` < velocity trajectory output file >
  Acceptable Values: UNIX filename
  Description: The binary DCD velocity trajectory filename. This file stores the trajectory of all atom velocities using the same format (binary DCD) as X-PLOR. If `velDCDfile` is defined, then `velDCDfreq` must also be defined.

- `velDCDfreq` < timesteps between writing velocities to trajectory file >
  Acceptable Values: positive integer
  Description: The number of timesteps between the writing of velocities to the trajectory file. The initial velocities will not be included in the trajectory file.

3.2.3 Standard output

NAMD logs a variety of summary information to standard output. The standard units used by NAMD are Angstroms for length, kcal/mol for energy, Kelvin for temperature, and bar for pressure. Wallclock or CPU times are given in seconds unless otherwise noted.

BOUNDARY energy is from spherical boundary conditions and harmonic restraints, while MISC energy is from external electric fields and various steering forces. TOTAL is the sum of the various potential energies, and the KINETIC energy. TOTAL2 uses a slightly different kinetic energy that is better conserved during equilibration in a constant energy ensemble. TOTAL3 is another variation with much smaller short-time fluctuations that is also adjusted to have the same running average as TOTAL2. Defects in constant energy simulations are much easier to spot in TOTAL3 than in TOTAL or TOTAL2.

PRESSURE is the pressure calculated based on individual atoms, while GPRESSURE incorporates hydrogen atoms into the heavier atoms to which they are bonded, producing smaller fluctuations. The TEMPAVG, PRESSAVG, and GPRESSAVG are the average of temperature and pressure values since the previous ENERGY output; for the first step in the simulation they will be identical to TEMP, PRESSURE, and GPRESSURE.

- `outputEnergies` < timesteps between energy output >
  Acceptable Values: positive integer
  Default Value: 1
  Description: The number of timesteps between each energy output of NAMD. This value specifies how often NAMD should output the current energy values to **stdout** (which can be redirected to a file). By default, this is done every step. For long simulations, the amount of output generated by NAMD can be greatly reduced by outputting the energies only occasionally.

- `mergeCrossterms` < add crossterm energy to dihedral? >
  Acceptable Values: yes or no
  Default Value: yes
  Description: If crossterm (or CMAP) terms are present in the potential, the energy is added to the dihedral energy to avoid altering the energy output format. Disable this feature to add a separate "CROSS" field to the output.

- `outputMomenta` < timesteps between momentum output >
  Acceptable Values: nonnegative integer
  Default Value: 0
  Description: The number of timesteps between each momentum output of NAMD. If specified and nonzero, linear and angular momenta will be output to **stdout**.

- `outputPressure` < timesteps between pressure output >
  Acceptable Values: nonnegative integer
  Default Value: 0

Description: The number of timesteps between each pressure output of NAMD. If specified and nonzero, atomic and group pressure tensors will be output to **stdout**.

- `outputTiming` < timesteps between timing output >
  Acceptable Values: nonnegative integer
  Default Value: the greater of `firstLdbStep` or 10× `outputEnergies`
  Description: The number of timesteps between each timing output of NAMD. If nonzero, CPU and wallclock times and memory usage will be output to **stdout**. These data are from node 0 only; CPU times and memory usage for other nodes may vary.

3.3 AMBER force field parameters

AMBER format PARM file and coordinate file can be read by NAMD, which allows one to use AMBER force field to carry out all types of simulations that NAMD has supported. NAMD can read PARM files in either the format used in AMBER 6 or the new format defined in AMBER 7. The output of the simulation (restart file, DCD file, etc.) will still be in traditional format that has been used in NAMD.

- `amber` < use AMBER format force field? >
  Acceptable Values: yes or no
  Default Value: no
  Description: If `amber` is set to on, then `parmfile` must be defined, and `structure` and `parameters` should not be defined.

- `parmfile` < AMBER format PARM file >
  Acceptable Values: UNIX filename
  Description: This file contains complete topology and parameter information of the system.

- `ambercoor` < AMBER format coordinate file >
  Acceptable Values: UNIX filename
  Description: This file contains the coordinates of all the atoms. Note that `coordinates` can also be used for PDB format coordinate file. When `amber` is set to on, either `ambercoor` or `coordinates` must be defined, but not both.

- `readexclusions` < Read exclusions from PARM file? >
  Acceptable Values: yes or no
  Default Value: yes
  Description: PARM file explicitly gives complete exclusion (including 1-4 exclusions) information. When `readexclusions` is set to on, NAMD will read all exclusions from PARM file and will not add any more; alternatively, if `readexclusions` is set to off, NAMD will ignore the exclusions in PARM file and will automatically generate them according to the exclusion policy specified by `exclude`.

- `scnb` < VDW 1-4 scaling factor >
  Acceptable Values: decimal ≥ 1.0
  Default Value: 2.0
  Description: Same meaning as SCNB in AMBER. Note that in NAMD, 1-4 vdw interactions are DIVIDED by `scnb`, whereas 1-4 electrostatic interactions are MULTIPLIED by `1-4scaling`. So `1-4scaling` should be set to the inverse of SCEE value used in AMBER.

Caveat:
1. Polarizable parameters in AMBER are not supported.
2. NAMD does not support the 10-12 potential terms in some old AMBER versions. When non-zero 10-12 parameter is encountered in PARM file, NAMD will terminate.
3. NAMD has several exclusion policy options, defined by `exclude`. The way AMBER dealing with exclusions corresponds to the "scaled1-4" in NAMD. So for simulations using AMBER force field, one would specify "exclude scaled1-4" in the configuration file, and set `1-4scaling` to the inverse value of SCEE as would be used in AMBER.
4. NAMD does not read periodic box lengths in PARM or coordinate file. They must be explicitly specified in NAMD configuration file.
5. By default, NAMD applies switching functions to the non-bond interactions within the cut-off distance, which helps to improve energy conservation, while AMBER does not use switching functions so it simply truncates the interactions at cutoff. However, if "authentic" AMBER cutoff simulations are desired, the switching functions could be turned off by specifying "switching off" in NAMD configuration file.
6. NAMD and AMBER may have different default values for some parameters (e.g., the tolerance of SHAKE). One should check other sections of this manual for accurate descriptions of the NAMD options.

Following are two examples of the NAMD configuration file to read AMBER force field and carry out simulation. They may help users to select proper NAMD options for AMBER force field. For the convenience of AMBER users, the AMBER 6 sander input files are given in the left for comparison, which would accomplish similar tasks in AMBER.

Example 1: Non-periodic boundary system, cutoff simulation

```
---AMBER----      ---NAMD---

 TITLE
 &cntrl
  ntb=0, igb=2,   # non-periodic, use cutoff for non-bond
  nstlim=1000,    numsteps       1000  # Num of total steps
  ntpr=50,        outputEnergies 50  # Energy output frequency
  ntwr=50,        restartfreq    50  # Restart file frequency
  ntwx=100,       DCDfreq        100  # Trajectory file frequency
  dt=0.001,       timestep       1  # in unit of fs (This is default)
  tempi=0.,       temperature    0  # Initial temp for velocity assignment
  cut=10.,        cutoff         10
                  switching      off  # Turn off the switching functions
  scee=1.2,       exclude        scaled1-4
                  1-4scaling     0.833333  # =1/1.2, default is 1.0
  scnb=2.0        scnb           2  # This is default
 &end
                  amber          on  # Specify this is AMBER force field
                  parmfile       prmtop  # Input PARM file
                  ambercoor      inpcrd  # Input coordinate file
                  outputname     md  # Prefix of output files
```

Example 2: Periodic boundary system, PME, NVE ensemble, using SHAKE algorithm

```
---AMBER----      ---NAMD---

 TITLE
 &cntrl
  ntc=2, ntf=2,   # SHAKE to the bond between each hydrogen and it mother atom
                  rigidBonds     all
  tol=0.0005,     rigidTolerance 0.0005  # Default is  0.00001
  nstlim=500,     numsteps       500  # Num of total steps
  ntpr=50,        outputEnergies 50  # Energy output frequency
  ntwr=100,       restartfreq    100  # Restart file frequency
  ntwx=100,       DCDfreq        100  # Trajectory file frequency
  dt=0.001,       timestep       1  # in unit of fs (This is default)
  tempi=300.,     temperature    300  # Initial temp for velocity assignment
  cut=9.,         cutoff         9
                  switching      off  # Turn off the switching functions
 &end
 &ewald           PME            on  # Use PME for electrostatic calculation
                  # Orthogonal periodic box size
  a=62.23,        cellBasisVector1   62.23  0  0
  b=62.23,        cellBasisVector2   0  62.23  0
  c=62.23,        cellBasisVector3   0  0  62.23
  nfft1=64,       PMEGridSizeX   64
  nfft2=64,       PMEGridSizeY   64
  nfft3=64,       PMEGridSizeZ   64
  ischrgd=1,      # NAMD doesn't force neutralization of charge
 &end
                  amber          on  # Specify this is AMBER force field
                  parmfile       FILENAME  # Input PARM file
                  ambercoor      FILENAME  # Input coordinate file
                  outputname     PREFIX  # Prefix of output files
                  exclude        scaled1-4
                  1-4scaling     0.833333  # =1/1.2, default is 1.0
```

3.4 GROMACS force field parameters

NAMD has the ability to load GROMACS ASCII topology (.top) and coordinate (.gro) files, which allows you to run most GROMACS simulations in NAMD. All simulation output will still be in the traditional NAMD formats.

- `gromacs` < use GROMACS format force field? >
  Acceptable Values: on or off
  Default Value: off
  Description: If `gromacs` is set to on, then `grotopfile` must be defined, and `structure` and `parameters` should not be defined.

- `grotopfile` < GROMACS format topology/parameter file >
  Acceptable Values: UNIX filename
  Description: This file contains complete topology and parameter information of the system.

- `grocoorfile` < GROMACS format coordinate file >
  Acceptable Values: UNIX filename
  Description: This file contains the coordinates of all the atoms. Note that `coordinates` can also be used for PDB format coordinate file. When `gromacs` is set to `on`, either `grocoorfile` or `coordinates` must be defined, but not both.

However, NAMD does not have support for many GROMACS-specific options:

- Dummies (fake atoms with positions generated from the positions of real atoms) are not supported.
- The GROMACS `pairs` section, where explicit 1–4 parameters are given between pairs of atoms, is not supported, since NAMD calculates its 1–4 interactions exclusively by type.
- Similarly, `exclusions` are not supported. The biggest problem here is that GROMACS RB dihedrals are supposed to imply exclusions, but NAMD does not support this.
- Constraints, restraints, and `settles` are not implemented in NAMD.
- In some cases, it may not work to override some but not all of the parameters for a bond, atom, etc. In this case, NAMD will generate an error and stop. The parser will sometimes not tolerate correct GROMACS files or fail to detect errors in badly formatted files.
- NAMD does not support all the types of bond potentials that exist in GROMACS, but approximates them with harmonic or sinusoidal potentials.
- NAMD does not read periodic box lengths in the coordinate file. They must be explicitly specified in the NAMD configuration file.

4 Creating PSF Structure Files

The `psfgen` structure building tool consists of a portable library of structure and file manipulation routines with a Tcl interface. Current capabilities include

- reading CHARMM topology files
- reading psf files in X-PLOR/NAMD format
- extracting sequence data from single segment PDB files
- generating a full molecular structure from sequence data
- applying patches to modify or link different segments
- writing NAMD and VMD compatible PSF structure files
- extracting coordinate data from PDB files
- constructing (guessing) missing atomic coordinates
- deleting selected atoms from the structure
- writing NAMD and VMD compatible PDB coordinate files

We are currently refining the interface of `psfgen` and adding features to create a complete molecular building solution. We welcome your feedback on this new tool.

4.1 Ordinary Usage

`psfgen` is currently distributed in two forms. One form is as a standalone program implemented as a Tcl interpreter which reads commands from standard output. You may use loops, variables, etc. as you would in a VMD or NAMD script. You may use psfgen interactively, but we expect it to be run most often with a script file redirected to standard input. The second form is as a Tcl package which can be imported into any Tcl application, including VMD. All the commands available to the standalone version of psfgen are available to the Tcl package; using `psfgen` within VMD lets you harness VMD's powerful atom selection capability, as well as instantly view the result of your structure building scripts. Examples of using `psfgen` both with and without VMD are provided in this document.

Generating PSF and PDB files for use with NAMD will typically consist of the following steps:

1. Preparing separate PDB files containing individual segments of protein, solvent, etc. before running `psfgen`.
2. Reading in the appropriate topology definition files and aliasing residue and atom names found in the PDB file to those found in the topology files. This will generally include selecting a default protonation state for histidine residues.
3. Generating the default structure using segment and pdb commands.
4. Applying additional patches to the structure.
5. Reading coordinates from the PDB files.

6. Deleting unwanted atoms, such as overlapping water molecules.

7. Guessing missing coordinates of hydrogens and other atoms.

8. Writing PSF and PDB files for use in NAMD.

4.1.1 Preparing separate PDB files

Many PDB files in the PDB databank contain multiple chains, corresponding to protein subunits, water, and other miscellaneous groups. Protein subunits are often identified by their chain ID in the PDB file. In `psfgen`, each of these groups must be assigned to their own *segment*. This applies most strictly in the case of protein chains, each of which must be assigned to its own segment so that N-terminal and C-terminal patches can be applied. You are free to group water molecules into whatever segments you choose.

Chains can be split up into their own PDB files using your favorite text editor and/or Unix shell commands, as illustrated in the BPTI example below. If you are using VMD you can also use atom selections to write pieces of the structure to separate files:

```
# Split a file containing protein and water into separate segments.
# Creates files named myfile_water.pdb, myfile_frag0.pdb, myfile_frag1.pdb,...
# Requires VMD.
mol load pdb myfile.pdb
set water [atomselect top water]
$water writepdb myfile_water.pdb
set protein [atomselect top protein]
set chains [lsort -unique [$protein get pfrag]]
foreach chain $chains {
  set sel [atomselect top "pfrag $chain"]
  $sel writepdb myfile_frag${chain}.pdb
}
```

4.1.2 Deleting unwanted atoms

The `delatom` command described below allows you to delete selected atoms from the structure. It's fine to remove atoms from your structure before building the PSF and PDB files, but you should never edit the PSF and PDB files created by `psfgen` by hand as it will probably mess up the internal numbering in the PSF file.

Very often the atoms you want to delete are water molecules that are either too far from the solute, or else outside of the periodic box you are trying to prepare. In either case VMD atom selections can be used to select the waters you want to delete. For example:

```
# Load a pdb and psf file into both psfgen and VMD.
resetpsf
readpsf myfile.psf
coordpdb myfile.pdb
mol load psf myfile.psf pdb myfile.pdb
# Select waters that are more than 10 Angstroms from the protein.
set badwater1 [atomselect top "name OH2 and not within 10 of protein"]
```

```
# Alternatively, select waters that are outside our periodic cell.
set badwater2 [atomselect top "name OH2 and (x<-30 or x>30 or y<-30 or>30
                              or z<-30 or z>30)"]
# Delete the residues corresponding to the atoms we selected.
foreach segid [$badwater1 get segid] resid [$badwater1 get resid] {
  delatom $segid $resid
}
# Have psfgen write out the new psf and pdb file (VMD's structure and
# coordinates are unmodified!).
writepsf myfile_chopwater.psf
writepdb myfile_chopwater.pdb
```

4.2 BPTI Example

To actually run this demo requires

- the program `psfgen` from any NAMD distribution,
- the CHARMM topology and parameter files `top_all22_prot.inp` and `par_all22_prot.inp` from `http://www.pharmacy.umaryland.edu/faculty/amackere/force_fields.htm`, and
- the BPTI PDB file `6PTI.pdb` available from the Protein Data Bank at `http://www.pdb.org/` by searching for `6PTI` and downloading the complete structure file in PDB format.

Building the BPTI structure

In this demo, we create the files `bpti.psf` and `bpti.pdb` in the output directory which can then be used for a simple NAMD simulation.

```
# File: bpti_example.tcl
# Requirements: topology file top_all22_prot.inp in directory toppar
#               PDB file 6PTI.pdb in current directory

# Create working directory; remove old output files
mkdir -p output
rm -f output/6PTI_protein.pdb output/6PTI_water.pdb

# (1) Split input PDB file into segments}
grep -v '^HETATM' 6PTI.pdb > output/6PTI_protein.pdb
grep 'HOH' 6PTI.pdb > output/6PTI_water.pdb

# (2) Embed the psfgen commands in this script
psfgen << ENDMOL

# (3) Read topology file
topology toppar/top_all22_prot.inp

# (4) Build protein segment
segment BPTI {
```

```
 pdb output/6PTI_protein.pdb
}

# (5) Patch protein segment
patch DISU BPTI:5 BPTI:55
patch DISU BPTI:14 BPTI:38
patch DISU BPTI:30 BPTI:51

# (6) Read protein coordinates from PDB file
pdbalias atom ILE CD1 CD    ; # formerly "alias atom ..."
coordpdb output/6PTI_protein.pdb BPTI

# (7) Build water segment
pdbalias residue HOH TIP3   ; # formerly "alias residue ..."
segment SOLV {
 auto none
 pdb output/6PTI_water.pdb
}

# (8) Read water coordinaes from PDB file
pdbalias atom HOH O OH2     ; # formerly "alias atom ..."
coordpdb output/6PTI_water.pdb SOLV

# (9) Guess missing coordinates
guesscoord

# (10) Write structure and coordinate files
writepsf output/bpti.psf
writepdb output/bpti.pdb

# End of psfgen commands
ENDMOL
```

Step-by-step explanation of the script:

(1) Split input PDB file into segments. 6PTI.pdb is the original file from the Protein Data Bank. It contains a single chain of protein and some PO4 and H2O HETATM records. Since each segment must have a separate input file, we remove all non-protein atom records using grep. If there were multiple chains we would have to split the file by hand. Create a second file containing only waters.

(2) Embed the psfgen commands in this script. Run the psfgen program, taking everything until "ENDMOL" as input. You may run psfgen interactively as well. Since psfgen is built on a Tcl interpreter, you may use loops, variables, etc., but you must use `$$` for variables when inside a shell script. If you want, run psfgen and enter the following commands manually.

(3) Read topology file. Read in the topology definitions for the residues we will create. This must match the parameter file used for the simulation as well. Multiple topology files may be read in since psfgen and NAMD use atom type names rather than numbers in psf files.

(4) Build protein segment. Actually build a segment, calling it BPTI and reading the sequence of residues from the stripped pdb file created above. In addition to the pdb command, we could specify residues explicitly. Both angles and dihedrals are generated automatically unless "auto none" is added (which is required to build residues of water). The commands "first" and "last" may be used to change the default patches for the ends of the chain. The structure is built when the closing } is encountered, and some errors regarding the first and last residue are normal.

(5) Patch protein segment. Some patch residues (those not used to begin or end a chain) are applied after the segment is built. These contain all angle and dihedral terms explicitly since they were already generated. In this case we apply the patch for a disulfide link three separate times.

(6) Read protein coordinates from PDB file. The same file used to generate the sequence is now read to extract coordinates. In the residue ILE, the atom CD is called CD1 in the pdb file, so we use "pdbalias atom" to define the correct name. If the segment names in the pdb file match the name we gave in the segment statement, then we don't need to specify it again; in this case we do specify the segment, so that all atoms in the pdb file must belong to the segment.

(7) Build water segment. Build a segment for the crystal waters. The residue type for water depends on the model, so here we alias HOH to TIP3. Because CHARMM uses an additional H-H bond we must disable generation of angles and dihedrals for segments containing water. Then read the pdb file.

(8) Read water coordinates from PDB file. Alias the atom type for water oxygen as well and read coordinates from the file to the segment SOLV. Hydrogen doesn't show up in crystal structures so it is missing from this pdb file.

(9) Guessing missing coordinates. The tolopogy file contains default internal coordinates which can be used to guess the locations of many atoms, hydrogens in particular. In the output pdb file, the occupancy field of guessed atoms will be set to 0, atoms which are known are set to 1, and atoms which could not be guessed are set to -1. Some atoms are "poorly guessed" if needed bond lengths and angles were missing from the topology file. Similarly, waters with missing hydrogen coordinates are given a default orientation.

Write structure and coordinate files. Now that all of the atoms and bonds have been created, we can write out the psf structure file for the system. We also create the matching coordinate pdb file. The psf and pdb files are a matched set with identical atom ordering as needed by NAMD.

Using generated files in NAMD.

The files bpti.pdb and bpti.psf can now be used with NAMD, but the initial coordinates require minimization first. The following is an example NAMD configuration file for the BPTI example.

```
# NAMD configuration file for BPTI

# molecular system
structure output/bpti.psf

# force field
paratypecharmm on
parameters toppar/par_all22_prot.inp
exclude scaled1-4
1-4scaling 1.0

# approximations
switching on
switchdist 8
cutoff 12
pairlistdist 13.5
margin 0
stepspercycle 20

#integrator
timestep 1.0

#output
outputenergies 10
outputtiming 100
binaryoutput no

# molecular system
coordinates output/bpti.pdb

#output
outputname output/bpti
dcdfreq 1000

#protocol
temperature 0
reassignFreq 1000
reassignTemp 25
reassignIncr 25
reassignHold 300

#script

minimize 1000

run 20000
```

4.3 Building solvent around a protein

The following script illustrates how **psfgen** and VMD can be used together to add water around a protein structure. It assumes you already have a psf and pdb file for your protein, as well as a box of water which is large enough to contain the protein. For more information on how atomselections can be used within VMD scripts, see the VMD User's Guide.

```
proc addwater { psffile pdbfile watpsf watpdb } {
# Create psf/pdb files that contain both our protein as well as
# a box of equilibrated water.  The water box should be large enough
# to easily contain our protein.
resetpsf
readpsf $psffile
readpsf $watpsf
coordpdb $pdbfile
coordpdb $watpdb

# Load the combined structure into VMD
writepsf combine.psf
writepdb combine.pdb
mol load psf combine.psf pdb combine.pdb

# Assume that the segid of the water in watpsf is QQQ
# We want to delete waters outside of a box ten Angstroms
# bigger than the extent of the protein.
set protein [atomselect top "not segid QQQ"]
set minmax [measure minmax $protein]
foreach {min max} $minmax { break }
foreach {xmin ymin zmin} $min { break }
foreach {xmax ymax zmax} $max { break }
    set xmin [expr $xmin - 10]
    set ymin [expr $ymin - 10]
    set zmin [expr $zmin - 10]
    set xmax [expr $xmax + 10]
    set ymax [expr $ymax + 10]
    set zmax [expr $zmax + 10]

# Center the water on the protein.  Also update the coordinates held
# by psfgen.
set wat [atomselect top "segid QQQ"]
$wat moveby [vecsub [measure center $protein] [measure center $wat]]
foreach atom [$wat get {segid resid name x y z}] {
foreach {segid resid name x y z} $atom { break }
coord $segid $resid $name [list $x $y $z]
}

# Select waters that we don't want in the final structure.
```

```
set outsidebox [atomselect top "segid QQQ and (x <= $xmin or y <= $ymin \
or z <= $zmin or x >= $xmax or y >= $ymax or z >= $xmax)"]
set overlap [atomselect top "segid QQQ and within 2.4 of (not segid QQQ)"]

# Get a list of all the residues that are in the two selections, and delete
# those residues from the structure.
set reslist [concat [$outsidebox get resid] [$overlap get resid]]
set reslist [lsort -unique -integer $reslist]

foreach resid $reslist {
delatom QQQ $resid
}

# That should do it - write out the new psf and pdb file.
writepsf solvate.psf
writepdb solvate.pdb

# Delete the combined water/protein molecule and load the system that
# has excess water removed.
mol delete top
mol load psf solvate.psf pdb solvate.pdb

# Return the size of the water box
return [list [list $xmin $ymin $zmin] [list $xmax $ymax $zmax]]
}
```

4.4 List of Commands

- `topology` [`list`] <*file name*>
  Purpose: Read in molecular topology definitions from file.
  Arguments: <*file name*>: CHARMM format topology file.
  `list`: Lists all currently specified topology files.
  `residues`: Return a list of the known residue topologies.
  `patches`: Return a list of the known residue patches.
  Context: Beginning of script, before segment. May call multiple times.

- `pdbalias residue` <*alternate name*> <*real name*>
  Purpose: Provide translations from residues found in PDB files to proper residue names read in from topology definition files. Proper names from topology files will be used in generated PSF and PDB files. This command also exists under the deprecated name `alias`.
  Arguments: <*alternate name*>: Residue name found in PDB file.
  <*real name*>: Residue name found in topology file.
  Context: Before reading sequence with pdb. May call multiple times.

- `segment` [`segids`] [`resids`] [`residue`] [`first`] [`last`] <*segment ID*> [*resid*] [*atom name*] { <*commands*> }
  Purpose: Build a segment of the molecule. A segment is typically a single chain of protein or DNA, with default patches applied to the termini. Segments may also contain pure solvent

or lipid. Options [segids] [resids] [residue] [first] [last] are used to query information about the specified segment.
Arguments: segids: Return a list of segids for the molecule in the current context.
resids: Return a list of resids for the molecule in the current context.
residue: Return the residue name of the residue in the given segment with the given resid.
atoms: Return a list of atoms for the given segment with the given resid.
coordinates: Return x, y, z coordinates for the given atom.
first: Returns the name of the patch that was applied to the beginning of the specified segment.
last: Returns the name of the patch that was applied to the end of the specified segment.
<*segment ID*>: Unique name for segment, 1–4 characters.
<*commands*>: Sequence of commands in Tcl syntax to build the primary structure of the segment, including auto, first, last, residue, pdb, etc.
Context: After topology definitions and residue aliases. May call multiple times. Structure information is generated at the end of every segment command.

- auto [angles] [dihedrals] [none]
  Purpose: Override default settings from topology file for automatic generation of angles and dihedrals for the current segment.
  Arguments: angles: Enable generation of angles from bonds.
  dihedrals: Enable generation of dihedrals from angles.
  none: Disable generation of angles and dihedrals.
  Context: Anywhere within segment, does not affect later segments.

- first <*patch name*>
  Purpose: Override default patch applied to first residue in segment. Default is read from topology file and may be residue-specific.
  Arguments: <*patch name*>: Single-target patch residue name or none.
  Context: Anywhere within segment, does not affect later segments.

- last <*patch name*>
  Purpose: Override default patch applied to last residue in segment. Default is read from topology file and may be residue-specific.
  Arguments: <*patch name*>: Single-target patch residue name or none.
  Context: Anywhere within segment, does not affect later segments.

- residue <*resid*> <*resname*> [*chain*]
  Purpose: Add a single residue to the end of the current segment.
  Arguments: <*resid*>: Unique name for residue, 1–5 characters, usually numeric. <*resname*>: Residue type name from topology file. <*chain*>: Single-character chain identifier.
  Context: Anywhere within segment.

- pdb <*file name*>
  Purpose: Extract sequence information from PDB file when building segment. Residue IDs will be preserved, residue names must match entries in the topology file or should be aliased before pdb is called.
  Arguments: <*file name*>: PDB file containing known or aliased residues.
  Context: Anywhere within segment.

- `mutate` <*resid*> <*resname*>
  Purpose: Change the type of a single residue in the current segment.
  Arguments: <*resid*>: Unique name for residue, 1–5 characters, usually numeric. <*resname*>: New residue type name from topology file.
  Context: Within segment, after target residue has been created.

- `patch` [`list`] <*patch residue name*> <*segid:resid*> [...]
  Purpose: Apply a patch to one or more residues. Patches make small modifications to the structure of residues such as converting one to a terminus, changing the protonation state, or creating disulphide bonds between a pair of residues.
  Arguments: `list`: Lists all patches applied explicitey using the command 'patch'.
  `listall`: Lists all currently applied patches including default patches.
  <*patch residue name*>: Name of patch residue from topology definition file.
  <*segid:resid*>: List of segment and residue pairs to which patch should be applied.
  Context: After one or more segments have been built.

- `regenerate` [`angles`] [`dihedrals`]
  Purpose: Remove all angles and/or dihedrals and completely regenerate them using the segment automatic generation algorithms. This is only needed if patches were applied that do not correct angles and bonds. Segment and file defaults are ignored, and angles/dihedrals for the entire molecule are regenerated from scratch.
  Arguments: `angles`: Enable generation of angles from bonds.
  `dihedrals`: Enable generation of dihedrals from angles.
  Context: After one or more segments have been built.

- `multiply` <*factor*> <*segid*[*:resid*[*:atomname*]]> [...]
  Purpose: Create multiple images of a set of atoms for use in locally enhanced sampling. The beta column of the output pdb file is set to 1...<*factor*> for each image. Multiple copies of bonds, angles, etc. are created. Atom, residue or segment names are not altered; images are distinguished only by beta value. This is not a normal molecular structure and may confuse other tools.
  Arguments: <*factor*>:
  <*segid:resid:atomname*>: segment, residue, or atom to be multiplied. If :resid is omitted the entire segment is multiplied; if :atomname is omitted the entire residue is multiplied. May be repeated as many times as necessary to include all atoms.
  Context: After one or more segments have been built, all patches applied, and coordinates guessed. The effects of this command may confuse other commands.

- `delatom` <*segid*> [*resid*] [*atom name*]
  Purpose: Delete one or more atoms. If only `segid` is specified, all atoms from that segment will be removed from the structure. If both `segid` and `resid` are specified, all atoms from just that residue will be removed. If `segid`, `resid`, and `atom name` are all specified, just a single atom will be removed.
  Arguments: <*segid*>: Name of segment.
  <*resid*>: Name of residue (optional).
  <*atom name*>: Name of atom (optional).
  Context: After all segments have been built and patched.

- `resetpsf`
  Purpose: Delete all segments in the structure. The topology definitions and aliases are left intact. If you want to clear the topology and aliases as well, use `psfcontext reset` instead.
  Arguments:
  Context: After one or more segments have been built.

- `psfcontext` [*context*] [`new`] [`delete`]
  Purpose: Switches between complete contexts, including structure, topology definitions, and aliases. If no arguments are provided, the current context is returned. If <*context*> or `new` is specified, a new context is entered and the old context is returned. If `delete` is also specified, the old context is destroyed and "deleted <*old context*>" is returned. An error is returned if the specified context does not exist or if `delete` was specified and the current context would still be in use. *It may be possible to write robust, error-tolerant code with this interface, but it would not be easy. Please employ the following revised* `psfcontext` *usage instead.*
  Arguments: <*context*>: Context ID returned by psfcontext.
  Context: At any time.

- `psfcontext reset`
  Purpose: Clears the structure, topology definitions, and aliases, creating clean environment just like a new context.
  Arguments:
  Context: At any time.

- `psfcontext create`
  Purpose: Creates a new context and returns its ID, but does not switch to it. This is different from `psfcontext new` above, which switches to the newly created context and returns the current context's ID.
  Arguments:
  Context: At any time.

- `psfcontext delete` <*context*>
  Purpose: Deletes the specified context. An error is returned if the specified context does not exist or would still be in use. This is different from `psfcontext` <*context*> `delete` above, which switches to the specified context and deletes the current one.
  Arguments: <*context*>: Context ID returned by psfcontext.
  Context: At any time.

- `psfcontext eval` <*context*> { <*commands*> }
  Purpose: Evaluates <*commands*> in the specified context, returning to the current context on exit. This should be totally robust, returning to the orignal context in case of errors and preventing its deletion when nested.
  Arguments: <*context*>: Context ID returned by `psfcontext create`.
  <*commands*>: Script to be executed in the specified context.
  Context: At any time.

- `psfcontext stats`
  Purpose: Returns the total numbers of contexts that have been created and destroyed. This is useful for checking if a script is leaking contexts.

Arguments:
Context: At any time.

- `writepsf` [`charmm`] [`x-plor`] [`cmap`] [`nocmap`] <*file name*>
  Purpose: Write out structure information as PSF file. A simplified session log is listed in the REMARKS section of the PSF file.
  Arguments: `charmm`: Use CHARMM format (numbers for atom types).
  `x-plor`: Use X-PLOR format (names for atom types), the default format required by NAMD.
  `cmap`: Write cross-term entries to PSF file if present, the default.
  `nocmap`: Do not write cross-term entries to PSF file, even if present.
  <*file name*>: PSF file to be generated.
  Context: After all segments have been built and patched.

- `readpsf` <*file name*>
  Purpose: Read in structure information from PSF file and adds it to the structure. It is an error if any segments in the PSF file already exist.
  Arguments: <*file name*>: PSF file in X-PLOR format (names for atom types).
  Context: Anywhere but within segment.

- `pdbalias atom` <*residue name*> <*alternate name*> <*real name*>
  Purpose: Provide translations from atom names found in PDB files to proper atom names read in from topology definition files. Proper names from topology files will be used in generated PSF and PDB files. This command also exists under the deprecated name `alias`.
  Arguments: <*residue name*>: Proper or aliased residue name.
  <*alternate name*>: Atom name found in PDB file.
  <*real name*>: Atom name found in topology file.
  Context: Before reading coordinates with coordpdb. May call multiple times.

- `coord` <*segid*> <*resid*> <*atomname*> <{ *x y z* }>
  Purpose: Set coordinates for a single atom.
  Arguments: <*segid*>: Segment ID of target atom.
  <*resid*>: Residue ID of target atom.
  <*atomname*>: Name of target atom.
  <{ *x y z* }>: Coordinates to be assigned.
  Context: After structure has been generated.

- `coordpdb` <*file name*> [*segid*]
  Purpose: Read coordinates from PDB file, matching segment, residue and atom names.
  Arguments: <*file name*>: PDB file containing known or aliased residues and atoms.
  <*segid*>: If specified override segment IDs in PDB file.
  Context: After segment has been generated and atom aliases defined.

- `guesscoord`
  Purpose: Guesses coordinates of atoms for which they were not explicitly set. Calculation is based on internal coordinate hints contained in toplogy definition files. When these are insufficient, wild guesses are attempted based on bond lengths of 1 Å and angles of 109°.
  Arguments: None.
  Context: After stucture has been generated and known coordinates read in.

- `writepdb` <*file name*>
  Purpose: Writes PDB file containing coordinates. Atoms order is identical to PSF file generated by writepsf (unless structure has been changed). The O field is set to 1 for atoms with known coordinates, 0 for atoms with guessed coordinates, and -1 for atoms with no coordinate data available (coordinates are set to 0 for these atoms).
  Arguments: <*file name*>: PDB file to be written.
  Context: After structure and coordinates are complete.

4.5 Example of a Session Log

The command "writepsf" prints a simple session log as "REMARKS" at the beginning of the PSF file. The log contains information about applied patches and used topology files which not stored in the standard records of PSF files. These informations are also available after a PSF file was read by command "readpsf". Here'a a simple axample:

```
PSF

       1 !NTITLE
 REMARKS original generated structure x-plor psf file
 REMARKS 4 patches were applied to the molecule.
 REMARKS topology 1LOV_autopsf-temp.top
 REMARKS segment P1 { first NTER; last CTER; auto angles dihedrals }
 REMARKS segment O1 { first NONE; last NONE; auto none  }
 REMARKS segment W1 { first NONE; last NONE; auto none  }
 REMARKS defaultpatch NTER P1:1
 REMARKS defaultpatch CTER P1:104
 REMARKS patch DISU P1:10  P1:2
 REMARKS patch DISU P1:103  P1:6

    1704 !NATOM
       1 P1   1    ALA  N    NH3   -0.300000       14.0070           0
...
```

All patches that were applied explicitely using the "patch" command are listed following the keyword "patch", but the patches that result from default patching like the first and last patches of a segment are marked as "defaultpatch". Further the segment based patching rules are listed along with the angle/dihedral autogeneration rules.

5 Basic Simulation Parameters

5.1 Non-bonded interaction parameters and computations

NAMD has a number of options that control the way that non-bonded interactions are calculated. These options are interrelated and can be quite confusing, so this section attempts to explain the behavior of the non-bonded interactions and how to use these parameters.

5.1.1 Non-bonded van der Waals interactions

The simplest non-bonded interaction is the van der Waals interaction. In NAMD, van der Waals interactions are always truncated at the cutoff distance, specified by `cutoff`. The main option that effects van der Waals interactions is the `switching` parameter. With this option set to `on`, a smooth switching function will be used to truncate the van der Waals potential energy smoothly at the cutoff distance. A graph of the van der Waals potential with this switching function is shown in Figure 1. If `switching` is set to `off`, the van der Waals energy is just abruptly truncated at the cutoff distance, so that energy may not be conserved.

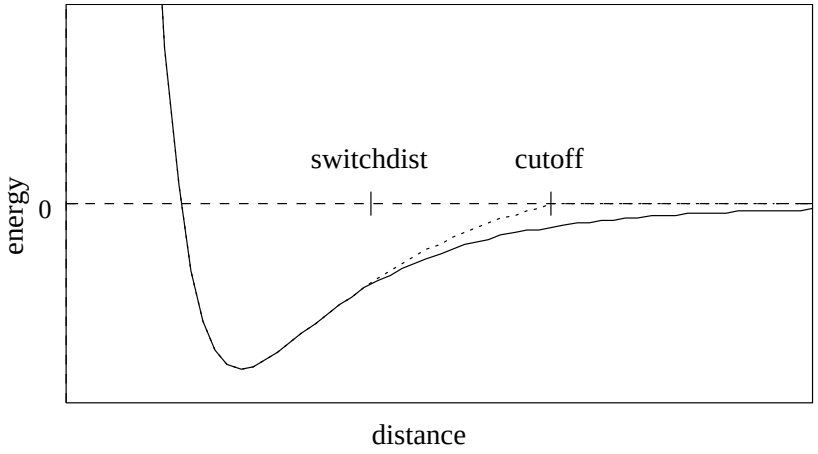

Figure 1: Graph of van der Waals potential with and without the application of the switching function. With the switching function active, the potential is smoothly reduced to 0 at the cutoff distance. Without the switching function, there is a discontinuity where the potential is truncated.

The switching function used is based on the X-PLOR switching function. The parameter `switchdist` specifies the distance at which the switching function should start taking effect to bring the van der Waals potential to 0 smoothly at the cutoff distance. Thus, the value of `switchdist` must always be less than that of `cutoff`.

5.1.2 Non-bonded electrostatic interactions

The handling of electrostatics is slightly more complicated due to the incorporation of multiple timestepping for full electrostatic interactions. There are two cases to consider, one where full electrostatics is employed and the other where electrostatics are truncated at a given distance.

First let us consider the latter case, where electrostatics are truncated at the cutoff distance. Using this scheme, all electrostatic interactions beyond a specified distance are ignored, or assumed to be zero. If `switching` is set to `on`, rather than having a discontinuity in the potential at the

cutoff distance, a shifting function is applied to the electrostatic potential as shown in Figure 2. As this figure shows, the shifting function shifts the entire potential curve so that the curve intersects the x-axis at the cutoff distance. This shifting function is based on the shifting function used by X-PLOR.

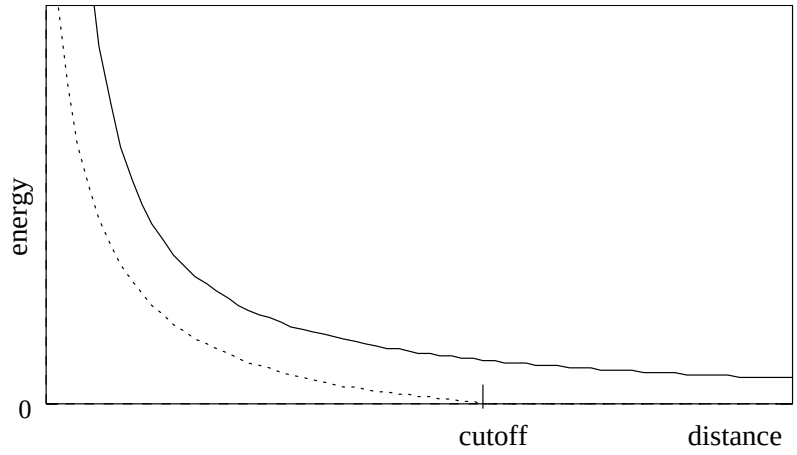

Figure 2: Graph showing an electrostatic potential with and without the application of the shifting function.

Next, consider the case where full electrostatics are calculated. In this case, the electrostatic interactions are not truncated at any distance. In this scheme, the `cutoff` parameter has a slightly different meaning for the electrostatic interactions — it represents the *local interaction distance*, or distance within which electrostatic pairs will be directly calculated every timestep. Outside of this distance, interactions will be calculated only periodically. These forces will be applied using a multiple timestep integration scheme as described in Section 5.2.

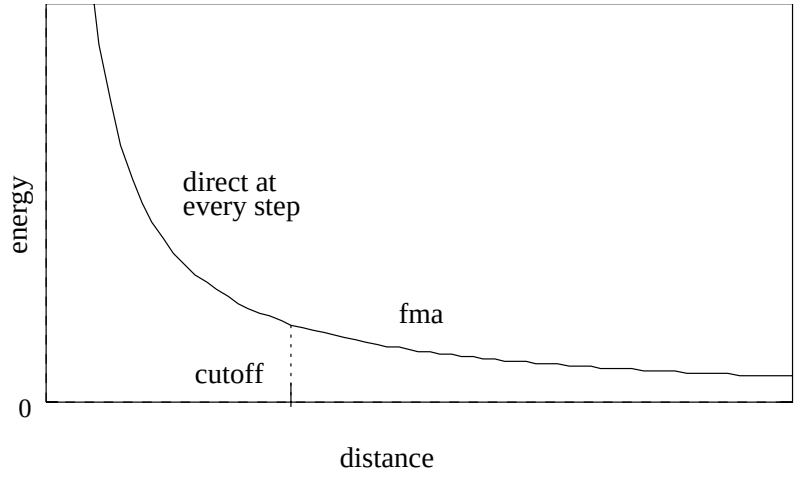

Figure 3: Graph showing an electrostatic potential when full electrostatics are used within NAMD, with one curve portion calculated directly and the other calculated using DPMTA.

5.1.3 Nonbonded interaction distance-testing

The last critical parameter for non-bonded interaction calculations is the parameter `pairlistdist`. To reduce the cost of performing the non-bonded interactions, NAMD uses a *non-bonded pair list* which contained all pairs of atoms for which non-bonded interactions should be calculated. Performing the search for pairs of atoms that should have their interactions calculated is an expensive operation. Thus, the pair list is only calculated periodically, at least once per cycle. Unfortunately, pairs of atoms move relative to each other during the steps between preparation of the pair list. Because of this, if the pair list were built to include only those pairs of atoms that are within the cutoff distance when the list is generated, it would be possible for atoms to drift closer together than the cutoff distance during subsequent timesteps and yet not have their non-bonded interactions calculated.

Let us consider a concrete example to better understand this. Assume that the pairlist is built once every ten timesteps and that the cutoff distance is 8.0 Å. Consider a pair of atoms A and B that are 8.1 Å apart when the pairlist is built. If the pair list includes only those atoms within the cutoff distance, this pair would not be included in the list. Now assume that after five timesteps, atoms A and B have moved to only 7.9 Å apart. A and B are now within the cutoff distance of each other, and should have their non-bonded interactions calculated. However, because the non-bonded interactions are based solely on the pair list and the pair list will not be rebuilt for another five timesteps, this pair will be ignored for five timesteps causing energy not to be conserved within the system.

To avoid this problem, the parameter `pairlistdist` allows the user to specify a distance greater than the `cutoff` distance for pairs to be included in the pair list, as shown in Figure 4. Pairs that are included in the pair list but are outside the cutoff distance are simply ignored. So in the above example, if the `pairlistdist` were set to 10.0 Å, then the atom pair A and B would be included in the pair list, even though the pair would initially be ignored because they are further apart than the cutoff distance. As the pair moved closer and entered the cutoff distance, because the pair was already in the pair list, the non-bonded interactions would immediately be calculated and energy conservation would be preserved. The value of `pairlistdist` should be chosen such that no atom pair moves more than `pairlistdist` − `cutoff` in one cycle. This will insure energy conservation and efficiency.

The `pairlistdist` parameter is also used to determine the minimum patch size. Unless the `splitPatch` parameter is explicitly set to `position`, hydrogen atoms will be placed on the same patch as the "mother atom" to which they are bonded. These *hydrogen groups* are then distance tested against each other using only a cutoff increased by the the value of the `hgroupCutoff` parameter. The size of the patches is also increased by this amount. NAMD functions correctly even if a hydrogen atom and its mother atom are separated by more than half of `hgroupCutoff` by breaking that group into its individual atoms for distance testing. Margin violation warning messages are printed if an atom moves outside of a safe zone surrounding the patch to which it is assigned, indicating that `pairlistdist` should be increased in order for forces to be calculated correctly and energy to be conserved.

Margin violations mean that atoms that are in non-neighboring patches may be closer than the cutoff distance apart. This may sometimes happen in constant pressure simulations when the cell shrinks (since the patch grid remains the same size). The workaround is to increase the margin parameter so that the simulation starts with fewer, larger patches. Restarting the simulation will also regenerate the patch grid.

In rare special circumstances atoms that are involved in bonded terms (bonds, angles, dihedrals,

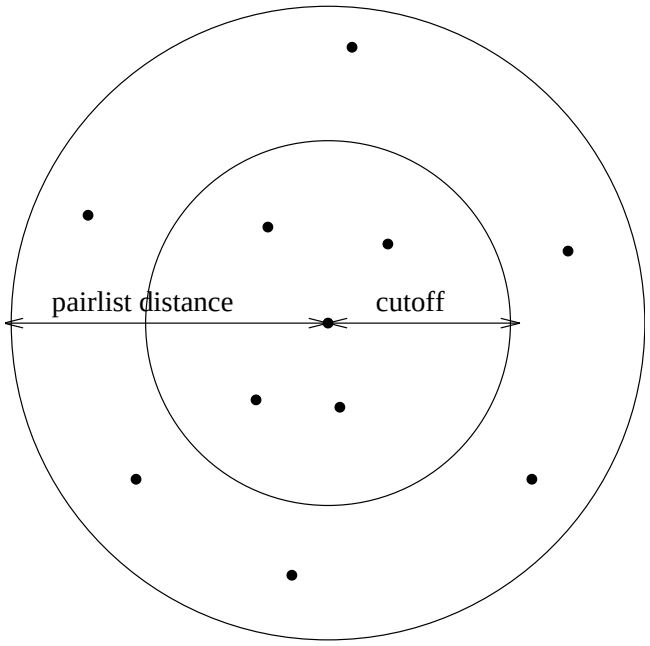

Figure 4: Depiction of the difference between the cutoff distance and the pair list distance. The pair list distance specifies a sphere that is slightly larger than that of the cutoff so that pairs are allowed to move in and out of the cutoff distance without causing energy conservation to be disturbed.

or impropers) or nonbonded exclusions (especially implicit exclusions due to bonds) will be placed on non-neighboring patches because they are more than the cutoff distance apart. This can result in the simulation dying with a message of "bad global exclusion count". If an "atoms moving too fast; simulation has become unstable", "bad global exclusion count", or similar error happens on the first timestep then there is likely something very wrong with the input coordinates, such as the atoms with uninitialized coordinates or different atom orders in the PSF and PDB file. Looking at the system in VMD will often reveal an abnormal structure. Be aware that the atom IDs in the "Atoms moving too fast" error message are 1-based, while VMD's atom indices are 0-based. If an "atoms moving too fast; simulation has become unstable", "bad global exclusion count", or similar error happens later in the simulation then the dynamics have probably become unstable, resulting in the system "exploding" apart. Energies printed at every timestep should show an exponential increase. This may be due to a timestep that is too long, or some other strange feature. Saving a trajectory of every step and working backwards in can also sometimes reveal the origin of the instability.

5.2 Full electrostatic integration

To further reduce the cost of computing full electrostatics, NAMD uses a multiple timestepping integration scheme. In this scheme, the total force acting on each atom is broken into two pieces, a quickly varying local component and a slower long range component. The local force component is defined in terms of a *splitting function*. The local force component consists of all bonded and van der Waals interactions as well as that portion of electrostatic interactions for pairs that are separated by less than the local interaction distance determined by the splitting function. The long range component consists only of electrostatic interactions outside of the local interaction distance. Since

the long range forces are slowly varying, they are not evaluated every timestep. Instead, they are evaluated every k timesteps, specified by the NAMD parameter `fullElectFrequency`. An impulse of k times the long range force is applied to the system every k timesteps (i.e., the r-RESPA integrator is used). For appropriate values of k, it is believed that the error introduced by this infrequent evaluation is modest compared to the error already incurred by the use of the numerical (Verlet) integrator. Improved methods for incorporating these long range forces are currently being investigated, with the intention of improving accuracy as well as reducing the frequency of long range force evaluations.

In the scheme described above, the van der Waals forces are still truncated at the local interaction distance. Thus, the van der Waals cutoff distance forms a lower limit to the local interaction distance. While this is believed to be sufficient, there are investigations underway to remove this limitation and provide full van der Waals calculations in $\mathcal{O}(N)$ time as well.

5.3 NAMD configuration parameters

5.3.1 Timestep parameters

- `numsteps` < number of timesteps >
  Acceptable Values: positive integer
  Description: The number of simulation timesteps to be performed. An integer greater than 0 is acceptable. The total amount of simulation time is `numsteps` × `timestep`.

- `timestep` < timestep size (fs) >
  Acceptable Values: non-negative decimal
  Default Value: 1.0
  Description: The timestep size to use when integrating each step of the simulation. The value is specified in femtoseconds.

- `firsttimestep` < starting timestep value >
  Acceptable Values: non-negative integer
  Default Value: 0
  Description: The number of the first timestep. This value is typically used only when a simulation is a continuation of a previous simulation. In this case, rather than having the timestep restart at 0, a specific timestep number can be specified.

- `stepspercycle` < timesteps per cycle >
  Acceptable Values: positive integer
  Default Value: 20
  Description: Number of timesteps in each cycle. Each cycle represents the number of timesteps between atom reassignments. For more details on non-bonded force evaluation, see Section 5.1.

5.3.2 Simulation space partitioning

- `cutoff` < local interaction distance common to both electrostatic and van der Waals calculations (Å) >
  Acceptable Values: positive decimal
  Description: See Section 5.1 for more information.

- `switching` < use switching function? >
  Acceptable Values: `on` or `off`
  Default Value: `on`
  Description: If `switching` is specified to be `off`, then a truncated cutoff is performed. If `switching` is turned `on`, then smoothing functions are applied to both the electrostatics and van der Waals forces. For a complete description of the non-bonded force parameters see Section 5.1. If `switching` is set to `on`, then `switchdist` must also be defined.

- `switchdist` < distance at which to activate switching/splitting function for electrostatic and van der Waals calculations (Å) >
  Acceptable Values: positive decimal ≤ `cutoff`
  Description: Distance at which the switching function should begin to take effect. This parameter only has meaning if `switching` is set to `on`. The value of `switchdist` must be less than or equal to the value of `cutoff`, since the switching function is only applied on the range from `switchdist` to `cutoff`. For a complete description of the non-bonded force parameters see Section 5.1.

- `limitdist` < maximum distance between pairs for limiting interaction strength(Å) >
  Acceptable Values: non-negative decimal
  Default Value: `0.`
  Description: The electrostatic and van der Waals potential functions diverge as the distance between two atoms approaches zero. The potential for atoms closer than `limitdist` is instead treated as $ar^2 + c$ with parameters chosen to match the force and potential at `limitdist`. This option should primarily be useful for alchemical free energy perturbation calculations, since it makes the process of creating and destroying atoms far less drastic energetically. The larger the value of `limitdist` the more the maximum force between atoms will be reduced. In order to not alter the other interactions in the simulation, `limitdist` should be less than the closest approach of any non-bonded pair of atoms; 1.3 Å appears to satisfy this for typical simulations but the user is encouraged to experiment. There should be no performance impact from enabling this feature.

- `pairlistdist` < distance between pairs for inclusion in pair lists (Å) >
  Acceptable Values: positive decimal ≥ `cutoff`
  Default Value: `cutoff`
  Description: A pair list is generated `pairlistsPerCycle` times each cycle, containing pairs of atoms for which electrostatics and van der Waals interactions will be calculated. This parameter is used when `switching` is set to `on` to specify the allowable distance between atoms for inclusion in the pair list. This parameter is equivalent to the X-PLOR parameter `CUTNb`. If no atom moves more than `pairlistdist`−`cutoff` during one cycle, then there will be no jump in electrostatic or van der Waals energies when the next pair list is built. Since such a jump is unavoidable when truncation is used, this parameter may only be specified when `switching` is set to `on`. If this parameter is not specified and `switching` is set to `on`, the value of `cutoff` is used. A value of at least one greater than `cutoff` is recommended.

- `splitPatch` < how to assign atoms to patches >
  Acceptable Values: `position` or `hydrogen`
  Default Value: `hydrogen`

Description: When set to `hydrogen`, hydrogen atoms are kept on the same patch as their parents, allowing faster distance checking and rigid bonds.

- `hgroupCutoff (Å)` < used for group-based distance testing >
  Acceptable Values: positive decimal
  Default Value: 2.5
  Description: This should be set to twice the largest distance which will ever occur between a hydrogen atom and its mother. Warnings will be printed if this is not the case. This value is also added to the margin.

- `margin` < extra length in patch dimension (Å) >
  Acceptable Values: positive decimal
  Default Value: 0.0
  Description: An internal tuning parameter used in determining the size of the cubes of space with which NAMD uses to partition the system. The value of this parameter will not change the physical results of the simulation. Unless you are very motivated to get the *very* best possible performance, just leave this value at the default.

- `pairlistMinProcs` < min procs for pairlists >
  Acceptable Values: positive integer
  Default Value: 1
  Description: Pairlists may consume a large amount of memory as atom counts, densities, and cutoff distances increase. Since this data is distributed across processors it is normally only problematic for small processor counts. Set pairlistMinProcs to the smallest number of processors on which the simulation can fit into memory when pairlists are used.

- `pairlistsPerCycle` < regenerate x times per cycle >
  Acceptable Values: positive integer
  Default Value: 2
  Description: Rather than only regenerating the pairlist at the beginning of a cycle, regenerate multiple times in order to better balance the costs of atom migration, pairlist generation, and larger pairlists.

- `outputPairlists` < how often to print warnings >
  Acceptable Values: non-negative integer
  Default Value: 0
  Description: If an atom moves further than the pairlist tolerance during a simulation (initially (pairlistdist - cutoff)/2 but refined during the run) any pairlists covering that atom are invalidated and temporary pairlists are used until the next full pairlist regeneration. All interactions are calculated correctly, but efficiency may be degraded. Enabling outputPairlists will summarize these pairlist violation warnings periodically during the run.

- `pairlistShrink` < tol *= (1 - x) on regeneration >
  Acceptable Values: non-negative decimal
  Default Value: 0.01
  Description: In order to maintain validity for the pairlist for an entire cycle, the pairlist tolerance (the distance an atom can move without causing the pairlist to be invalidated) is adjusted during the simulation. Every time pairlists are regenerated the tolerance is reduced by this fraction.

- `pairlistGrow` < tol *= (1 + x) on trigger >
  Acceptable Values: non-negative decimal
  Default Value: 0.01
  Description: In order to maintain validity for the pairlist for an entire cycle, the pairlist tolerance (the distance an atom can move without causing the pairlist to be invalidated) is adjusted during the simulation. Every time an atom exceeds a trigger criterion that is some fraction of the tolerance distance, the tolerance is increased by this fraction.

- `pairlistTrigger` < trigger is atom beyond (1 - x) * tol >
  Acceptable Values: non-negative decimal
  Default Value: 0.3
  Description: The goal of pairlist tolerance adjustment is to make pairlist invalidations rare while keeping the tolerance as small as possible for best performance. Rather than monitoring the (very rare) case where atoms actually move more than the tolerance distance, we reduce the trigger tolerance by this fraction. The tolerance is increased whenever the trigger tolerance is exceeded, as specified by pairlistGrow.

5.3.3 Basic dynamics

- `exclude` < exclusion policy to use >
  Acceptable Values: `none`, `1-2`, `1-3`, `1-4`, or `scaled1-4`
  Description: This parameter specifies which pairs of bonded atoms should be excluded from non-bonded interactions. With the value of `none`, no bonded pairs of atoms will be excluded. With the value of `1-2`, all atom pairs that are directly connected via a linear bond will be excluded. With the value of `1-3`, all `1-2` pairs will be excluded along with all pairs of atoms that are bonded to a common third atom (i.e., if atom A is bonded to atom B and atom B is bonded to atom C, then the atom pair A-C would be excluded). With the value of `1-4`, all `1-3` pairs will be excluded along with all pairs connected by a set of two bonds (i.e., if atom A is bonded to atom B, and atom B is bonded to atom C, and atom C is bonded to atom D, then the atom pair A-D would be excluded). With the value of `scaled1-4`, all `1-3` pairs are excluded and all pairs that match the `1-4` criteria are modified. The electrostatic interactions for such pairs are modified by the constant factor defined by `1-4scaling`. The van der Waals interactions are modified by using the special 1-4 parameters defined in the parameter files.

- `temperature` < initial temperature (K) >
  Acceptable Values: positive decimal
  Description: Initial temperature value for the system. Using this option will generate a random velocity distribution for the initial velocities for all the atoms such that the system is at the desired temperature. Either the `temperature` or the `velocities/binvelocities` option must be defined to determine an initial set of velocities. Both options cannot be used together.

- `COMmotion` < allow initial center of mass motion? >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: Specifies whether or not motion of the center of mass of the entire system is allowed. If this option is set to `no`, the initial velocities of the system will be adjusted to

remove center of mass motion of the system. Note that this does not preclude later center-of-mass motion due to external forces such as random noise in Langevin dynamics, boundary potentials, and harmonic restraints.

- `zeroMomentum` < remove center of mass drift due to PME >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: If enabled, the net momentum of the simulation and any resultant drift is removed before every full electrostatics step. This correction should conserve energy and have minimal impact on parallel scaling. This feature should only be used for simulations that would conserve momentum except for the slight errors in PME. (Features such as fixed atoms, harmonic restraints, steering forces, and Langevin dynamics do not conserve momentum; use in combination with these features should be considered experimental.) Since the momentum correction is delayed, enabling outputMomenta will show a slight nonzero linear momentum but there should be no center of mass drift.

- `dielectric` < dielectric constant for system >
  Acceptable Values: decimal ≥ 1.0
  Default Value: 1.0
  Description: Dielectric constant for the system. A value of 1.0 implies no modification of the electrostatic interactions. Any larger value will lessen the electrostatic forces acting in the system.

- `nonbondedScaling` < scaling factor for nonbonded forces >
  Acceptable Values: decimal ≥ 0.0
  Default Value: 1.0
  Description: Scaling factor for electrostatic and van der Waals forces. A value of 1.0 implies no modification of the interactions. Any smaller value will lessen the nonbonded forces acting in the system.

- `1-4scaling` < scaling factor for 1-4 interactions >
  Acceptable Values: $0 \leq$ decimal ≤ 1
  Default Value: 1.0
  Description: Scaling factor for 1-4 interactions. This factor is only used when the `exclude` parameter is set to `scaled1-4`. In this case, this factor is used to modify the electrostatic interactions between 1-4 atom pairs. If the `exclude` parameter is set to anything but `scaled1-4`, this parameter has no effect regardless of its value.

- `vdwGeometricSigma` < use geometric mean to combine L-J sigmas >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: Use geometric mean, as required by OPLS, rather than traditional arithmetic mean when combining Lennard-Jones sigma parameters for different atom types.

- `seed` < random number seed >
  Acceptable Values: positive integer
  Default Value: pseudo-random value based on current UNIX clock time
  Description: Number used to seed the random number generator if `temperature` or `langevin` is selected. This can be used so that consecutive simulations produce the same

results. If no value is specified, NAMD will choose a pseudo-random value based on the current UNIX clock time. The random number seed will be output during the simulation startup so that its value is known and can be reused for subsequent simulations. Note that if Langevin dynamics are used in a parallel simulation (i.e., a simulation using more than one processor) even using the same seed will *not* guarantee reproducible results.

- `rigidBonds` < controls if and how ShakeH is used >
  Acceptable Values: `none`, `water`, `all`
  Default Value: `none`
  Description: When `water` is selected, the hydrogen-oxygen and hydrogen-hydrogen distances in waters are constrained to the nominal length or angle given in the parameter file, making the molecules completely rigid. When `rigidBonds` is `all`, waters are made rigid as described above and the bond between each hydrogen and the (one) atom to which it is bonded is similarly constrained. For the default case `none`, no lengths are constrained.

- `rigidTolerance` < allowable bond-length error for ShakeH (Å) >
  Acceptable Values: positive decimal
  Default Value: 1.0e-8
  Description: The ShakeH algorithm is assumed to have converged when all constrained bonds differ from the nominal bond length by less than this amount.

- `rigidIterations` < maximum ShakeH iterations >
  Acceptable Values: positive integer
  Default Value: 100
  Description: The maximum number of iterations ShakeH will perform before giving up on constraining the bond lengths. If the bond lengths do not converge, a warning message is printed, and the atoms are left at the final value achieved by ShakeH. Although the default value is 100, convergence is usually reached after fewer than 10 iterations.

- `rigidDieOnError` < maximum ShakeH iterations >
  Acceptable Values: `on` or `off`
  Default Value: `on`
  Description: Exit and report an error if rigidTolerance is not achieved after rigidIterations.

- `useSettle` < Use SETTLE for waters. >
  Acceptable Values: `on` or `off`
  Default Value: `on`
  Description: If rigidBonds are enabled then use the non-iterative SETTLE algorithm to keep waters rigid rather than the slower SHAKE algorithm.

5.3.4 DPMTA parameters

DPMTA is no longer included in the released NAMD binaries. We recommend that you instead use PME with a periodic system because it conserves energy better, is more efficient, and is better parallelized. If you must have the fast multipole algorithm you may compile NAMD yourself.

These parameters control the options to DPMTA, an algorithm used to provide full electrostatic interactions. DPMTA is a modified version of the FMA (Fast Multipole Algorithm) and, unfortu-

nately, most of the parameters still refer to FMA rather than DPMTA for historical reasons. Don't be confused!

For a further description of how exactly full electrostatics are incorporated into NAMD, see Section 5.2. For a greater level of detail about DPMTA and the specific meaning of its options, see the DPMTA distribution which is available via anonymous FTP from the site `ftp.ee.duke.edu` in the directory `/pub/SciComp/src`.

- `FMA` < use full electrostatics? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not the DPMTA algorithm from Duke University should be used to compute the full electrostatic interactions. If set to `on`, DPMTA will be used with a multiple timestep integration scheme to provide full electrostatic interactions as detailed in Section 5.2. *DPMTA is no longer included in released binaries.*

- `FMALevels` < number of levels to use in multipole expansion >
  Acceptable Values: positive integer
  Default Value: 5
  Description: Number of levels to use for the multipole expansion. This parameter is only used if `FMA` is set to `on`. A value of 4 should be sufficient for systems with less than 10,000 atoms. A value of 5 or greater should be used for larger systems.

- `FMAMp` < number of multipole terms to use for FMA >
  Acceptable Values: positive integer
  Default Value: 8
  Description: Number of terms to use in the multipole expansion. This parameter is only used if `FMA` is set to `on`. If the `FMAFFT` is set to `on`, then this value must be a multiple of 4. The default value of 8 should be suitable for most applications.

- `FMAFFT` < use DPMTA FFT enhancement? >
  Acceptable Values: `on` or `off`
  Default Value: `on`
  Description: Specifies whether or not the DPMTA code should use the FFT enhancement feature. This parameter is only used if `FMA` is set to `on`. If `FMAFFT` is set to `on`, the value of `FMAMp` must be set to a multiple of 4. This feature offers substantial benefits only for values of `FMAMp` of 8 or greater. This feature will substantially increase the amount of memory used by DPMTA.

- `FMAtheta` < DPMTA theta parameter (radians) >
  Acceptable Values: decimal
  Default Value: 0.715
  Description: This parameter specifies the value of the theta parameter used in the DPMTA calculation. The default value is based on recommendations by the developers of the code.

- `FMAFFTBlock` < blocking factor for FMA FFT >
  Acceptable Values: positive integer
  Default Value: 4
  Description: The blocking factor for the FFT enhancement to DPMTA. This parameter

is only used if both `FMA` and `FMAFFT` are set to `on`. The default value of 4 should be suitable for most applications.

5.3.5 PME parameters

PME stands for Particle Mesh Ewald and is an efficient full electrostatics method for use with periodic boundary conditions. None of the parameters should affect energy conservation, although they may affect the accuracy of the results and momentum conservation.

- `PME` < Use particle mesh Ewald for electrostatics? >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: Turns on particle mesh Ewald.

- `PMETolerance` < PME direct space tolerance >
  Acceptable Values: positive decimal
  Default Value: 10^{-6}
  Description: Affects the value of the Ewald coefficient and the overall accuracy of the results.

- `PMEInterpOrder` < PME interpolation order >
  Acceptable Values: positive integer
  Default Value: 4 (cubic)
  Description: Charges are interpolated onto the grid and forces are interpolated off using this many points, equal to the order of the interpolation function plus one.

- `PMEGridSpacing` < maximum space between grid points >
  Acceptable Values: positive real
  Description: The grid spacing partially determines the accuracy and efficiency of PME. If any of the grid sizes below are not set, then PMEGridSpacing must be set (recommended value is 1.0 Å) and will be used to calculate them. If a grid size is set, then the grid spacing must be at least PMEGridSpacing (if set, or a very large default of 1.5).

- `PMEGridSizeX` < number of grid points in x dimension >
  Acceptable Values: positive integer
  Description: The grid size partially determines the accuracy and efficiency of PME. For speed, `PMEGridSizeX` should have only small integer factors (2, 3 and 5).

- `PMEGridSizeY` < number of grid points in y dimension >
  Acceptable Values: positive integer
  Description: The grid size partially determines the accuracy and efficiency of PME. For speed, `PMEGridSizeY` should have only small integer factors (2, 3 and 5).

- `PMEGridSizeZ` < number of grid points in z dimension >
  Acceptable Values: positive integer
  Description: The grid size partially determines the accuracy and efficiency of PME. For speed, `PMEGridSizeZ` should have only small integer factors (2, 3 and 5).

- `PMEProcessors` < processors for FFT and reciprocal sum >
  Acceptable Values: positive integer

Default Value: larger of x and y grid sizes up to all available processors
Description: For best performance on some systems and machines, it may be necessary to restrict the amount of parallelism used. Experiment with this parameter if your parallel performance is poor when PME is used.

- `FFTWEstimate` < Use estimates to optimize FFT? >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: Do not optimize FFT based on measurements, but on FFTW rules of thumb. This reduces startup time, but may affect performance.

- `FFTWUseWisdom` < Use FFTW wisdom archive file? >
  Acceptable Values: `yes` or `no`
  Default Value: `yes`
  Description: Try to reduce startup time when possible by reading FFTW "wisdom" from a file, and saving wisdom generated by performance measurements to the same file for future use. This will reduce startup time when running the same size PME grid on the same number of processors as a previous run using the same file.

- `FFTWWisdomFile` < name of file for FFTW wisdom archive >
  Acceptable Values: file name
  Default Value: FFTW_NAMD_*version_platform*.txt
  Description: File where FFTW wisdom is read and saved. If you only run on one platform this may be useful to reduce startup times for all runs. The default is likely sufficient, as it is version and platform specific.

- `useDPME` < Use old DPME code? >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: Switches to old DPME implementation of particle mesh Ewald. The new code is faster and allows non-orthogonal cells so you probably just want to leave this option turned off. If you set `cellOrigin` to something other than $(0, 0, 0)$ the energy may differ slightly between the old and new implementations. *DPME is no longer included in released binaries.*

5.3.6 Full direct parameters

The direct computation of electrostatics is not intended to be used during real calculations, but rather as a testing or comparison measure. Because of the $\mathcal{O}(N^2)$ computational complexity for performing direct calculations, this is *much* slower than using DPMTA or PME to compute full electrostatics for large systems. In the case of periodic boundary conditions, the nearest image convention is used rather than a full Ewald sum.

- `FullDirect` < calculate full electrostatics directly? >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: Specifies whether or not direct computation of full electrostatics should be performed.

5.3.7 Multiple timestep parameters

One of the areas of current research being studied using NAMD is the exploration of better methods for performing multiple timestep integration. Currently the only available method is the impulse-based Verlet-I or r-RESPA method which is stable for timesteps up to 4 fs for long-range electrostatic forces, 2 fs for short-range nonbonded forces, and 1 fs for bonded forces Setting `rigid all` (i.e., using SHAKE) increases these timesteps to 6 fs, 2 fs, and 2 fs respectively but eliminates bond motion for hydrogen. The mollified impulse method (MOLLY) reduces the resonance which limits the timesteps and thus increases these timesteps to 6 fs, 2 fs, and 1 fs while retaining all bond motion.

- `fullElectFrequency` < number of timesteps between full electrostatic evaluations >
  Acceptable Values: positive integer factor of `stepspercycle`
  Default Value: `nonbondedFreq`
  Description: This parameter specifies the number of timesteps between each full electrostatics evaluation. It is recommended that `fullElectFrequency` be chosen so that the product of `fullElectFrequency` and `timestep` does not exceed 4.0 unless `rigidBonds all` or `molly on` is specified, in which case the upper limit is perhaps doubled.

- `nonbondedFreq` < timesteps between nonbonded evaluation >
  Acceptable Values: positive integer factor of `fullElectFrequency`
  Default Value: 1
  Description: This parameter specifies how often short-range nonbonded interactions should be calculated. Setting `nonbondedFreq` between 1 and `fullElectFrequency` allows triple timestepping where, for example, one could evaluate bonded forces every 1 fs, short-range nonbonded forces every 2 fs, and long-range electrostatics every 4 fs.

- `MTSAlgorithm` < MTS algorithm to be used >
  Acceptable Values: `impulse/verletI` or `constant/naive`
  Default Value: `impulse`
  Description: Specifies the multiple timestep algorithm used to integrate the long and short range forces. `impulse/verletI` is the same as r-RESPA. `constant/naive` is the stale force extrapolation method.

- `longSplitting` < how should long and short range forces be split? >
  Acceptable Values: `xplor`, `c1`
  Default Value: `c1`
  Description: Specifies the method used to split electrostatic forces between long and short range potentials. The `xplor` option uses the X-PLOR shifting function, and the `c1` splitting uses the following C^1 continuous shifting function [16]:

  $SW(r_{ij}) = 0$ if $|\vec{r}_{ij}| > R_{off}$
  $SW(r_{ij}) = 1$ if $|\vec{r}_{ij}| \leq R_{on}$
  if $R_{off} > |\vec{r}_{ij}| \geq R_{on}$

  where

  R_{on} is a constant defined using the configuration value `switchdist`

  R_{off} is specified using the configuration value `cutoff`

- `molly` < use mollified impulse method (MOLLY)? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: This method eliminates the components of the long range electrostatic forces which contribute to resonance along bonds to hydrogen atoms, allowing a fullElectFrequency of 6 (vs. 4) with a 1 fs timestep without using `rigidBonds all`. You may use `rigidBonds water` but using `rigidBonds all` with MOLLY makes no sense since the degrees of freedom which MOLLY protects from resonance are already frozen.

- `mollyTolerance` < allowable error for MOLLY >
  Acceptable Values: positive decimal
  Default Value: 0.00001
  Description: Convergence criterion for MOLLY algorithm.

- `mollyIterations` < maximum MOLLY iterations >
  Acceptable Values: positive integer
  Default Value: 100
  Description: Maximum number of iterations for MOLLY algorithm.

6 Additional Simulation Parameters

6.1 Constraints and Restraints

6.1.1 Harmonic constraint parameters

The following describes the parameters for the harmonic constraints feature of NAMD. Actually, this feature should be referred to as harmonic restraints rather than constraints, but for historical reasons the terminology of harmonic constraints has been carried over from X-PLOR. This feature allows a harmonic restraining force to be applied to any set of atoms in the simulation.

- `constraints` < are constraints active? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not harmonic constraints are active. If it is set to `off`, then no harmonic constraints are computed. If it is set to `on`, then harmonic constraints are calculated using the values specified by the parameters `consref`, `conskfile`, `conskcol`, and `consexp`.

- `consexp` < exponent for harmonic constraint energy function >
  Acceptable Values: positive, even integer
  Default Value: 2
  Description: Exponent to be use in the harmonic constraint energy function. This value must be a positive integer, and only even values really make sense. This parameter is used only if `constraints` is set to `on`.

- `consref` < PDB file containing constraint reference positions >
  Acceptable Values: UNIX file name
  Description: PDB file to use for reference positions for harmonic constraints. Each atom that has an active constraint will be constrained about the position specified in this file.

- `conskfile` < PDB file containing force constant values >
  Acceptable Values: UNIX filename
  Description: PDB file to use for force constants for harmonic constraints.

- `conskcol` < column of PDB file containing force constant >
  Acceptable Values: `X`, `Y`, `Z`, `O`, or `B`
  Description: Column of the PDB file to use for the harmonic constraint force constant. This parameter may specify any of the floating point fields of the PDB file, either X, Y, Z, occupancy, or beta-coupling (temperature-coupling). Regardless of which column is used, a value of 0 indicates that the atom should not be constrained. Otherwise, the value specified is used as the force constant for that atom's restraining potential.

- `constraintScaling` < scaling factor for harmonic constraint energy function >
  Acceptable Values: positive
  Default Value: 1.0
  Description: The harmonic constraint energy function is multiplied by this parameter, making it possible to gradually turn off constraints during equilibration. This parameter is used only if `constraints` is set to `on`.

- `selectConstraints` < Restrain only selected Cartesian components of the coordinates? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: This option is useful to restrain the positions of atoms to a plane or a line in space. If active, this option will ensure that only selected Cartesian components of the coordinates are restrained. E.g.: Restraining the positions of atoms to their current z values with no restraints in x and y will allow the atoms to move in the x-y plane while retaining their original z-coordinate. Restraining the x and y values will lead to free motion only along the z coordinate.

- `selectConstrX` < Restrain X components of coordinates >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Restrain the Cartesian x components of the positions.

- `selectConstrY` < Restrain Y components of coordinates >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Restrain the Cartesian y components of the positions.

- `selectConstrZ` < Restrain Z components of coordinates >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Restrain the Cartesian z components of the positions.

6.1.2 Fixed atoms parameters

Atoms may be held fixed during a simulation. NAMD avoids calculating most interactions in which all affected atoms are fixed unless `fixedAtomsForces` is specified.

- `fixedAtoms` < are there fixed atoms? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not fixed atoms are present.

- `fixedAtomsForces` < are forces between fixed atoms calculated? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not forces between fixed atoms are calculated. This option is required to turn fixed atoms off in the middle of a simulation. These forces will affect the pressure calculation, and you should leave this option off when using constant pressure if the coordinates of the fixed atoms have not been minimized. The use of constant pressure with significant numbers of fixed atoms is not recommended.

- `fixedAtomsFile` < PDB file containing fixed atom parameters >
  Acceptable Values: UNIX filename
  Default Value: `coordinates`
  Description: PDB file to use for the fixed atom flags for each atom. If this parameter is not specified, then the PDB file specified by `coordinates` is used.

- `fixedAtomsCol` < column of PDB containing fixed atom parameters >
  Acceptable Values: `X`, `Y`, `Z`, `O`, or `B`
  Default Value: `O`
  Description: Column of the PDB file to use for the containing fixed atom parameters for each atom. The coefficients can be read from any floating point column of the PDB file. A value of 0 indicates that the atom is not fixed.

6.2 Energy Minimization

6.2.1 Conjugate gradient parameters

The default minimizer uses a sophisticated conjugate gradient and line search algorithm with much better performance than the older velocity quenching method. The method of conjugate gradients is used to select successive search directions (starting with the initial gradient) which eliminate repeated minimization along the same directions. Along each direction, a minimum is first bracketed (rigorously bounded) and then converged upon by either a golden section search, or, when possible, a quadratically convergent method using gradient information.

For most systems, it just works.

- `minimization` < Perform conjugate gradient energy minimization? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Turns efficient energy minimization `on` or `off`.

- `minTinyStep` < first initial step for line minimizer >
  Acceptable Values: positive decimal
  Default Value: 1.0e-6
  Description: If your minimization is immediately unstable, make this smaller.

- `minBabyStep` < max initial step for line minimizer >
  Acceptable Values: positive decimal
  Default Value: 1.0e-2
  Description: If your minimization becomes unstable later, make this smaller.

- `minLineGoal` < gradient reduction factor for line minimizer >
  Acceptable Values: positive decimal
  Default Value: 1.0e-4
  Description: Varying this might improve conjugate gradient performance.

6.2.2 Velocity quenching parameters

You can perform energy minimization using a simple quenching scheme. While this algorithm is not the most rapidly convergent, it is sufficient for most applications. There are only two parameters for minimization: one to activate minimization and another to specify the maximum movement of any atom.

- `velocityQuenching` < Perform old-style energy minimization? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Turns slow energy minimization `on` or `off`.

- `maximumMove` < maximum distance an atom can move during each step (Å) >
  Acceptable Values: positive decimal
  Default Value: 0.75 × `cutoff/stepsPerCycle`
  Description: Maximum distance that an atom can move during any single timestep of minimization. This is to insure that atoms do not go flying off into space during the first few timesteps when the largest energy conflicts are resolved.

6.3 Temperature Control and Equilibration

6.3.1 Langevin dynamics parameters

NAMD is capable of performing Langevin dynamics, where additional damping and random forces are introduced to the system. This capability is based on that implemented in X-PLOR which is detailed in the X-PLOR *User's Manual* [7], although a different integrator is used.

- `langevin` < use Langevin dynamics? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not Langevin dynamics active. If set to `on`, then the parameter `langevinTemp` must be set and the parameters `langevinFile` and `langevinCol` can optionally be set to control the behavior of this feature.

- `langevinTemp` < temperature for Langevin calculations (K) >
  Acceptable Values: positive decimal
  Description: Temperature to which atoms affected by Langevin dynamics will be adjusted. This temperature will be roughly maintained across the affected atoms through the addition of friction and random forces.

- `langevinDamping` < damping coefficient for Langevin dynamics (1/ps) >
  Acceptable Values: positive decimal
  Default Value: per-atom values from PDB file
  Description: Langevin coupling coefficient to be applied to all atoms (unless `langevinHydrogen` is `off`, in which case only non-hydrogen atoms are affected). If not given, a PDB file is used to obtain coefficients for each atom (see `langevinFile` and `langevinCol` below).

- `langevinHydrogen` < Apply Langevin dynamics to hydrogen atoms? >
  Acceptable Values: `on` or `off`
  Default Value: `on`
  Description: If `langevinDamping` is set then setting `langevinHydrogen` to `off` will turn off Langevin dynamics for hydrogen atoms. This parameter has no effect if Langevin coupling coefficients are read from a PDB file.

- `langevinFile` < PDB file containing Langevin parameters >
  Acceptable Values: UNIX filename
  Default Value: `coordinates`
  Description: PDB file to use for the Langevin coupling coefficients for each atom. If this parameter is not specified, then the PDB file specified by `coordinates` is used.

- `langevinCol` < column of PDB from which to read coefficients >
  Acceptable Values: `X`, `Y`, `Z`, `O`, or `B`

Default Value: `O`
Description: Column of the PDB file to use for the Langevin coupling coefficients for each atom. The coefficients can be read from any floating point column of the PDB file. A value of 0 indicates that the atom will remain unaffected.

6.3.2 Temperature coupling parameters

NAMD is capable of performing temperature coupling, in which forces are added or reduced to simulate the coupling of the system to a heat bath of a specified temperature. This capability is based on that implemented in X-PLOR which is detailed in the X-PLOR *User's Manual* [7].

- `tCouple` < perform temperature coupling? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not temperature coupling is active. If set to `on`, then the parameter `tCoupleTemp` must be set and the parameters `tCoupleFile` and `tCoupleCol` can optionally be set to control the behavior of this feature.

- `tCoupleTemp` < temperature for heat bath (K) >
  Acceptable Values: positive decimal
  Description: Temperature to which atoms affected by temperature coupling will be adjusted. This temperature will be roughly maintained across the affected atoms through the addition of forces.

- `tCoupleFile` < PDB file with tCouple parameters >
  Acceptable Values: UNIX filename
  Default Value: `coordinates`
  Description: PDB file to use for the temperature coupling coefficient for each atom. If this parameter is not specified, then the PDB file specified by `coordinates` is used.

- `tCoupleCol` < column of PDB from which to read coefficients >
  Acceptable Values: `X`, `Y`, `Z`, `O`, or `B`
  Default Value: `O`
  Description: Column of the PDB file to use for the temperature coupling coefficient for each atom. This value can be read from any floating point column of the PDB file. A value of 0 indicates that the atom will remain unaffected.

6.3.3 Temperature rescaling parameters

NAMD allows equilibration of a system by means of temperature rescaling. Using this method, all of the velocities in the system are periodically rescaled so that the entire system is set to the desired temperature. The following parameters specify how often and to what temperature this rescaling is performed.

- `rescaleFreq` < number of timesteps between temperature rescaling >
  Acceptable Values: positive integer
  Description: The equilibration feature of NAMD is activated by specifying the number of timesteps between each temperature rescaling. If this value is given, then the `rescaleTemp` parameter must also be given to specify the target temperature.

- `rescaleTemp` < temperature for equilibration (K) >
  Acceptable Values: positive decimal
  Description: The temperature to which all velocities will be rescaled every `rescaleFreq` timesteps. This parameter is valid only if `rescaleFreq` has been set.

6.3.4 Temperature reassignment parameters

NAMD allows equilibration of a system by means of temperature reassignment. Using this method, all of the velocities in the system are periodically reassigned so that the entire system is set to the desired temperature. The following parameters specify how often and to what temperature this reassignment is performed.

- `reassignFreq` < number of timesteps between temperature reassignment >
  Acceptable Values: positive integer
  Description: The equilibration feature of NAMD is activated by specifying the number of timesteps between each temperature reassignment. If this value is given, then the `reassignTemp` parameter must also be given to specify the target temperature.

- `reassignTemp` < temperature for equilibration (K) >
  Acceptable Values: positive decimal
  Default Value: `temperature` if set, otherwise none
  Description: The temperature to which all velocities will be reassigned every `reassignFreq` timesteps. This parameter is valid only if `reassignFreq` has been set.

- `reassignIncr` < temperature increment for equilibration (K) >
  Acceptable Values: decimal
  Default Value: 0
  Description: In order to allow simulated annealing or other slow heating/cooling protocols, `reassignIncr` will be added to `reassignTemp` after each reassignment. (Reassignment is carried out at the first timestep.) The `reassignHold` parameter may be set to limit the final temperature. This parameter is valid only if `reassignFreq` has been set.

- `reassignHold` < holding temperature for equilibration (K) >
  Acceptable Values: positive decimal
  Description: The final temperature for reassignment when `reassignIncr` is set; `reassignTemp` will be held at this value once it has been reached. This parameter is valid only if `reassignIncr` has been set.

6.4 Boundary Conditions

In addition to periodic boundary conditions, NAMD provides spherical and cylindrical boundary potentials to contain atoms in a given volume. To apply more general boundary potentials written in Tcl, use `tclBC` as described in Sec. 6.6.9.

6.4.1 Spherical harmonic boundary conditions

NAMD provides spherical harmonic boundary conditions. These boundary conditions can consist of a single potential or a combination of two potentials. The following parameters are used to define these boundary conditions.

- `sphericalBC` < use spherical boundary conditions? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not spherical boundary conditions are to be applied to the system. If set to `on`, then `sphericalBCCenter`, `sphericalBCr1` and `sphericalBCk1` must be defined, and `sphericalBCexp1`, `sphericalBCr2`, `sphericalBCk2`, and `sphericalBCexp2` can optionally be defined.

- `sphericalBCCenter` < center of sphere (Å) >
  Acceptable Values: position
  Description: Location around which sphere is centered.

- `sphericalBCr1` < radius for first boundary condition (Å) >
  Acceptable Values: positive decimal
  Description: Distance at which the first potential of the boundary conditions takes effect. This distance is a radius from the center.

- `sphericalBCk1` < force constant for first potential >
  Acceptable Values: non-zero decimal
  Description: Force constant for the first harmonic potential. A positive value will push atoms toward the center, and a negative value will pull atoms away from the center.

- `sphericalBCexp1` < exponent for first potential >
  Acceptable Values: positive, even integer
  Default Value: 2
  Description: Exponent for first boundary potential. The only likely values to use are 2 and 4.

- `sphericalBCr2` < radius for second boundary condition (Å) >
  Acceptable Values: positive decimal
  Description: Distance at which the second potential of the boundary conditions takes effect. This distance is a radius from the center. If this parameter is defined, then `sperical BCk2` must also be defined.

- `sphericalBCk2` < force constant for second potential >
  Acceptable Values: non-zero decimal
  Description: Force constant for the second harmonic potential. A positive value will push atoms toward the center, and a negative value will pull atoms away from the center.

- `sphericalBCexp2` < exponent for second potential >
  Acceptable Values: positive, even integer
  Default Value: 2
  Description: Exponent for second boundary potential. The only likely values to use are 2 and 4.

6.4.2 Cylindrical harmonic boundary conditions

NAMD provides cylindrical harmonic boundary conditions. These boundary conditions can consist of a single potential or a combination of two potentials. The following parameters are used to define these boundary conditions.

- `cylindricalBC` < use cylindrical boundary conditions? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not cylindrical boundary conditions are to be applied to the system. If set to `on`, then `cylindricalBCCenter`, `cylindricalBCr1`, `cylindricalBCl1` and `cylindricalBCk1` must be defined, and `cylindricalBCAxis`, `cylindricalBCexp1`, `cylindricalBCr2`, `cylindricalBCl2`, `cylindricalBCk2`, and `cylindricalBCexp2` can optionally be defined.

- `cylindricalBCCenter` < center of cylinder (Å) >
  Acceptable Values: position
  Description: Location around which cylinder is centered.

- `cylindricalBCAxis` < axis of cylinder (Å) >
  Acceptable Values: `x`, `y`, or `z`
  Description: Axis along which cylinder is aligned.

- `cylindricalBCr1` < radius for first boundary condition (Å) >
  Acceptable Values: positive decimal
  Description: Distance at which the first potential of the boundary conditions takes effect along the non-axis plane of the cylinder.

- `cylindricalBCl1` < distance along cylinder axis for first boundary condition (Å) >
  Acceptable Values: positive decimal
  Description: Distance at which the first potential of the boundary conditions takes effect along the cylinder axis.

- `cylindricalBCk1` < force constant for first potential >
  Acceptable Values: non-zero decimal
  Description: Force constant for the first harmonic potential. A positive value will push atoms toward the center, and a negative value will pull atoms away from the center.

- `cylindricalBCexp1` < exponent for first potential >
  Acceptable Values: positive, even integer
  Default Value: 2
  Description: Exponent for first boundary potential. The only likely values to use are 2 and 4.

- `cylindricalBCr2` < radius for second boundary condition (Å) >
  Acceptable Values: positive decimal
  Description: Distance at which the second potential of the boundary conditions takes effect along the non-axis plane of the cylinder. If this parameter is defined, then `cylindricalBCl2` and `sphericalBCk2` must also be defined.

- `cylindricalBCl2` < radius for second boundary condition (Å) >
  Acceptable Values: positive decimal
  Description: Distance at which the second potential of the boundary conditions takes effect along the cylinder axis. If this parameter is defined, then `cylindricalBCr2` and `sphericalBCk2` must also be defined.

- `cylindricalBCk2` < force constant for second potential >
  Acceptable Values: non-zero decimal
  Description: Force constant for the second harmonic potential. A positive value will push atoms toward the center, and a negative value will pull atoms away from the center.

- `cylindricalBCexp2` < exponent for second potential >
  Acceptable Values: positive, even integer
  Default Value: 2
  Description: Exponent for second boundary potential. The only likely values to use are 2 and 4.

6.4.3 Periodic boundary conditions

NAMD provides periodic boundary conditions in 1, 2 or 3 dimensions. The following parameters are used to define these boundary conditions.

- `cellBasisVector1` < basis vector for periodic boundaries (Å) >
  Acceptable Values: vector
  Default Value: 0 0 0
  Description: Specifies a basis vector for periodic boundary conditions.

- `cellBasisVector2` < basis vector for periodic boundaries (Å) >
  Acceptable Values: vector
  Default Value: 0 0 0
  Description: Specifies a basis vector for periodic boundary conditions.

- `cellBasisVector3` < basis vector for periodic boundaries (Å) >
  Acceptable Values: vector
  Default Value: 0 0 0
  Description: Specifies a basis vector for periodic boundary conditions.

- `cellOrigin` < center of periodic cell (Å) >
  Acceptable Values: position
  Default Value: 0 0 0
  Description: When position rescaling is used to control pressure, this location will remain constant. Also used as the center of the cell for wrapped output coordinates.

- `extendedSystem` < XSC file to read cell parameters from >
  Acceptable Values: file name
  Description: In addition to .coor and .vel output files, NAMD generates a .xsc (eXtended System Configuration) file which contains the periodic cell parameters and extended system variables, such as the strain rate in constant pressure simulations. Periodic cell parameters will be read from this file if this option is present, ignoring the above parameters.

- `XSTfile` < XST file to write cell trajectory to >
  Acceptable Values: file name
  Description: NAMD can also generate a .xst (eXtended System Trajectory) file which contains a record of the periodic cell parameters and extended system variables during the simulation. If `XSTfile` is defined, then `XSTfreq` must also be defined.

- `XSTfreq` < how often to append state to XST file >
  Acceptable Values: positive integer
  Description: Like the `DCDfreq` option, controls how often the extended system configuration will be appended to the XST file.

- `wrapWater` < wrap water coordinates around periodic boundaries? >
  Acceptable Values: on or off
  Default Value: off
  Description: Coordinates are normally output relative to the way they were read in. Hence, if part of a molecule crosses a periodic boundary it is not translated to the other side of the cell on output. This option alters this behavior for water molecules only.

- `wrapAll` < wrap all coordinates around periodic boundaries? >
  Acceptable Values: on or off
  Default Value: off
  Description: Coordinates are normally output relative to the way they were read in. Hence, if part of a molecule crosses a periodic boundary it is not translated to the other side of the cell on output. This option alters this behavior for all contiguous clusters of bonded atoms.

- `wrapNearest` < use nearest image to cell origin when wrapping coordinates? >
  Acceptable Values: on or off
  Default Value: off
  Description: Coordinates are normally wrapped to the diagonal unit cell centered on the origin. This option, combined with `wrapWater` or `wrapAll`, wraps coordinates to the nearest image to the origin, providing hexagonal or other cell shapes.

6.5 Pressure Control

Constant pressure simulation (and pressure calculation) require periodic boundary conditions. Pressure is controlled by dynamically adjusting the size of the unit cell and rescaling all atomic coordinates (other than those of fixed atoms) during the simulation.

Pressure values in NAMD output are in bar. PRESSURE is the pressure calculated based on individual atoms, while GPRESSURE incorporates hydrogen atoms into the heavier atoms to which they are bonded, producing smaller fluctuations. The TEMPAVG, PRESSAVG, and GPRESSAVG are the average of temperature and pressure values since the previous ENERGY output; for the first step in the simulation they will be identical to TEMP, PRESSURE, and GPRESSURE.

The phenomenological pressure of bulk matter reflects averaging in both space and time of the sum of a large positive term (the kinetic pressure, nRT/V), and a large cancelling negative term (the static pressure). The instantaneous pressure of a simulation cell as simulated by NAMD will have mean square fluctuations (according to David Case quoting Section 114 of *Statistical Physics* by Landau and Lifshitz) of $kT/(V\beta)$, where β is the compressibility, which is RMS of roughly 100 bar for a 10,000 atom biomolecular system. Much larger fluctuations are regularly observed in practice.

The instantaneous pressure for a biomolecular system is well defined for "internal" forces that are based on particular periodic images of the interacting atoms, conserve momentum, and are translationally invariant. When dealing with externally applied forces such as harmonic constraints, fixed atoms, and various steering forces, NAMD bases its pressure calculation on the relative

positions of the affected atoms in the input coordinates and assumes that the net force will average to zero over time. For time periods during with the net force is non-zero, the calculated pressure fluctuations will include a term proportional to the distance to the affected from the user-defined cell origin. A good way to observe these effects and to confirm that pressure for external forces is handled reasonably is to run a constant volume cutoff simulation in a cell that is larger than the molecular system by at least the cutoff distance; the pressure for this isolated system should average to zero over time.

Because NAMD's impluse-basd multiple timestepping system alters the balance between bonded and non-bonded forces from every timestep to an average balance over two steps, the calculated pressure on even and odd steps will be different. The PRESSAVG and GPRESSAVG fields provide the average over the non-printed intermediate steps. If you print energies on every timestep you will see the effect clearly in the PRESSURE field.

The following options affect all pressure control methods.

- `useGroupPressure` < group or atomic quantities >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: Pressure can be calculated using either the atomic virial and kinetic energy (the default) or a hydrogen-group based pseudo-molecular virial and kinetic energy. The latter fluctuates less and is required in conjunction with rigidBonds (SHAKE).

- `useFlexibleCell` < anisotropic cell fluctuations >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: NAMD allows the three orthogonal dimensions of the periodic cell to fluctuate independently when this option is enabled.

- `useConstantRatio` < constant shape in first two cell dimensions >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: When enabled, NAMD keeps the ratio of the unit cell in the x-y plane constant while allowing fluctuations along all axes. The `useFlexibleCell` option is required for this option.

- `useConstantArea` < constant area and normal pressure conditions >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: When enabled, NAMD keeps the dimension of the unit cell in the x-y plane constant while allowing fluctuations along the z axis. This is not currently implemented in Berendsen's method.

6.5.1 Berendsen pressure bath coupling

NAMD provides constant pressure simulation using Berendsen's method. The following parameters are used to define the algorithm.

- `BerendsenPressure` < use Berendsen pressure bath coupling? >
  Acceptable Values: `on` or `off`

Default Value: `off`
Description: Specifies whether or not Berendsen pressure bath coupling is active. If set to `on`, then the parameters `BerendsenPressureTarget`, `BerendsenPressureCompressibility` and `BerendsenPressureRelaxationTime` must be set and the parameter `BerendsenPressureFreq` can optionally be set to control the behavior of this feature.

- `BerendsenPressureTarget` < target pressure (bar) >
Acceptable Values: positive decimal
Description: Specifies target pressure for Berendsen's method. A typical value would be 1.01325 bar, atmospheric pressure at sea level.

- `BerendsenPressureCompressibility` < compressibility (bar^{-1}) >
Acceptable Values: positive decimal
Description: Specifies compressibility for Berendsen's method. A typical value would be 4.57E-5 bar^{-1}, corresponding to liquid water. The higher the compressibility, the more volume will be adjusted for a given pressure difference. The compressibility and the relaxation time appear only as a ratio in the dynamics, so a larger compressibility is equivalent to a smaller relaxation time.

- `BerendsenPressureRelaxationTime` < relaxation time (fs) >
Acceptable Values: positive decimal
Description: Specifies relaxation time for Berendsen's method. If the instantaneous pressure did not fluctuate randomly during a simulation and the compressibility estimate was exact then the inital pressure would decay exponentially to the target pressure with this time constant. Having a longer relaxation time results in more averaging over pressure measurements and hence smaller fluctuations in the cell volume. A reasonable choice for relaxation time would be 100 fs. The compressibility and the relaxation time appear only as a ratio in the dynamics, so a larger compressibility is equivalent to a smaller relaxation time.

- `BerendsenPressureFreq` < how often to rescale positions >
Acceptable Values: positive multiple of `nonbondedFrequency` and `fullElectFrequency`
Default Value: `nonbondedFrequency` or `fullElectFrequency` if used
Description: Specifies number of timesteps between position rescalings for Berendsen's method. Primarily to deal with multiple timestepping integrators, but also to reduce cell volume fluctuations, cell rescalings can occur on a longer interval. This could reasonably be between 1 and 20 timesteps, but the relaxation time should be at least ten times larger.

6.5.2 Nosé-Hoover Langevin piston pressure control

NAMD provides constant pressure simulation using a modified Nosé-Hoover method in which Langevin dynamics is used to control fluctuations in the barostat. This method should be combined with a method of temperature control, such as Langevin dynamics, in order to simulate the NPT ensemble.

The Langevin piston Nose-Hoover method in NAMD is a combination of the Nose-Hoover constant pressure method as described in GJ Martyna, DJ Tobias and ML Klein, "Constant pressure molecular dynamics algorithms", J. Chem. Phys 101(5), 1994, with piston fluctuation control implemented using Langevin dynamics as in SE Feller, Y Zhang, RW Pastor and BR Brooks, "Constant pressure molecular dynamics simulation: The Langevin piston method", J. Chem. Phys. 103(11), 1995.

The equations of motion are:

$$\begin{aligned} r' &= p/m + e'r \\ p' &= F - e'p - gp + R \\ V' &= 3Ve' \\ e'' &= 3V/W(P - P_0) - g_e e' + R_e/W \\ W &= 3N\tau^2 kT \\ < R^2 > &= 2mgkT/h \\ \tau &= \text{oscillationperiod} \\ < R_e^2 > &= 2Wg_e kT/h \end{aligned}$$

Here, W is the mass of piston, R is noise on atoms, and R_e is the noise on the piston.

The user specifies the desired pressure, oscillation and decay times of the piston, and temperature of the piston. The compressibility of the system is not required. In addition, the user specifies the damping coefficients and temperature of the atoms for Langevin dynamics.

The following parameters are used to define the algorithm.

- `LangevinPiston` < use Langevin piston pressure control? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not Langevin piston pressure control is active. If set to `on`, then the parameters `LangevinPistonTarget`, `LangevinPistonPeriod`, `LangevinPistonDecay` and `LangevinPistonTemp` must be set.

- `LangevinPistonTarget` < target pressure (bar) >
  Acceptable Values: positive decimal
  Description: Specifies target pressure for Langevin piston method. A typical value would be 1.01325 bar, atmospheric pressure at sea level.

- `LangevinPistonPeriod` < oscillation period (fs) >
  Acceptable Values: positive decimal
  Description: Specifies barostat oscillation time scale for Langevin piston method. If the instantaneous pressure did not fluctuate randomly during a simulation and the decay time was infinite (no friction) then the cell volume would oscillate with this angular period. Having a longer period results in more averaging over pressure measurements and hence slower fluctuations in the cell volume. A reasonable choice for the piston period would be 200 fs.

- `LangevinPistonDecay` < damping time scale (fs) >
  Acceptable Values: positive decimal
  Description: Specifies barostat damping time scale for Langevin piston method. A value larger than the piston period would result in underdamped dynamics (decaying ringing in the cell volume) while a smaller value approaches exponential decay as in Berendsen's method above. A smaller value also corresponds to larger random forces with increased coupling to the Langevin temperature bath. Typically this would be chosen equal to or smaller than the piston period, such as 100 fs.

- `LangevinPistonTemp` < noise temperature (K) >
  Acceptable Values: positive decimal

Description: Specifies barostat noise temperature for Langevin piston method. This should be set equal to the target temperature for the chosen method of temperature control.

- `SurfaceTensionTarget` < Surface tension target (dyn/cm) >
  Acceptable Values: decimal
  Default Value: 0.0
  Description: Specifies surface tension target. Must be used with `useFlexibleCell` and periodic boundary conditions. The pressure specified in `LangevinPistonTarget` becomes the pressure along the z axis, and surface tension is applied in the x-y plane.

- `StrainRate` < initial strain rate >
  Acceptable Values: decimal triple (x y z)
  Default Value: 0. 0. 0.
  Description: Optionally specifies the initial strain rate for pressure control. Is overridden by value read from file specified with `extendedSystem`. There is typically no reason to set this parameter.

- `ExcludeFromPressure` < Should some atoms be excluded from pressure rescaling? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not to exclude some atoms from pressure rescaling. The coordinates and velocites of such atoms are not rescaled during constant pressure simulations, though they do contribute to the virial calculation. May be useful for membrane protein simulation. EXPERIMENTAL.

- `ExcludeFromPressureFile` < File specifying excluded atoms >
  Acceptable Values: PDB file
  Default Value: coordinates file
  Description: PDB file with one column specifying which atoms to exclude from pressure rescaling. Specify 1 for excluded and 0 for not excluded.

- `ExcludeFromPressureCol` < Column in PDB file for specifying excluded atoms >
  Acceptable Values: O, B, X, Y, or Z
  Default Value: O
  Description: Specifies which column of the pdb file to check for excluded atoms.

6.6 Applied Forces and Analysis

There are several ways to apply external forces to simulations with NAMD. These are described below.

6.6.1 Constant Forces

NAMD provides the ability to apply constant forces to some atoms. There are two parameters that control this feature.

- `constantForce` < Apply constant forces? >
  Acceptable Values: yes or no
  Default Value: no
  Description: Specifies whether or not constant forces are applied.

- `consForceFile` < PDB file containing forces to be applied >
  Acceptable Values: UNIX filename
  Description: The X, Y, Z and occupancy (O) fields of this file are read to determine the constant force vector of each atom, which is (X,Y,Z)*O, in unit of kcal/(mol*Å). The occupancy (O) serves as a scaling factor, which could expand the range of the force applied. (One may be unable to record very large or very small numbers in the data fields of a PDB file due to limited space). Zero forces are ignored.

  Specifying `consforcefile` is optional; constant forces may be specifed or updated between runs by using the consForceConfig command.

- `consForceScaling` < Scaling factor for constant forces >
  Acceptable Values: decimal
  Default Value: 1.0
  Description: Scaling factor by which constant forces are multiplied. May be changed between run commands.

6.6.2 External Electric Field

NAMD provides the ability to apply a constant electric field to the molecular system being simulated. Energy due to the external field will be reported in the MISC column and may be discontinuous in simulations using periodic boundary conditions if, for example, a charged hydrogen group moves outside of the central cell. There are two parameters that control this feature.

- `eFieldOn` < apply electric field? >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: Specifies whether or not an electric field is applied.

- `eField` < electric field vector >
  Acceptable Values: vector of decimals (x y z)
  Description: Vector which describes the electric field to be applied. Units are kcal/(mol Å e), which is natural for simulations. This parameter may be changed between `run` commands, allowing a square wave or other approximate wave form to be applied.

6.6.3 Moving Constraints

Moving constraints feature works in conjunction with the Harmonic Constraints (see an appropriate section of the User's guide). The reference positions of all constraints will move according to

$$\vec{r}(t) \;=\; \vec{r}_0 \;+\; \vec{v}t\,. \tag{1}$$

A velocity vector $\vec{v}$ (`movingConsVel`) needs to be specified.

The way the moving constraints work is that the moving reference position is calculated every integration time step using Eq. 1, where $\vec{v}$ is in Å/timestep, and t is the current timestep (i.e., `firstTimestep` plus however many timesteps have passed since the beginning of NAMD run). Therefore, one should be careful when restarting simulations to appropriately update the `firstTimestep` parameter in the NAMD configuration file or the reference position specified in the reference PDB file.

NOTE: NAMD actually calculates the constraints potential with $U = k(x - x_0)^d$ and the force with $F = dk(x - x_0)$, where d is the exponent `consexp`. The result is that if one specifies some value for the force constant k in the PDB file, effectively, the force constant is $2k$ in calculations. This caveat was removed in SMD feature.

The following parameters describe the parameters for the moving harmonic constraint feature of NAMD.

- `movingConstraints` < Are moving constraints active >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Should moving restraints be applied to the system. If set to `on`, then `movingConsVel` must be defined. May not be used with `rotConstraints`.

- `movingConsVel` < Velocity of the reference position movement >
  Acceptable Values: vector in Å/timestep
  Description: The velocity of the reference position movement. Gives both absolute value and direction

6.6.4 Rotating Constraints

The constraints parameters are specified in the same manner as for usual (static) harmonic constraints. The reference positions of all constrained atoms are then rotated with a given angular velocity about a given axis. If the force constant of the constraints is sufficiently large, the constrained atoms will follow their reference positions.

A rotation matrix M about the axis unit vector v is calculated every timestep for the angle of rotation corresponding to the current timestep. angle $= \Omega t$, where Ω is the angular velocity of rotation.

From now on, all quantities are 3D vectors, except the matrix M and the force constant K.

The current reference position R is calculated from the initial reference position R_0 (at $t = 0$), $R = M(R_0 - P) + P$, where P is the pivot point.

Coordinates of point N can be found as $N = P + ((R - P) \cdot v)v$. Normal from the atom pos to the axis is, similarly, normal $= (P + ((X - P) \cdot v)v) - X$ The force is, as usual, $F = K(R - X)$; This is the force applied to the atom in NAMD (see below). NAMD does not know anything about the torque applied. However, the torque applied to the atom can be calculated as a vector product torque $= F \times normal$ Finally, the torque applied to the atom with respect to the axis is the projection of the torque on the axis, i.e., $torque_{proj} = torque \cdot v$

If there are atoms that have to be constrained, but not moved, this implementation is not suitable, because it will move *all* reference positions.

Only one of the moving and rotating constraints can be used at a time.

Using very soft springs for rotating constraints leads to the system lagging behind the reference positions, and then the force is applied along a direction different from the "ideal" direction along the circular path.

Pulling on N atoms at the same time with a spring of stiffness K amounts to pulling on the whole system by a spring of stiffness NK, so the overall behavior of the system is as if you are pulling with a very stiff spring if N is large.

In both moving and rotating constraints the force constant that you specify in the constraints pdb file is multiplied by 2 for the force calculation, i.e., if you specified $K = 0.5$ kcal/mol/Å^2 in the

pdb file, the force actually calculated is $F = 2K(R - X) = 1$ kcal/mol/Å^2 $(R - X)$. SMD feature of namd2 does the calculation without multiplication of the force constant specified in the config file by 2.

- `rotConstraints` < Are rotating constraints active >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Should rotating restraints be applied to the system. If set to `on`, then `rotConsAxis`, `rotConsPivot` and `rotConsVel` must be defined. May not be used with `movingConstraints`.

- `rotConsAxis` < Axis of rotation >
  Acceptable Values: vector (may be unnormalized)
  Description: Axis of rotation. Can be any vector. It gets normalized before use. If the vector is 0, no rotation will be performed, but the calculations will still be done.

- `rotConsPivot` < Pivot point of rotation >
  Acceptable Values: position in Å
  Description: Pivot point of rotation. The rotation axis vector only gives the direction of the axis. Pivot point places the axis in space, so that the axis goes through the pivot point.

- `rotConsVel` < Angular velocity of rotation >
  Acceptable Values: rate in degrees per timestep
  Description: Angular velocity of rotation, degrees/timestep.

6.6.5 Targeted Molecular Dynamics (TMD)

In TMD, subset of atoms in the simulation is guided towards a final 'target' structure by means of steering forces. At each timestep, the RMS distance between the current coordinates and the target structure is computed (after first aligning the target structure to the current coordinates). The force on each atom is given by the gradient of the potential

$$U_{TMD} = \frac{1}{2}\frac{k}{N}\left[RMS(t) - RMS^*(t)\right]^2 \tag{2}$$

where $RMS(t)$ is the instantaneous best-fit RMS distance of the current coordinates from the target coordinates, and $RMS^*(t)$ evolves linearly from the initial RMSD at the first TMD step to the final RMSD at the last TMD step. The spring constant k is scaled down by the number N of targeted atoms.

- `TMD` < Is TMD active >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Should TMD steering forces be applied to the system. If TMD is enabled, `TMDk`, `TMDFile`, and `TMDLastStep` must be defined in the input file as well.

- `TMDk` < Elastic constant for TMD forces >
  Acceptable Values: Positive value in $kcal/mol/$Å^2.
  Description: The value of k in Eq. 2. A value of 200 seems to work well in many cases.

- `TMDOutputFreq` < How often to print TMD output >
  Acceptable Values: Positive integer
  Default Value: 1
  Description: TMD output consists of lines of the form `TMD ts targetRMS currentRMS` where `ts` is the timestep, `targetRMS` is the target RMSD at that timestep, and `currentRMS` is the actual RMSD.

- `TMDFile` < File for TMD information >
  Acceptable Values: Path to PDB file
  Description: Target atoms are those whose occupancy (O) is nonzero in the TMD PDB file. The file must contain the same number of atoms as the structure file. The coordinates for the target structure are also taken from the targeted atoms in this file. Non-targeted atoms are ignored.

- `TMDFirstStep` < first TMD timestep >
  Acceptable Values: Positive integer
  Default Value: 0
  Description:

- `TMDLastStep` < last TMD timestep >
  Acceptable Values: Positive integer
  Description: TMD forces are applied only between `TMDFirstStep` and `TMDLastStep`. The target RMSD evolves linearly in time from the initial to the final target value.

- `TMDInitialRMSD` < target RMSD at first TMD step >
  Acceptable Values: Non-negative value in Å
  Default Value: from coordinates
  Description: In order to perform TMD calculations that involve restarting a previous NAMD run, be sure to specify `TMDInitialRMSD` with the same value in each NAMD input file, and use the NAMD parameter `firstTimestep` in the continuation runs so that the target RMSD continues from where the last run left off.

- `TMDFinalRMSD` < target RMSD at last TMD step >
  Acceptable Values: Non-negative value in Å
  Default Value: 0
  Description: If no `TMDInitialRMSD` is given, the initial RMSD will be calculated at the first TMD step. `TMDFinalRMSD` may be less than or greater than `TMDInitialRMSD`, depending on whether the system is to be steered towards or away from a target structure, respectively. Forces are applied only if $RMS(t)$ is betwween `TMDInitialRMSD` and $RMS*(t)$; in other words, only if the current RMSD fails to keep pace with the target value.

6.6.6 Steered Molecular Dynamics (SMD)

The SMD feature is independent from the harmonic constraints, although it follows the same ideas. In both SMD and harmonic constraints, one specifies a PDB file which indicates which atoms are 'tagged' as constrained. The PDB file also gives initial coordinates for the constraint positions. One also specifies such parameters as the force constant(s) for the constraints, and the velocity with which the constraints move.

There are two major differences between SMD and harmonic constraints:

- In harmonic constraints, each tagged atom is harmonically constrained to a reference point which moves with constant velocity. In SMD, it is the *center of mass* of the tagged atoms which is constrained to move with constant velocity.
- In harmonic constraints, each tagged atom is constrained in all three spatial dimensions. In SMD, tagged atoms are constrained *only along the constraint direction*.

The center of mass of the SMD atoms will be harmonically constrained with force constant k (`SMDk`) to move with velocity v (`SMDVel`) in the direction $\vec{n}$ (`SMDDir`). SMD thus results in the following potential being applied to the system:

$$U(\vec{r}_1, \vec{r}_2, ..., t) \; = \; \frac{1}{2} k \left[vt - (\vec{R}(t) - \vec{R}_0) \cdot \vec{n} \right]^2 . \tag{3}$$

Here, $t \equiv N_{ts} dt$ where N_{ts} is the number of elapsed timesteps in the simulation and dt is the size of the timestep in femtoseconds. Also, $\vec{R}(t)$ is the current center of mass of the SMD atoms and R_0 is the initial center of mass as defined by the coordinates in `SMDFile`. Vector $\vec{n}$ is normalized by NAMD before being used.

Output NAMD provides output of the current SMD data. The frequency of output is specified by the `SMDOutputFreq` parameter in the configuration file. Every `SMDOutputFreq` timesteps NAMD will print the current timestep, current position of the center of mass of the restrained atoms, and the current force applied to the center of mass (in piconewtons, pN). The output line starts with word `SMD`

Parameters The following parameters describe the parameters for the SMD feature of NAMD.

- `SMD` < Are SMD features active >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Should SMD harmonic constraint be applied to the system. If set to `on`, then `SMDk`, `SMDFile`, `SMDVel`, and `SMDDir` must be defined. Specifying `SMDOutputFreq` is optional.
- `SMDFile` < SMD constraint reference position >
  Acceptable Values: UNIX filename
  Description: File to use for the initial reference position for the SMD harmonic constraints. All atoms in this PDB file with a nonzero value in the *occupancy* column will be tagged as SMD atoms. The coordinates of the tagged SMD atoms will be used to calculate the initial center of mass. During the simulation, this center of mass will move with velocity `SMDVel` in the direction `SMDDir`. The actual atom order in this PDB file must match that in the structure or coordinate file, since the atom number field in this PDB file will be ignored.
- `SMDk` < force constant to use in SMD simulation >
  Acceptable Values: positive real
  Description: SMD harmonic constraint force constant. Must be specified in kcal/mol/Å^2. The conversion factor is 1 kcal/mol = 69.479 pN Å.
- `SMDVel` < Velocity of the SMD reference position movement >
  Acceptable Values: nonzero real, Å/timestep
  Description: The velocity of the SMD center of mass movement. Gives the absolute value.

- `SMDDir` < Direction of the SMD center of mass movement >
  Acceptable Values: non-zero vector
  Description: The direction of the SMD reference position movement. The vector does not have to be normalized, it is normalized by NAMD before being used.

- `SMDOutputFreq` < frequency of SMD output >
  Acceptable Values: positive integer
  Default Value: 1
  Description: The frequency in timesteps with which the current SMD data values are printed out.

6.6.7 Interactive Molecular Dynamics (IMD)

NAMD now works directly with VMD to allow you to view and interactively steer your simulation. With IMD enabled, you can connect to NAMD at any time during the simulation to view the current state of the system or perform interactive steering.

- `IMDon` < is IMD active? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not to listen for an IMD connection.

- `IMDport` < port number to expect a connection on >
  Acceptable Values: positive integer
  Description: This is a free port number on the machine that node 0 is running on. This number will have to be entered into VMD.

- `IMDfreq` < timesteps between sending coordinates >
  Acceptable Values: positive integer
  Description: This allows coordinates to be sent less often, which may increase NAMD performance or be necessary due to a slow network.

- `IMDwait` < wait for an IMD connection? >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: If `no`, NAMD will proceed with calculations whether a connection is present or not. If `yes`, NAMD will pause at startup until a connection is made, and pause when the connection is lost.

- `IMDignore` < ignore interactive steering forces >
  Acceptable Values: `yes` or `no`
  Default Value: `no`
  Description: If `yes`, NAMD will ignore any steering forces generated by VMD to allow a simulation to be monitored without the possibility of perturbing it.

6.6.8 Tcl Forces and Analysis

NAMD provides a limited Tcl scripting interface designed for applying forces and performing on-the-fly analysis. This interface is efficient if only a few coordinates, either of individual atoms or

centers of mass of groups of atoms, are needed. In addition, information must be requested one timestep in advance. To apply forces individually to a potentially large number of atoms, use `tclBC` instead as described in Sec. 6.6.9. The following configuration parameters are used to enable the Tcl interface:

- `tclForces` < is Tcl interface active? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not Tcl interface is active. If it is set to `off`, then no Tcl code is executed. If it is set to `on`, then Tcl code specified in `tclForcesScript` parameters is executed.

- `tclForcesScript` < input for Tcl interface >
  Acceptable Values: file or {script}
  Description: Must contain either the name of a Tcl script file or the script itself between { and } (may include multiple lines). This parameter may occur multiple times and scripts will be executed in order of appearance. The script(s) should perform any required initialization on the Tcl interpreter, including requesting data needed during the first timestep, and define a procedure `calcforces { }` to be called every timestep.

At this point only low-level commands are defined. In the future this list will be expanded. Current commands are:

- `print <anything>`
  This command should be used instead of `puts` to display output. For example, "`print Hello World`".

- `atomid <segname> <resid> <atomname>`
  Determines atomid of an atom from its segment, residue, and name. For example, "`atomid br 2 N`".

- `addatom <atomid>`
  Request coordinates of this atom for next force evaluation, and the calculated total force on this atom for current force evaluation. Request remains in effect until `clearconfig` is called. For example, "`addatom 4`" or "`addatom [atomid br 2 N]`".

- `addgroup <atomid list>`
  Request center of mass coordinates of this group for next force evaluation. Returns a group ID which is of the form `gN` where `N` is a small integer. This group ID may then be used to find coordinates and apply forces just like a regular atom ID. Aggregate forces may then be applied to the group as whole. Request remains in effect until `clearconfig` is called. For example, "`set groupid [addgroup { 14 10 12 }]`".

- `clearconfig`
  Clears the current list of requested atoms. After `clearconfig`, calls to `addatom` and `addgroup` can be used to build a new configuration.

- `getstep`
  Returns the current step number.

- `loadcoords <varname>`
  Loads requested atom and group coordinates (in Å) into a local array. `loadcoords` should only be called from within the `calcforces` procedure. For example, "`loadcoords p`" and "`print $p(4)`".

- `loadforces <varname>`
  Loads the forces applied in the previous timestep (in kcal mol^{-1} $Å^{-1}$) into a local array. `loadforces` should only be called from within the `calcforces` procedure. For example, "`loadforces f`" and "`print $f(4)`".

- `loadtotalforces <varname>`
  Loads the total forces on each requested atom in the previous time step (in kcal $mol^{-1}Å^{-1}$) into a local array. The total force also includes external forces. Note that the "`loadforces`" command returns external forces applied by the user. Therefore, one can subtract the external force on an atom from the total force on this atom to get the pure force arising from the simulation system.

- `loadmasses <varname>`
  Loads requested atom and group masses (in amu) into a local array. `loadmasses` should only be called from within the `calcforces` procedure. For example, "`loadcoords m`" and "`print $m(4)`".

- `addforce <atomid|groupid> <force vector>`
  Applies force (in kcal mol^{-1} $Å^{-1}$) to atom or group. `addforce` should only be called from within the `calcforces` procedure. For example, "`addforce $groupid { 1. 0. 2. }`".

- `addenergy <energy (kcal/mol)>`
  This command adds the specified energy to the MISC column (and hence the total energy) in the energy output. For normal runs, the command does not affect the simulation trajectory at all, and only has an artificial effect on its energy output. However, it can indeed affect minimizations.

With the commands above and the functionality of the Tcl language, one should be able to perform any on-the-fly analysis and manipulation. To make it easier to perform certain tasks, some Tcl routines are provided below.

Several vector routines (`vecadd`, `vecsub`, `vecscale`) from the VMD Tcl interface are defined. Please refer to VMD manual for their usage.

The following routines take atom coordinates as input, and return some geometry parameters (bond, angle, dihedral).

- `getbond <coor1> <coor2>`
  Returns the length of the bond between the two atoms. Actually the return value is simply the distance between the two coordinates. "coor1" and "coor2" are coordinates of the atoms.

- `getangle <coor1> <coor2> <coor3>`
  Returns the angle (from 0 to 180) defined by the three atoms. "coor1", "coor2" and "coor3" are coordinates of the atoms.

- `getdihedral <coor1> <coor2> <coor3> <coor4>`
  Returns the dihedral (from -180 to 180) defined by the four atoms. "coor1", "coor2", "coor3" and "coor4" are coordinates of the atoms.

The following routines calculate the derivatives (gradients) of some geometry parameters (angle, dihedral).

- `anglegrad <coor1> <coor2> <coor3>`
  An angle defined by three atoms is a function of their coordinates: $\theta\left(\vec{r_1}, \vec{r_2}, \vec{r_3}\right)$ (in radian). This command takes the coordinates of the three atoms as input, and returns a list of $\{\frac{\partial\theta}{\partial\vec{r_1}}\ \frac{\partial\theta}{\partial\vec{r_2}}\ \frac{\partial\theta}{\partial\vec{r_3}}\}$. Each element of the list is a 3-D vector in the form of a Tcl list.
- `dihedralgrad <coor1> <coor2> <coor3> <coor4>`
  A dihedral defined by four atoms is a function of their coordinates: $\phi\left(\vec{r_1}, \vec{r_2}, \vec{r_3}, \vec{r_4}\right)$ (in radian). This command takes the coordinates of the four atoms as input, and returns a list of $\{\frac{\partial\phi}{\partial\vec{r_1}}\ \frac{\partial\phi}{\partial\vec{r_2}}\ \frac{\partial\phi}{\partial\vec{r_3}}\ \frac{\partial\phi}{\partial\vec{r_4}}\}$. Each element of the list is a 3-D vector in the form of a Tcl list.

As an example, here's a script which applies a harmonic constraint (reference position being 0) to a dihedral. Note that the "addenergy" line is not really necessary – it simply adds the calculated constraining energy to the MISC column, which is displayed in the energy output.

```
tclForcesScript {
  # The IDs of the four atoms defining the dihedral
  set aid1 112
  set aid2 123
  set aid3 117
  set aid4 115

  # The "spring constant" for the harmonic constraint
  set k 3.0

  addatom $aid1
  addatom $aid2
  addatom $aid3
  addatom $aid4

  set PI 3.1416

  proc calcforces {} {

    global aid1 aid2 aid3 aid4 k PI

    loadcoords p

    # Calculate the current dihedral
    set phi [getdihedral $p($aid1) $p($aid2) $p($aid3) $p($aid4)]
    # Change to radian
    set phi [expr $phi*$PI/180]

    # (optional) Add this constraining energy to "MISC" in the energy output
    addenergy [expr $k*$phi*$phi/2.0]
```

```
    # Calculate the "force" along the dihedral according to the harmonic constraint
    set force [expr -$k*$phi]

    # Calculate the gradients
    foreach {g1 g2 g3 g4} [dihedralgrad $p($aid1) $p($aid2) $p($aid3) $p($aid4)] {}

    # The force to be applied on each atom is proportional to its
    # corresponding gradient
    addforce $aid1 [vecscale $g1 $force]
    addforce $aid2 [vecscale $g2 $force]
    addforce $aid3 [vecscale $g3 $force]
    addforce $aid4 [vecscale $g4 $force]
  }
}
```

6.6.9 Tcl Boundary Forces

While the `tclForces` interface described above is very flexible, it is only efficient for applying forces to a small number of pre-selected atoms. Applying forces individually to a potentially large number of atoms, such as applying boundary conditions, is much more efficient with the `tclBC` facility described below.

- `tclBC` < are Tcl boundary forces active? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not Tcl interface is active. If it is set to `off`, then no Tcl code is executed. If it is set to `on`, then Tcl code specified in the `tclBCScript` parameter is executed.

- `tclBCScript` < input for Tcl interface >
  Acceptable Values: {script}
  Description: Must contain the script itself between { and } (may include multiple lines). This parameter may occur only once. The script(s) should perform any required initialization on the Tcl interpreter and define a procedure `calcforces <step> <unique> [args...]` to be called every timestep.

- `tclBCArgs` < extra args for tclBC calcforces command >
  Acceptable Values: {args...}
  Description: The string (or Tcl list) provided by this option is appended to the tclBC calcforces command arguments. This parameter may appear multiple times during a run in order to alter the parameters of the boundary potential function.

The script provided in `tclBCScript` and the `calcforces` procedure it defines are executed in multiple Tcl interpreters, one for every processor that owns patches. These `tclBC` interpreters do not share state with the Tcl interpreter used for `tclForces` or config file parsing. The `calcforces` procedure is passed as arguments the current timestep, a "unique" flag which is non-zero for exactly one Tcl interpreter in the simulation (that on the processor of patch zero), and any arguments

provided to the most recent `tclBCArgs` option. The "unique" flag is useful to limit printing of messages, since the command is invoked on multiple processors.

The `print`, `vecadd`, `vecsub`, `vecscale`, `getbond`, `getangle`, `getdihedral`, `anglegrad`, and `dihedralgrad` commands described under `tclForces` are available at all times.

The `wrapmode <mode>` command, available in the `tclBCScript` or the `calcforces` procedure, determines how coordinates obtained in the calcforces procedure are wrapped around periodic boundaries. The options are:

- `patch`, (default) the position in NAMD's internal patch data structure, requires no extra calculation and is almost the same as `cell`
- `input`, the position corresponding to the input files of the simulation
- `cell`, the equivalent position in the unit cell centered on the `cellOrigin`
- `nearest`, the equivalent position nearest to the `cellOrigin`

The following commands are available from within the `calcforces` procedure:

- `nextatom`
  Sets the internal counter to a new atom and return 1, or return 0 if all atoms have been processed (this may even happen the first call). This should be called as the condition of a while loop, i.e., `while {[nextatom]} { ... }` to iterate over all atoms. One one atom may be accessed at a time.
- `dropatom`
  Excludes the current atom from future iterations on this processor until `cleardrops` is called. Use this to eliminate extra work when an atom will not be needed for future force calculations. If the atom migrates to another processor it may reappear, so this call should be used only as an optimization.
- `cleardrops`
  All available atoms will be iterated over by `nextatom` as if `dropatom` had never been called.
- `getcoord`
  Returns a list {x y z} of the position of the current atom wrapped in the periodic cell (if there is one) in the current wrapping mode as specified by `wrapmode`.
- `getcell`
  Returns a list of 1–4 vectors containing the cell origin (center) and as many basis vectors as exist, i.e., `{{ox oy oz} {ax ay az} {bx by bz} {cx cy cz}}`. It is more efficient to set the wrapping mode than to do periodic image calculations in Tcl.
- `getmass`
  Returns the mass of the current atom.
- `getcharge`
  Returns the charge of the current atom.
- `getid`
  Returns the 1-based ID of the current atom.

- `addforce {<fx> <fy> <fz>}`
  Adds the specified force to the current atom for this step.

- `addenergy <energy>`
  Adds potential energy to the BOUNDARY column of NAMD output.

As an example, these spherical boundary condition forces:

```
sphericalBC         on
sphericalBCcenter   0.0,0.0,0.0
sphericalBCr1       48
sphericalBCk1       10
sphericalBCexp1     2
```

Are replicated in the following script:

```
tclBC on
tclBCScript {
  proc veclen2 {v1} {
    foreach {x1 y1 z1} $v1 { break }
    return [expr $x1*$x1 + $y1*$y1 + $z1*$z1]
  }

  # wrapmode input
  # wrapmode cell
  # wrapmode nearest
  # wrapmode patch ;# the default

  proc calcforces {step unique R K} {
    if { $step % 20 == 0 } {
      cleardrops
      # if $unique { print "clearing dropped atom list at step $step" }
    }
    set R [expr 1.*$R]
    set R2 [expr $R*$R]
    set tol 2.0
    set cut2 [expr ($R-$tol)*($R-$tol)]

    while {[nextatom]} {
      # addenergy 1 ; # monitor how many atoms are checked
      set rvec [getcoord]
      set r2 [veclen2 $rvec]
      if { $r2 < $cut2 } {
        dropatom
        continue
      }
      if { $r2 > $R2 } {
        # addenergy 1 ; # monitor how many atoms are affected
```

```
        set r [expr sqrt($r2)]
        addenergy [expr $K*($r - $R)*($r - $R)]
        addforce [vecscale $rvec [expr -2.*$K*($r-$R)/$r]]
      }
    }
  }
}

tclBCArgs {48.0 10.0}
```

6.6.10 External Program Forces

This feature allows an external program to be called to calculate forces at every force evaluation, taking all atom coordinates as input.

- `extForces` < Apply external program forces? >
  Acceptable Values: yes or no
  Default Value: no
  Description: Specifies whether or not external program forces are applied.

- `extForcesCommand` < Force calculation command >
  Acceptable Values: UNIX shell command
  Description: This string is the argument to the system() function at every forces evaluation and should read coordinates from the file specified by extCoordFilename and write forces to the file specified by extForceFilename.

- `extCoordFilename` < Temporary coordinate file >
  Acceptable Values: UNIX filename
  Description: Atom coordinates are written to this file, which should be read by the extForcesCommand. The format is one line of "atomid charge x y z" for every atom followed by three lines with the periodic cell basis vectors "a.x a.y a.z", "b.x b.y b.z", and "c.x c.y c.z". The atomid starts at 1 (not 0). For best performance the file should be in /tmp and not on a network-mounted filesystem.

- `extForceFilename` < Temporary force file >
  Acceptable Values: UNIX filename
  Description: Atom forces are read from this file after extForcesCommand in run. The format is one line of "atomid replace fx fy fz" for every atom followed by the energy on a line by itself and then, optionally, three lines of the virial "v.xx v.xy v.xz", "v.yx v.yy v.yz", "v.zx v.zy v.zz" where, e.g., v.xy = - fx * y for a non-periodic force. The atomid starts at 1 (not 0) and all atoms must be present and in order. The energy is added to the MISC output field. The replace flag should be 1 if the external program force should replace the forces calculated by NAMD for that atom and 0 if the forces should be added. For best performance the file should be in /tmp and not on a network-mounted filesystem.

6.7 Free Energy of Conformational Change Calculations

NAMD incorporates methods for performing free energy of conformational change perturbation calculations. The system is efficient if only a few coordinates, either of individual atoms or centers

of mass of groups of atoms, are needed. The following configuration parameters are used to enable free energy perturbation:

- `freeEnergy` < is free energy perturbation active? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not free energy perturbation is active. If it is set to `off`, then no free energy perturbation is performed. If it is set to `on`, then the free energy perturbation calculation specified in `freeEnergyConfig` parameters is executed.

- `freeEnergyConfig` < free energy perturbation script >
  Acceptable Values: file or {script}
  Description: Must contain either the name of a free energy perturbation script file or the script itself between { and } (may include multiple lines). This parameter may occur multiple times and scripts will be executed in order of appearance. The format of the free energy perturbation script is described below.

The following sections describe the format of the free energy perturbation script.

6.7.1 User-Supplied Conformational Restraints

These restraints extend the scope of the available restraints beyond that provided by the harmonic position restraints. Each restraint is imposed with a potential energy term, whose form depends on the type of the restraint.

Fixed Restraints

Position restraint (1 atom): force constant K_f, and reference position $\overrightarrow{r_{ref}}$

$$E = (K_f/2)\left(|\overrightarrow{r_i} - \overrightarrow{r_{ref}}|\right)^2$$

Stretch restraint (2 atoms): force constant K_f, and reference distance d_{ref}

$$E = (K_f/2)\left(d_i - d_{ref}\right)^2$$

Bend restraint (3 atoms): force constant K_f, and reference angle θ_{ref}

$$E = (K_f/2)\left(\theta_i - \theta_{ref}\right)^2$$

Torsion restraint (4 atoms): energy barrier E_0, and reference angle χ_{ref}

$$E = (E_0/2)\left\{1 - \cos\left(\chi_i - \chi_{ref}\right)\right\}$$

Forcing restraints

Position restraint (1 atom): force constant K_f, and two reference positions $\overrightarrow{r_0}$ and $\overrightarrow{r_1}$

$$E = (K_f/2)\left(|\overrightarrow{r_i} - \overrightarrow{r_{ref}}|\right)^2$$
$$\overrightarrow{r_{ref}} = \lambda\overrightarrow{r_1} + (1-\lambda)\ \overrightarrow{r_0}$$

Stretch restraint (2 atoms): force constant K_f, and two reference distances d_0 and d_1

$$E = (K_f/2)\left(d_i - d_{ref}\right)^2$$
$$d_{ref} = d_1 + (1-\lambda)\, d_0$$

Bend restraint (3 atoms): force constant K_f, and two reference angles θ_0 and θ_1

$$E = (K_f/2)\left(\theta_i - \theta_{ref}\right)^2$$
$$\theta_{ref} = \lambda\theta_1 + (1-\lambda)\,\theta_0$$

Torsion restraint (4 atoms): energy barrier E_0, and two reference angles χ_0 and χ_1

$$E = (E_0/2)\left\{1 - \cos\left(\chi_i - \chi_{ref}\right)\right\}$$
$$\chi_{ref} = \lambda\chi_1 + (1-\lambda)\,\chi_0$$

The forcing restraints depend on the coupling parameter, λ, specified in a conformational forcing calculation. For example, the restraint distance, d_{ref}, depends on λ, and as λ changes two atoms or centers-of-mass are forced closer together or further apart. In this case $K_f = K_{f,0}$, the value supplied at input.

Alternatively, the value of K_f may depend upon the coupling parameter λ according to:
$K_f = K_{f,0}\lambda$

Bounds

Position bound (1 atom): Force constant K_f, reference position $\overrightarrow{r_{ref}}$, and upper or lower reference distance, d_{ref}

Upper bound:

$$E = (K_f/2)\,(d_i - d_{ref})^2 \text{ for } d_i > d_{ref}, \text{ else } E = 0.$$

Lower bound:

$$E = (K_f/2)\,(d_i - d_{ref})^2 \text{ for } d_i < d_{ref}, \text{ else } E = 0.$$

$$d_i^2 = (|\overrightarrow{r_i} - \overrightarrow{r_{ref}}|)^2$$

Distance bound (2 atoms): Force constant K_f, and upper or lower reference distance, d_{ref}

Upper bound:

$$E = (K_f/2)\,(d_{ij} - d_{ref})^2 \text{ for } d_{ij} > d_{ref}, \text{ else } E = 0.$$

Lower bound:

$$E = (K_f/2)\,(d_{ij} - d_{ref})^2 \text{ for } d_{ij} < d_{ref}, \text{ else } E = 0.$$

Angle bound (3 atoms): Force constant K_f, and upper or lower reference angle, θ_{ref}

Upper bound:

$$E = (K_f/2)\,(\theta - \theta_{ref})^2 \text{ for } \theta > \theta_{ref}, \text{ else } E = 0.$$

Lower bound:

$$E = (K_f/2)\,(\theta - \theta_{ref})^2 \text{ for } \theta < \theta_{ref}, \text{ else } E = 0.$$

Torsion bound (4 atoms): An upper and lower bound must be provided together. Energy gap E_0, lower AND upper reference angles, χ_1 and χ_2, and angle interval, $\Delta\chi$.

$$\begin{array}{llll} \chi_1 & < \chi & < \chi_2: & E = 0 \\ (\chi_1 - \Delta\chi) & < \chi & < \chi_1: & E = (G/2)\,\{1 - \cos(\chi - \chi_1)\} \\ \chi_2 & < \chi & (\chi_2 + \Delta\chi): & E = (G/2)\,\{1 - \cos(\chi - \chi_2)\} \\ (\chi_2 + \Delta\chi) & < \chi & (\chi_1 - \Delta\chi + 2\pi): & E = G \end{array}$$

$$G = E_0/\{1 - \cos(\Delta\chi)\}$$

Bounds may be used in pairs, to set a lower and upper bound. Torsional bounds always are defined in pairs.

6.7.2 Free Energy Calculations

Conformational forcing / Potential of mean force

In conformational forcing calculations, structural parameters such as atomic positions, interatomic distances, and dihedral angles are forced to change by application of changing restraint potentials. For example, the distance between two atoms can be restrained by a potential to a

mean distance that is varied during the calculation. The free energy change (or potential of mean force, pmf) for the process can be estimated during the simulation.

The potential is made to depend on a coupling parameter, λ, whose value changes during the simulation. In potential of mean force calculations, the reference value of the restraint potential depends on λ. Alternately, the force constant for the restraint potential may change in proportion to the coupling parameter. Such a calculation gives the value of a restraint free energy, i.e., the free energy change of the system due to imposition of the restraint potential.

Methods for computing the free energy

With conformational forcing (or with molecular transformation calculations) one obtains a free energy difference for a process that is forced on the system by changing the potential energy function that determines the dynamics of the system. One always makes the changing potential depend on a coupling parameter, λ. By convention, λ can have values only in the range from 0 to 1, and a value of $\lambda = 0$ corresponds to one defined state and a value of $\lambda = 1$ corresponds to the other defined state. Intermediate values of λ correspond to intermediate states; in the case of conformational forcing calculations these intermediate states are physically realizable, but in the case of molecular transformation calculations they are not.

The value of λ is changed during the simulation. In the first method provided here, the change in λ is stepwise, while in the second method it is virtually continuous.

Multi-configurational thermodynamic integration (MCTI).

In MCTI one accumulates $\langle \partial U/\partial\lambda \rangle$ at several values of λ, and from these averages estimates the integral

$$-\Delta A = \int \langle \partial U/\partial\lambda \rangle \, d\lambda$$

With this method, the precision of each $\langle \partial U/\partial\lambda \rangle$ can be estimated from the fluctuations of the time series of $\partial U/\partial\lambda$.

Slow growth.

In slow growth, λ is incremented by $\delta\lambda = \pm 1/N_{step}$ after each dynamics integration time-step, and the pmf is estimated as

$$-\Delta A = \Sigma \, (\partial U/\partial\lambda) \, \delta\lambda$$

Typically, slow growth is done in cycles of: equilibration at $\lambda = 0$, change to $\lambda = 1$, equilibration at $\lambda = 1$, change to $\lambda = 0$. It is usual to estimate the precision of slow growth simulations from the results of successive cycles.

6.7.3 Options for Conformational Restraints

User-supplied restraint and bounds specifications

```
urestraint {
  n * (restraint or bound specification)          // see below
}
```

Restraint Specifications (not coupled to pmf calculations)

posi	ATOM	kf = KF	ref = (X Y Z)
dist	2 x ATOM	kf = KF	ref = D
angle	3 x ATOM	kf = KF	ref = A
dihe	4 x ATOM	barr = B	ref = A

Bound Specifications (not coupled to pmf calculations)

posi bound	ATOM	kf = KF	[low = (X Y Z D) or hi = (X Y Z D)]
dist bound	2 x ATOM	kf = KF	[low = D or hi = D]
angle bound	3 x ATOM	kf = KF	[low = A or hi = A]
dihe bound	4 x ATOM	gap = E	low = A0 hi = A1 delta = A2

Forcing Restraint Specifications (coupled to pmf calculations)

posi pmf	ATOM	kf=KF	low = (X0 Y0 Z0) hi = (X1 Y1 Z1)
dist pmf	2 x ATOM	kf=KF	low = D0 hi = D1
angle pmf	3 x ATOM	kf=KF	low = A0 hi = A1
dihe pmf	4 x ATOM	barr=B	low = A0 hi = A1

Units

Input item	Units
E, B	kcal/mol
X, Y, Z, D	
A	degrees
K_f	kcal/(mol ^{2}) or kcal/(mol rad^2)

6.7.4 Options for ATOM Specification

The designation ATOM, above, stands for one of the following forms:

A single atom
(segname, resnum, atomname)
Example: (insulin, 10, ca)

All atoms of a single residue
(segname, resnum)
Example: (insulin, 10)

A list of atoms
group { (segname, resnum, atomname), (segname, resnum, atomname), ... }
Example: group { (insulin, 10, ca), (insulin, 10, cb), (insulin, 11, cg) }

All atoms in a list of residues
group { (segname, resnum), (segname, resnum), ... }
Example: group { (insulin, 10), (insulin, 12), (insulin, 14) }

All atoms in a range of residues
group { (segname, resnum) to (segname, resnum) }
Example: group { (insulin, 10) to (insulin, 12) }

One or more atomnames in a list of residues
group { atomname: (segname, resnum), (segname, resnum), ... }
group { (atomname, atomname, ...): (segname, resnum), (segname, resnum), ... }
Examples: group { ca: (insulin, 10), (insulin, 12), (insulin, 14) }
group { (ca, cb, cg): (insulin, 10), (insulin, 12), (insulin, 14) }
group { (ca, cb): (insulin, 10), (insulin, 12) cg: (insulin, 11), (insulin, 12) }

Note: Within a group, atomname is in effect until a new atomname is used, or the keyword all is used. atomname will not carry over from group to group. This note applies to the paragraph below.

One or more atomnames in a range of residues

group { atomname: (segname, resnum) to (segname, resnum) }
group { (atomname, atomname, ...): (segname, resnum) to (segname, resnum) }
Examples: group { ca: (insulin, 10) to (insulin, 14) }
group { (ca, cb, cg): (insulin, 10) to (insulin, 12) }
group { (ca, cb): (insulin, 10) to (insulin, 12) all: (insulin, 13) }

6.7.5 Options for Potential of Mean Force Calculation

The pmf and mcti blocks, below, are used to simultaneously control all forcing restraints specified in urestraint above. These blocks are performed consecutively, in the order they appear in the config file. The pmf block is used to either a) smoothly vary λ from 0 $\rightarrow$1 or 1 $\rightarrow$0, or b) set lambda. The mcti block is used to vary λ from 0 $\rightarrow$1 or 1 $\rightarrow$0 in steps, so that λ is fixed while $dU/d\lambda$ is accumulated.

Lamba control for slow growth

pmf {
task = [up, down, stop, grow, fade, or nogrow]
time = T [fs, ps, or ns] (default = ps)
lambda = Y (value of λ; only needed for stop and nogrow)
lambdat = Z (value of λ_t; only needed for grow, fade, and nogrow) (default = 0)
print = P [fs, ps, or ns] or noprint (default = ps)
}

up, down, stop:	λ is applied to the reference values.
grow, fade, nogrow:	λ is applied to K_f. A fixed value, λ_t, is used to determine the ref. values.
up, grow:	λ changes from 0 $\rightarrow$1. (no value of λ is required)
down, fade:	λ changes from 1 $\rightarrow$0. (no value of λ is required)
stop, nogrow:	dU/dλ is accumulated (for single point MCTI)

Lambda control for automated MCTI

mcti {
task = [stepup, stepdown, stepgrow, or stepfade]
equiltime = T1 [fs, ps, or ns] (default = ps)
accumtime = T2 [fs, ps, or ns] (default = ps)
numsteps = N
lambdat = Z (value of λ_t; only needed for stepgrow, and stepfade) (default = 0)
print = P [fs, ps, or ns] or noprint (default = ps)
}

stepup, stepdown:	λ is applied to the reference values.
stepgrow, stepfade:	λ is applied to K_f. A fixed value, λ_t, is used to determine the ref. values.
stepup, stepgrow:	λ changes from 0 $\rightarrow$1. (no value of λ is required)
stepdown, stepfade:	λ changes from 1 $\rightarrow$0. (no value of λ is required)

For each task, λ changes in steps of (1.0/N) from 0 $\rightarrow$1 or 1 $\rightarrow$0. At each step, no data is accumulated for the initial period T1, then dU/dλ is accumulated for T2. Therefore, the total duration of an mcti block is (T1+T2) x N.

6.7.6 Examples

Fixed restraints

```
// 1. restrain the position of the ca atom of residue 0.
// 2. restrain the distance between the ca's of residues 0 and 10 to 5.2Å
// 3. restrain the angle between the ca's of residues 0-10-20 to 90^o .
// 4. restrain the dihedral angle between the ca's of residues 0-10-20-30 to 180^o .
// 5. restrain the angle between the centers-of-mass of residues 0-10-20 to 90^o .
urestraint {
 posi (insulin, 0, ca) kf=20 ref=(10, 11, 11)
 dist (insulin, 0, ca) (insulin, 10, ca) kf=20 ref=5.2
 angle (insulin, 0, ca) (insulin, 10, ca) (insulin, 20, ca) kf=20 ref=90
 dihe (insulin, 0, ca) (insulin, 10, ca) (insulin, 20, ca) (insulin, 30, ca) barr=20 ref=180
 angle (insulin, 0) (insulin, 10) (insulin, 20) kf=20 ref=90
}
```

```
// 1.    restrain the center of mass of three atoms of residue 0.
// 2.    restrain the distance between (the COM of 3 atoms of residue 0) to (the COM of 3 atoms of residue 10).
// 3.    restrain the dihedral angle of (10,11,12)-(15,16,17,18)-(20,22)-(30,31,32,34,35) to 90^o
//       ( (ca of 10 to 12), (ca, cb, cg of 15 to 18), (all atoms of 20 and 22), (ca of 30, 31, 32, 34, all atoms of 35) ).
urestraint {
 posi group {(insulin, 0, ca), (insulin, 0, cb), (insulin, 0, cg)} kf=20 ref=(10, 11, 11)
   dist   group {(insulin, 0, ca), (insulin, 0, cb), (insulin, 0, cg)}
          group {(insulin, 10, ca), (insulin, 10, cb), (insulin, 10, cg)} kf=20 ref=6.2
  dihe    group {ca: (insulin, 10) to (insulin, 12)}
          group {(ca, cb, cg): (insulin, 15) to (insulin, 18)}
          group {(insulin, 20), (insulin, 22)}
          group {ca: (insulin, 30) to (insulin, 32), (insulin, 34), all: (insulin, 35)} barr=20 ref=90
}
```

Bound specifications

```
// 1.      impose an upper bound if an atom's position strays too far from a reference position.
//         (add an energy term if the atom is more than 10Å from (2.0, 2.0, 2.0) ).
// 2&3.    impose lower and upper bounds on the distance between the ca's of residues 5 and 15.
//         (if the separation is less than 5.0Å or greater than 12.0Å add an energy term).
// 4.      impose a lower bound on the angle between the centers-of-mass of residues 3-6-9.
//         (if the angle goes lower than 90^o  apply a restraining potential).
urestraint {
 posi bound (insulin, 3, cb) kf=20 hi = (2.0, 2.0, 2.0, 10.0)
 dist bound (insulin, 5, ca) (insulin, 15, ca) kf=20 low = 5.0
 dist bound (insulin, 5, ca) (insulin, 15, ca) kf=20 hi = 12.0
 angle bound (insulin, 3) (insulin, 6) (insulin, 9) kf=20 low=90.0
}
```

```
// torsional bounds are defined as pairs. this example specifies upper and lower bounds on the
// dihedral angle, χ, separating the planes of the 1-2-3 residues and the 2-3-4 residues.
// The energy is 0 for:              -90^o  ¡ χ  ¡ 120^o
// The energy is 20 kcal/mol for:    130^o  ¡ χ  ¡ 260^o
// Energy rises from 0 → 20 kcal/mol as χ increases from 120^o →  130^o , and decreases from –90^o → –100^o.
```

```
urestraint {
  dihe bound (insulin 1) (insulin 2) (insulin 3) (insulin 4) gap=20 low=-90 hi=120 delta=10
}
```

Forcing restraints

```
  // a forcing restraint will be imposed on the distance between the centers-of-mass of residues (10 to 15) and
  // residues (30 to 35). low=20.0, hi=10.0, indicates that the reference distance is 20.0at λ=0, and 10.0at λ=1.
urestraint {
    dist pmf   group { (insulin, 10) to (insulin, 15) }
               group { (insulin, 30) to (insulin, 35) } kf=20, low=20.0, hi=10.0
}

  // 1. during the initial 10 ps, increase the strength of the forcing restraint to full strength: 0 → 20 kcal/(mol 2)
  // 2. next, apply a force to slowly close the distance from 20 to 10 (λ changes from 0 → 1)
  // 3. accumulate dU/dλ for another 10 ps. ( stays fixed at 1)
  // 4. force the distance back to its initial value of 20 ( changes from 1 → 0)
pmf {
  task = grow
  time = 10 ps
  print = 1 ps
}
pmf {
  task = up
  time = 100 ps
}
pmf {
  task = stop
  time = 10 ps
}
pmf {
  task = down
  time = 100 ps
}

  // 1.     force the distance to close from 20 to 10 in 5 steps. (λ changes from 0 →  1:   0.2, 0.4, 0.6, 0.8, 1.0)
  //       at each step equilibrate for 10 ps, then collect dU/dλ for another 10 ps.
  //       ref = 18, 16, 14, 12, 10 , duration = (10 + 10) x 5 = 100 ps.
  // 2.     reverse the step above (λ  changes from 1 → 0:   0.8, 0.6, 0.4, 0.2, 0.0)
mcti {
  task = stepup
  equiltime = 10 ps
  accumtime = 10 ps
  numsteps = 5
  print = 1 ps
}
mcti {
  task = stepdown
}
```

6.7.7 Appendix

Gradient for position restraint

$E = (K_f/2)\left(|\overrightarrow{r_i} - \overrightarrow{r_{ref}}|\right)^2$

$E = (K_f/2)\left\{(x_i - x_{ref})^2 + (y_i - y_{ref})^2 + (z_i - z_{ref})^2\right\}$

$\nabla(E) = K_f\left\{(x_i - x_{ref})\,\overrightarrow{i} + (y_i - y_{ref})\,\overrightarrow{j} + (z_i - z_{ref})\,\overrightarrow{k}\right\}$

Gradient for stretch restraint

$E = (K_f/2)\,(d_i - d_{ref})^2$

$d_i = \left\{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2\right\}^{1/2}$

$\nabla(E) = K_f\,(d_i - d_{ref}) \cdot \nabla(di)$

for atom 2 moving, and atom 1 fixed

$\nabla(d_i) = 1/2\left\{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2\right\}^{-1/2}\left\{2\,(x_2 - x_1) + 2\,(y_2 - y_1) + 2\,(z_2 - z_1)\right\}$

$\nabla(d_i) = \left\{(x_2 - x_1)\,\overrightarrow{i} + (y_2 - y_1)\,\overrightarrow{j} + (z_2 - z_1)\,\overrightarrow{k}\right\}/d_i$

$\nabla(E) = K_f\left\{(d_i - d_{ref})/d_i\right\}\left\{(x_2 - x_1)\,\overrightarrow{i} + (y_2 - y_1)\,\overrightarrow{j} + (z_2 - z_1)\,\overrightarrow{k}\right\}$

Gradient for bend restraint

$E = (K_f/2)\,(\theta_i - \theta_{ref})^2$

Atoms at positions A-B-C

distances: (A to B) = c; (A to C) = b; (B to C) = a;

$\theta_i = \cos^{-1}(u) = \cos^{-1}\left\{\left(a^2 + c^2 - b^2\right)/(2ac)\right\}$

$\nabla(E) = K_f\,(\theta_i - \theta_{ref}) \cdot \nabla(\theta_i)$

$\nabla(\theta_i) = \frac{-1}{\sqrt{1-u^2}} \cdot \nabla(u)$

for atom A moving, atoms B & C fixed (distances b and c change)

$\nabla(u) = \left\{-b/(ac)\right\} \cdot \nabla(b) + \left\{-a/\left(2c^2\right) + 1/(2a) + b^2/\left(2ac^2\right)\right\} \cdot \nabla(c)$

$\nabla(b) = \left\{(x_A - x_C)\,\overrightarrow{i} + (y_A - y_C)\,\overrightarrow{j} + (z_A - z_C)\,\overrightarrow{k}\right\}/b$

$\nabla(c) = \left\{(x_A - x_B)\,\overrightarrow{i} + (y_A - y_B)\,\overrightarrow{j} + (z_A - z_B)\,\overrightarrow{k}\right\}/c$

for atom B moving, atoms A & C fixed (distances a and c change)

$\nabla(u) = \left\{1/(2c) + -c/(2a^2) + b^2/(2a^2c)\right\} \cdot \nabla(a) + \left\{-a/\left(2c^2\right) + 1/(2a) + b^2/\left(2ac^2\right)\right\} \cdot \nabla(c)$

$\nabla(a) = \left\{(x_B - x_C)\,\overrightarrow{i} + (y_B - y_C)\,\overrightarrow{j} + (z_B - z_C)\,\overrightarrow{k}\right\}/a$

$\nabla(c) = \left\{(x_B - x_A)\,\overrightarrow{i} + (y_B - y_A)\,\overrightarrow{j} + (z_B - z_A)\,\overrightarrow{k}\right\}/c$

for atom C moving, atoms A & B fixed (distances a and b change)

$\nabla(u) = \left\{-b/(ac)\right\} \cdot \nabla(b) + \left\{-c/\left(2a^2\right) + 1/(2c) + b^2/\left(2ac^2\right)\right\} \cdot \nabla(a)$

$\nabla(b) = \left\{(x_C - x_A)\,\overrightarrow{i} + (y_C - y_A)\,\overrightarrow{j} + (z_C - z_A)\,\overrightarrow{k}\right\}/b$

$\nabla(a) = \left\{(x_C - x_B)\,\overrightarrow{i} + (y_C - y_B)\,\overrightarrow{j} + (z_C - z_B)\,\overrightarrow{k}\right\}/a$

Gradient for dihedral angle restraint

$E = (E_0/2)\left\{1 - \cos\left(\chi_i - \chi_{ref}\right)\right\}$

Atoms at positions A-B-C-D

$\chi_i = \cos^{-1}(u) = \cos^{-1}\left(\frac{(\overrightarrow{CD}\times\overrightarrow{CB})\bullet(\overrightarrow{BC}\times\overrightarrow{BA})}{\left|\overrightarrow{CD}\times\overrightarrow{CB}\right|\left|\overrightarrow{BC}\times\overrightarrow{BA}\right|}\right)$ AND

$\chi_i = \sin^{-1}(v) = \sin^{-1}\left(\frac{(\overrightarrow{CD}\times\overrightarrow{CB})\times(\overrightarrow{BC}\times\overrightarrow{BA})}{\left|\overrightarrow{CD}\times\overrightarrow{CB}\right|\left|\overrightarrow{BC}\times\overrightarrow{BA}\right|} \bullet \frac{\overrightarrow{CB}}{\left|\overrightarrow{CB}\right|}\right)$

$$\nabla(E) = (E_0/2)\left\{\sin\left(\chi_i - \chi_{ref}\right)\right\} \cdot \nabla(\chi_i)$$
$$\nabla(\chi_i) = \frac{-1}{\sqrt{1-u^2}} \cdot \nabla(u)$$

$$\begin{aligned}\overrightarrow{CD} \times \overrightarrow{CB} = \quad & ((y_D - y_C)(z_B - z_C) - (z_D - z_C)(y_B - y_C))\,\overrightarrow{i} + \\ & ((z_D - z_C)(x_B - x_C) - (x_D - x_C)(z_B - z_C))\,\overrightarrow{j} + \\ & ((x_D - x_C)(y_B - y_C) - (y_D - y_C)(x_B - x_C))\,\overrightarrow{k} \\ = \quad & p_1\,\overrightarrow{i} + p_2\,\overrightarrow{j} + p_3\,\overrightarrow{k}\end{aligned}$$

$$\begin{aligned}\overrightarrow{BC} \times \overrightarrow{BA} = \quad & ((y_C - y_B)(z_A - z_B) - (z_C - z_B)(y_A - y_B))\,\overrightarrow{i} + \\ & ((z_C - z_B)(x_A - x_B) - (x_C - x_B)(z_A - z_B))\,\overrightarrow{j} + \\ & ((x_C - x_B)(y_A - y_B) - (y_C - y_B)(x_A - x_B))\,\overrightarrow{k} \\ = \quad & p_4\,\overrightarrow{i} + p_5\,\overrightarrow{j} + p_6\,\overrightarrow{k}\end{aligned}$$

$$u = \frac{p_1 p_4 + p_2 p_5 + p_3 p_6}{\sqrt{p_1^2+p_2^2+p_3^2}\sqrt{p_4^2+p_5^2+p_6^2}}$$

$$\begin{aligned}\nabla(u) = \quad & \frac{p_1 \cdot \nabla(p_4) + p_2 \cdot \nabla(p_5) + p_3 \cdot \nabla(p_6)}{\sqrt{p_1^2+p_2^2+p_3^2}\sqrt{p_4^2+p_5^2+p_6^2}} + \\ & \frac{p_1 p_4 + p_2 p_5 + p_3 p_6}{\sqrt{p_1^2+p_2^2+p_3^2}} \left(-1/2\left(p_4^2+p_5^2+p_6^2\right)^{-3/2}\left(2p_4 \cdot \nabla(p_4) + 2p_5 \cdot \nabla(p_5) + 2p_6 \cdot \nabla(p_6)\right)\right) + \\ & \frac{p_1 p_4 + p_2 p_5 + p_3 p_6}{\sqrt{p_4^2+p_5^2+p_6^2}} \left(-1/2\left(p_1^2+p_2^2+p_3^2\right)^{-3/2}\left(2p_1 \cdot \nabla(p_1) + 2p_2 \cdot \nabla(p_2) + 2p_3 \cdot \nabla(p_3)\right)\right)\end{aligned}$$

for atom A moving, atoms B, C, & D fixed

$$\begin{aligned}\nabla(p_1) &= (0.0)\,\overrightarrow{i} + (0.0)\,\overrightarrow{j} + (0.0)\,\overrightarrow{k} \\ \nabla(p_2) &= (0.0)\,\overrightarrow{i} + (0.0)\,\overrightarrow{j} + (0.0)\,\overrightarrow{k} \\ \nabla(p_3) &= (0.0)\,\overrightarrow{i} + (0.0)\,\overrightarrow{j} + (0.0)\,\overrightarrow{k} \\ \nabla(p_4) &= (0.0)\,\overrightarrow{i} + (z_B - z_C)\,\overrightarrow{j} + (y_C - y_B)\,\overrightarrow{k} \\ \nabla(p_5) &= (z_C - z_B)\,\overrightarrow{i} + (0.0)\,\overrightarrow{j} + (x_B - x_C)\,\overrightarrow{k} \\ \nabla(p_6) &= (y_B - y_C)\,\overrightarrow{i} + (x_C - x_B)\,\overrightarrow{j} + (0.0)\,\overrightarrow{k}\end{aligned}$$

for atom B moving, atoms A, C, & D fixed

$$\begin{aligned}\nabla(p_1) &= (0.0)\,\overrightarrow{i} + (z_C - z_D)\,\overrightarrow{j} + (y_D - y_C)\,\overrightarrow{k} \\ \nabla(p_2) &= (z_D - z_C)\,\overrightarrow{i} + (0.0)\,\overrightarrow{j} + (x_C - x_D)\,\overrightarrow{k} \\ \nabla(p_3) &= (y_C - y_D)\,\overrightarrow{i} + (x_D - x_C)\,\overrightarrow{j} + (0.0)\,\overrightarrow{k} \\ \nabla(p_4) &= (0.0)\,\overrightarrow{i} + (z_C - z_A)\,\overrightarrow{j} + (y_A - y_C)\,\overrightarrow{k} \\ \nabla(p_5) &= (z_A - z_C)\,\overrightarrow{i} + (0.0)\,\overrightarrow{j} + (x_C - x_A)\,\overrightarrow{k} \\ \nabla(p_6) &= (y_C - y_A)\,\overrightarrow{i} + (x_A - x_C)\,\overrightarrow{j} + (0.0)\,\overrightarrow{k}\end{aligned}$$

Gradient for forcing position restraint

$$E = (K_f/2)\left(|\overrightarrow{r_i} - \overrightarrow{r_{ref}}|\right)^2$$
$$r_{ref} = \lambda\overrightarrow{r_1} + (1-\lambda)\,\overrightarrow{r_0}$$

$$\begin{aligned}dE/d\lambda = \quad & K_f \times \quad \left((x_i - x_{ref})^2 + (y_i - y_{ref})^2 + (z_i - z_{ref})^2\right)^{1/2} \times \\ & 1/2\left((x_i - x_{ref})^2 + (y_i - y_{ref})^2 + (z_i - z_{ref})^2\right)^{-1/2} \times \\ & (2\,(x_i - x_{ref})\,(x_0 - x_1) + 2\,(y_i - y_{ref})\,(y_0 - y_1) + 2\,(z_i - z_{ref})\,(z_0 - z_1))\end{aligned}$$

$$dE/d\lambda = K_f \times ((x_i - x_{ref})\,(x_0 - x_1) + (y_i - y_{ref})\,(y_0 - y_1) + (z_i - z_{ref})\,(z_0 - z_1))$$

Gradient for forcing stretch restraint

$E = (K_f/2)\,(d_i - d_{ref})^2$
$d_{ref} = \lambda d_1 + (1-\lambda)\,d_0$
$dE/d\lambda = K_f \;\times\; (d_i - d_{ref}) \;\times\; (d_0 - d_1)$

Gradient for forcing bend restraint
$E = (K_f/2)\,(\theta_i - \theta_{ref})^2$
$\theta_{ref} = \lambda\theta_1 + (1-\lambda)\,\theta_0$
$dE/d\lambda = K_f \;\times\; (\theta_i - \theta_{ref}) \;\times\; (\theta_0 - \theta_1)$

Gradient for forcing dihedral restraint
$E = (E_0/2)\,(1 - \cos(\chi_i - \chi_{ref}))$
$\chi_{ref} = \lambda\chi_1 + (1-\lambda)\,\chi_0$
$dE/d\lambda = (E_0/2) \;\times\; \sin(\chi_i - \chi_{ref}) \;\times\; (\chi_0 - \chi_1)$

6.8 Adaptive Biasing Force Calculations

This feature has been contributed to NAMD by the following authors:

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6.8.1 Introduction and theoretical background

Strictly speaking, a potential of mean force (PMF) is the reversible work supplied to the system to bring two solvated particles, or ensembles of particles, from an infinite separation to some contact distance: [8]

$$w(r) = -\frac{1}{\beta}\ln g(r) \tag{4}$$

Here, $g(r)$ is the pair correlation function of the two particles, or ensembles thereof. The vocabulary "PMF" has, however, been extended to a wide range of reaction coordinates that go far beyond simple interatomic or intermolecular distances. In this perspective, generalization of equation (4) is not straightforward. This explains why it may be desirable to turn to a definition suitable for any type of reaction coordinate, ξ:

$$A(\xi) = -\frac{1}{\beta}\ln \mathcal{P}_\xi + A_0 \tag{5}$$

$A(\xi)$ is the free energy of the state defined by a particular value of ξ, which corresponds to an iso–ξ hypersurface in phase space. A_0 is a constant and $\mathcal{P}_\xi$ is the probability density to find the chemical system of interest at ξ.

The connection between the derivative of the free energy with respect to the reaction coordinate, $\mathrm{d}A(\xi)/\mathrm{d}\xi$, and the forces exerted along the latter may be written as: [28, 12]

$$\frac{\mathrm{d}A(\xi)}{\mathrm{d}\xi} = \left\langle \frac{\partial \mathcal{V}(\mathbf{x})}{\partial \xi} - \frac{1}{\beta}\frac{\partial \ln |J|}{\partial \xi} \right\rangle_{\xi} = -\langle F_{\xi} \rangle_{\xi} \tag{6}$$

where $|J|$ is the determinant of the Jacobian for the transformation from generalized to Cartesian coordinates. The first term of the ensemble average corresponds to the Cartesian forces exerted on the system, derived from the potential energy function, $\mathcal{V}(\mathbf{x})$. The second contribution is a geometric correction arising from the change in the metric of the phase space due to the use of generalized coordinates. It is worth noting, that, contrary to its instantaneous component, F_{ξ}, only the average force, $\langle F_{\xi} \rangle_{\xi}$, is physically meaningful.

In the framework of the average biasing force (ABF) approach, [11, 24] F_{ξ} is accumulated in small windows or bins of finite size, $\delta\xi$, thereby providing an estimate of the derivative $\mathrm{d}A(\xi)/\mathrm{d}\xi$ defined in equation (6). The force applied along the reaction coordinate, ξ, to overcome free energy barriers is defined by:

$$\mathbf{F}^{\mathrm{ABF}} = \boldsymbol{\nabla}_{\boldsymbol{x}} \widetilde{A} = -\langle F_{\xi} \rangle_{\xi} \, \boldsymbol{\nabla}_{\boldsymbol{x}} \xi \tag{7}$$

where $\widetilde{A}$ denotes the current estimate of the free energy and $\langle F_{\xi} \rangle_{\xi}$, the current average of F_{ξ}.

As sampling of the phase space proceeds, the estimate $\boldsymbol{\nabla}_{\boldsymbol{x}} \widetilde{A}$ is progressively refined. The biasing force, $\mathbf{F}^{\mathrm{ABF}}$, introduced in the equations of motion guarantees that in the bin centered about ξ, the force acting along the reaction coordinate averages to zero over time. Evolution of the system along ξ is, therefore, governed mainly by its self–diffusion properties.

A particular feature of the instantaneous force, F_{ξ}, is its tendency to fluctuate significantly. As a result, in the beginning of an ABF simulation, the accumulated average in each bin will generally take large, inaccurate values. Under these circumstances, applying the biasing force along ξ according to equation (7) may severely perturb the dynamics of the system, thereby biasing artificially the accrued average, and, thus, impede convergence. To avoid such undesirable effects, no biasing force is applied in a bin centered about ξ until a reasonable number of force samples has been collected. When the user–defined minimum number of samples is reached, the biasing force is introduced progressively in the form of a linear ramp. For optimal efficiency, this minimal number of samples should be adjusted on a system–dependent basis.

In addition, to alleviate the deleterious effects caused by abrupt variations of the force, the corresponding fluctuations are smoothed out, using a weighted running average over a preset number of adjacent bins, in lieu of the average of the current bin itself. It is, however, crucial to ascertain that the free energy profile varies regularly in the ξ–interval, over which the average is performed.

To obtain an adequate sampling in reasonable simulation times, it is recommended to split long reaction pathways into consecutive ranges of ξ. In contrast with probability–based methods, ABF does *not* require that these windows overlap by virtue of the continuity of the force across the the reaction pathway.

A more comprehensive discussion of the theoretical basis of the method and its implementation in NAMD can be found in [15].

6.8.2 Using the NAMD implementation of the adaptive biasing force method

The ABF method has been implemented as a suite of Tcl routines that can be invoked from the main configuration file used to run molecular dynamics simulations with NAMD.

The routines can be invoked by including the following command in the configuration file:

```
source <path to>/lib/abf/abf.tcl
```

where `<path to>/lib/abf/abf.tcl` is the complete path to the main ABF file. The other Tcl files of the ABF package must be located in the same directory.

A second option for loading the ABF module is to source the `lib/init.tcl` file distributed with NAMD, and then use the Tcl package facility. The file may be sourced in the config file:

```
source <path to>/lib/init.tcl
package require abf
```

Or, to make the config file portable, the init file may be the first config file passed to NAMD:

```
namd2 <path to>/lib/init.tcl myconfig.namd
```

and then the config file need only contain:

```
package require abf
```

Note that the ABF code makes use of the `TclForces` and `TclForcesScript` commands. As a result, NAMD configuration files should not call the latter directly when running ABF.

6.8.3 Parameters for ABF simulations

The following parameters have been defined to control ABF calculations. They may be set using the folowing syntax:

`abf <keyword> <value>`

where `<value>` may be a number, a word or a Tcl list. Keywords are not case–sensitive.

- `coordinate` < Type of reaction coordinate used in the ABF simulation >
  Acceptable Values: `distance`, `distance-com`, `abscissa`, `zCoord`, `zCoord-1atom` or `xyDistance`
  Description: As a function of the system of interest, a number of alternative reaction coordinates may be considered. The ABF code is modular: RC–specific code for each RC is contained in a separate Tcl file. Additional RCs, tailored for a particular problem, may be added by creating a new file providing the required Tcl procedures. Existing files such as `distance.tcl` are thoroughly commented, and should provide a good basis for the coding of additional coordinates, together with [15].

  (1) `distance` — corresponds to the distance separating two selected atoms:
  `abf1`: index of the first atom of the reaction coordinate;
  `abf2`: index of the second atom of the reaction coordinate.

  (2) `distance-com` — corresponds to the distance separating the center of mass of two sets of atoms, *e.g.*the distance between the centroid of two benzene molecules:
  `abf1`: list of indices of atoms participating to the first center of mass;
  `abf2`: list of indices of atoms participating to the second center of mass.

(3) `abscissa` — corresponds to the distance between the centers of mass of two sets of atoms along a given direction:
`direction`: a vector (Tcl list of three real numbers) defining the direction of interest
`abf1`: list of indices of atoms participating to the first center of mass;
`abf2`: list of indices of atoms participating to the second center of mass.

(4) `zCoord` — corresponds to the distance separating two groups of atoms along the z-direction of Cartesian space. This reaction coordinate is useful for the estimation of transfer free energies between two distinct media:
`abf1`: list of indices of reference atoms
`abf2`: list of indices of atoms of interest — *e.g.*a solute

(5) `zCoord-1atom` — is similar to `zCoord`, but using a single atom of interest
`abf1`: list of indices of reference atoms
`abf2`: index of an atom of interest

(6) `xyDistance` — is the distance between the centers of mass of two atom groups, projected on the (x, y) plane:
`abf1`: list of indices of atoms participating to the first center of mass;
`abf2`: list of indices of atoms participating to the second center of mass.

- `xiMin` < Lower bound of the reaction coordinate >
  Acceptable Values: decimal number, in Å
  Description: Lower limit of the reaction coordinate, ξ, below which no sampling is performed.

- `xiMax` < Upper bound of the reaction coordinate >
  Acceptable Values: decimal number, in Å
  Description: Upper limit of the reaction coordinate, ξ, beyond which no sampling is performed.

- `dxi` < Width of the bins in which the forces are accumulated >
  Acceptable Values: decimal number, in Å
  Description: Width, $\delta\xi$, of the bins in which the instantaneous components of the force, F_ξ, are collected. The choice of this variable is dictated by the nature of the system and how rapidly the free energy changes as a function of ξ.

- `forceConst` < Force constant applied at the borders of the reaction coordinate >
  Acceptable Values: positive decimal number, in kcal/mol/Å^2
  Default Value: 10.0
  Description: If this force constant is nonzero, a harmonic bias is enforced at the borders

of the reaction coordinate, *i.e.*at both `xiMin` and `xiMax`, to guarantee that sampling will be confined between these two values.

- `dSmooth` < Length over which force data is averaged when computing the ABF >
  Acceptable Values: positive decimal number, in Å
  Default Value: 0.0
  Description: To avoid abrupt variations in the average force and in the free energy, fluctuations are smoothed out by means of a weighted running average over adjacent bins on each side of ξ. When the free energy derivative varies slowly, smoothing can be performed across several contiguous bins. Great attention should be paid, however, when the free energy varies sharply with ξ.

- `fullSamples` < Number of samples in a bin prior to application of the ABF >
  Acceptable Values: positive integer
  Default Value: 200
  Description: To avoid nonequilibrium effects in the dynamics of the system, due to large fluctuations of the force exerted along the reaction coordinate, ξ, it is recommended to apply the biasing force only after a reasonable estimate of the latter has been obtained.

- `outFile` < Output file of an ABF calculation >
  Acceptable Values: Unix filename
  Default Value: `abf.dat`
  Description: Output file containing, for each value of the reaction coordinate, ξ, the free energy, $A(\xi)$, the average force, $\langle F_\xi \rangle$, and the number of samples accrued in the bin.

- `historyFile` < History of the force data over time >
  Acceptable Values: Unix filename
  Default Value: `none`
  Description: This file contains a history of the information stored in `outFile`, and is written every tenth update of `outFile`. Data for different timesteps are separated by & signs for easier visualization using the Grace plotting software. This is useful for assessing the convergence of the free energy profile.

- `inFiles` < Input files for an ABF calculation >
  Acceptable Values: Tcl list of Unix filenames
  Default Value: empty list
  Description: Input files containing the same data as in `outFileName`, and that may, therefore, be used to restart an ABF simulation. The new free energies and forces will then be written out based on the original information supplied by these files. This command may also be used to combine data obtained from separate runs.

- `outputFreq` < Frequency at which `outFileName` is updated >
  Acceptable Values: positive integer
  Default Value: 5000
  Description: The free energy, $A(\xi)$, the average force, $\langle F_\xi \rangle$, and the number of samples accrued in the bin will be written to the ABF output file every `ABFoutFreq` timesteps.

- `writeXiFreq` < Frequency at which the time series of ξ is written >
  Acceptable Values: positive integer
  Default Value: 0
  Description: If this parameter is nonzero, the instantaneous value of the reaction coordinate, ξ, is written in the NAMD standard output every `writeXiFreq` time steps.

- `distFile` < Output file containing force distributions >
  Acceptable Values: Unix filename
  Default Value: `none`
  Description: Output file containing a distribution of the instantaneous components of the force, F_ξ, for every bin comprised between `xiMin` and `xiMax`. This is useful for performing error analysis for the resulting free energy profile

- `fMax` < Half–width of the force histograms >
  Acceptable Values: positive decimal number, in kcal/mol/Å
  Default Value: 60.0
  Description: When force distributions are written in `distFile`, the histogram collects F_ξ values ranging from $-$`fMax` to $+$`fMax`.

- `moveBoundary` < Number of samples beyond which `xiMin` and `xiMax` are updated >
  Acceptable Values: positive integer
  Default Value: 0
  Description: Slow relaxation in the degrees of freedom orthogonal to the reaction coordinate, ξ, results in a non–uniform sampling along the latter. To force exploration of ξ in quasi non–ergodic situations, the boundaries of the reaction pathway may be modified dynamically when a preset minimum number of samples is attained. As a result, the interval between `xiMin` and `xiMax` is progressively narrowed down as this threshold is being reached for all values of ξ. It should be clearly understood that uniformity of the sampling is artificial and is only used to force diffusion along ξ. Here, uniform sampling does not guarantee the proper convergence of the simulation.

- `restraintList` < Apply external restraints >
  Acceptable Values: list of formatted entries
  Default Value: empty list
  Description: For a detailed description of this feature, see next subsection.

- `applyBias` < Apply a biasing force in the simulation ? >
  Acceptable Values: `yes` or `no`
  Default Value: `yes`
  Description: By default, a biasing force is applied along the reaction coordinate, ξ, in ABF calculations. It may be, however, desirable to set this option to `no` to monitor the evolution of the system along ξ and collect the forces and the free energy, yet, without introducing any bias in the simulation.

- `usMode` < Run umbrella sampling simulation ? >
  Acceptable Values: `yes` or `no`

Default Value: `no`

Description: When setting this option, an "umbrella sampling" [30] calculation is performed, supplying a probability distribution for the reaction coordinate, ξ. As an initial guess of the biases required to overcome the free energy barriers, use can be made of a previous ABF simulation — *cf.* `inFiles`. In addition, specific restraints may be defined using the `restraintList` feature described below.

6.8.4 Including restraints in ABF simulations

In close connection with the possibility to run umbrella sampling simulations, the ABF module of NAMD also includes the capability to add sets of restraints to confine the system in selected regions of configurational space. Incorporation of harmonic restraints may be invoked using a syntax similar in spirit to that adopted in the conformational free energy module of NAMD:

```
abf restraintList {
   angle1  {angle {A 1 CA} {G 1 N3} {G 1 N1}          40.0 30.0}
   dihe1   {dihe  {A 1 O1} {A 1 CA} {A 1 O2} {G 1 N3} 40.0  0.0}
   dihe2   {dihe  {A 1 CA} {A 1 O2} {G 1 N2} {G 1 N3} 40.0  0.0}
}
```

The general syntax of an item of this list is:

```
name {type atom1 atom2 [atom3] [atom4] k reference}
```

where `name` could be any word used to refer to the restraint in the NAMD output. `type` is the type of restraint, *i.e.*a distance, `dist`, a valence angle, `angle`, or a dihedral angle, `dihe`. Definition of the successive atoms follows the syntax of NAMD conformation free energy calculations. `k` is the force constant of the harmonic restraint, the unit of which depends on `type`. `reference` is the reference, target value of the restrained coordinate.

Aside from `dist`, `angle` and `dihe`, which correspond to harmonic restraints, linear ramps have been added for distances, using the specific keyword `distLin`. In this particular case, generally useful in umbrella sampling free energy calculations, the syntax is:

```
name {distLin atom1 atom2 F r1 r2}
```

where `F` is the force in kcal/mol/Å. The restraint is applied over the interval between `r1` and `r2`.

The `harm` restraint applies, onto one single atom, a harmonic potential of the form

$$V(x,y,z) = \frac{1}{2}k_x(x-x_0)^2 + \frac{1}{2}k_y(y-y_0)^2 + \frac{1}{2}k_z(z-z_0)^2$$

This way, atoms may be restrained to the vicinity of a plane, an axis, or a point, depending on the number of nonzero force constants. The syntax is:

```
name {harm atom {kx ky kz} {x0 y0 z0} }
```

6.8.5 Important recommendations when running ABF simulations

The formalism implemented in NAMD had been originally devised in the framework of unconstrained MD. Holonomic constraints may, however, be introduced without interfering with the computation of the bias and, hence, the PMF, granted that some precautions are taken.

Either of the following strategies may be adopted:

(1) Atoms involved in the computation of F_ξ do not participate in constrained degrees of freedom. If, for instance, chemical bonds between hydrogen and heavy atoms are frozen, ξ could be chosen as a distance between atoms that are not involved in a constraint.

In some cases, not all atoms used for defining ξ are involved in the computation of the force component F_ξ. Specifically, reference atoms `abf1` in the RC types `zCoord` and `zCoord-1atom` are not taken into account in F_ξ. Therefore, constraints involving those atoms have no effect on the ABF protocol.

(2) The definition of ξ involves atoms forming constrained bonds. In this case, the effect of constraints on ABF can be eliminated by using a group–based RC built on atom groups containing both "ends" of all rigid bonds involved, *i.e.*hydrogens together with their mother atom.

For example, if the distance from a methane molecule to the center of mass of a water lamella is studied with the `zCoord` RC by taking water oxygens as a reference (`abf1`) and all five atoms of methane as the group of interest (`abf2`):

- Water molecules may be constrained because the reference atoms are not used to compute the force component;
- C—H bonds in methane may be constrained as well, because the contributions of constraint forces on the carbon and hydrogens to F_ξ will cancel out.

6.8.6 Example of input file for computing potentials of mean force

In this example, the system consists of a short, ten-residue peptide, formed by L-alanine amino acids. Reversible folding/unfolding of this peptide is carried out using as a reaction coordinate the carbon atom of the first and the last carbonyl groups — ξ, hence, corresponds to a a simple interatomic distance, defined by the keyword `distance`. The reaction pathway is explored between 12 and 32 Å, *i.e.*, over a distance of 20 Å, in a single window. The variations of the free energy derivative are soft enough to warrant the use of bins with a width of 0.2 Å, in which forces are accrued.

```
source                ~/lib/abf/abf.tcl

abf coordinate        distance

abf abf1              4
abf abf2              99

abf dxi               0.2
abf xiMin             12.0
```

```
abf xiMax              32.0
abf outFile            deca-alanine.dat
abf fullSamples        500
abf inFiles            {}
abf distFile           deca-alanine.dist
abf dSmooth            0.4
```

Here, the ABF is applied after 500 samples have been collected, which, in vacuum, have proven to be sufficient to get a reasonable estimate of $\langle F_\xi \rangle$.

6.9 Alchemical Free Energy Perturbation Calculations

This feature has been contributed to NAMD by the following authors:

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6.9.1 Introduction

Theoretical background A method to perform alchemical free energy perturbation (FEP) [32, 4, 31, 29, 19, 14, 21, 9, 10] is available in NAMD. Within the FEP framework, the free energy difference between two alternate states, a and b, is expressed by:

$$\Delta A_{a\rightarrow b} = -\frac{1}{\beta} \ln \left\langle \exp \left\{ -\beta \left[\mathcal{H}_b(\mathbf{x}, \mathbf{p}_x) - \mathcal{H}_a(\mathbf{x}, \mathbf{p}_x) \right] \right\} \right\rangle_a \tag{8}$$

Here, $\beta^{-1} \equiv k_B T$, where k_B is the Boltzmann constant, T is the temperature. $\mathcal{H}_a(\mathbf{x}, \mathbf{p}_x)$ and $\mathcal{H}_b(\mathbf{x}, \mathbf{p}_x)$ are the Hamiltonians characteristic of states a and b, respectively. $\langle \cdots \rangle_a$ denotes an ensemble average over configurations representative of the initial, reference state, a.

Convergence of equation (8) implies that low–energy configurations of the target state, b, are also configurations of the reference state, a, thus resulting in an appropriate overlap of the corresponding ensembles — see Figure 5. In practice, transformation between the two thermodynamic states is replaced by a series of transformations between non–physical, intermediate states along a well–delineated pathway that connects a to b. This pathway is characterized by a general extent parameter, often referred to as "coupling parameter" [4, 21, 17, 18], λ, that makes the Hamiltonian and, hence, the free energy, a continuous function of this parameter between a and b:

$$\Delta A_{a\rightarrow b} = -\frac{1}{\beta} \sum_{i=1}^{N} \ln \left\langle \exp \left\{ -\beta \left[\mathcal{H}(\mathbf{x}, \mathbf{p}_x; \lambda_{i+1}) - \mathcal{H}(\mathbf{x}, \mathbf{p}_x; \lambda_i) \right] \right\} \right\rangle_i \tag{9}$$

Here, N stands for the number of intermediate stages, or "windows" between the initial and the final states — see Figure 5.

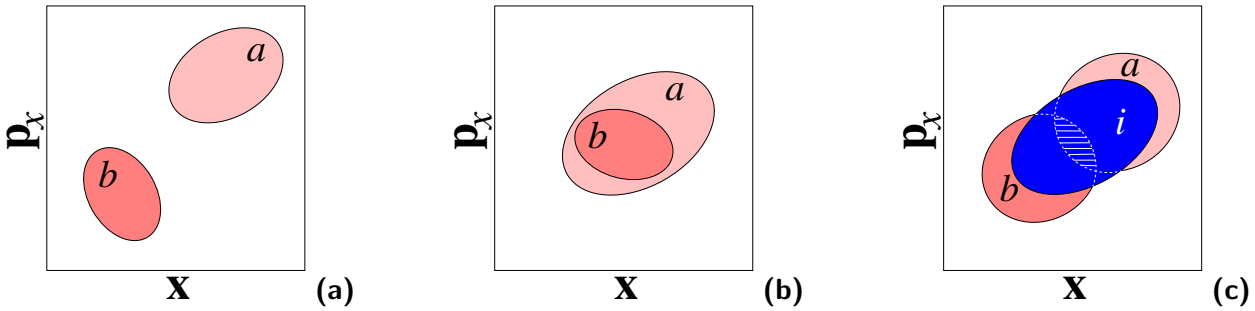

Figure 5: Convergence of an FEP calculation. If the ensembles representative of states a and b are too disparate, equation (8) will not converge **(a)**. If, in sharp contrast, the configurations of state b form a subset of the ensemble of configurations characteristic of state a, the simulation is expected to converge **(b)**. The difficulties reflected in case **(a)** may be alleviated by the introduction of mutually overlapping intermediate states that connect a to b **(c)**. It should be mentioned that in practice, the kinetic contribution, $\mathcal{T}(\mathbf{p}_x)$, is assumed to be identical for state a and state b.

The dual–topology paradigm In a typical FEP setup involving the transformation of one chemical species into an alternate one in the course of the simulation, the atoms in the molecular topology can be classified into three groups, (i) a group of atoms that do not change during the simulation — *e.g.*the environment, (ii) the atoms describing the reference state, a, of the system, and (iii) the atoms that correspond to the target state, b, at the end of the alchemical transformation. The atoms representative of state a should *never* interact with those of state b throughout the MD simulation. Such a setup, in which atoms of both the initial and the final states of the system are present in the molecular topology file — *i.e.*the `psf` file — is characteristic of the so–called "dual topology" paradigm [13, 23, 2]. The hybrid Hamiltonian of the system, which is a function of the general extent parameter, λ, that connects smoothly state a to state b, is calculated as a linear combination of the corresponding Hamiltonians:

$$\mathcal{H}(\mathbf{x}, \mathbf{p}_x; \lambda) = \mathcal{H}_0(\mathbf{x}, \mathbf{p}_x) + \lambda\mathcal{H}_b(\mathbf{x}, \mathbf{p}_x) + (1 - \lambda)\mathcal{H}_a(\mathbf{x}, \mathbf{p}_x) \tag{10}$$

where $\mathcal{H}_a(\mathbf{x}, \mathbf{p}_x)$ describes the interaction of the group of atoms representative of the reference state, a, with the rest of the system. $\mathcal{H}_b(\mathbf{x}, \mathbf{p}_x)$ characterizes the interaction of the target topology, b, with the rest of the system. $\mathcal{H}_0(\mathbf{x}, \mathbf{p}_x)$ is the Hamiltonian describing those atoms that do not undergo any transformation during the MD simulation.

For instance, in the point mutation of an alanine side chain into that of glycine, by means of an FEP calculation, the topology of both the methyl group of alanine and the hydrogen borne by the C_α in glycine co–exist throughout the simulation (see Figure 6), yet without actually seeing each other.

The energy and forces are defined as a function of λ, in such a fashion that the interaction of the methyl group of alanine with the rest of the protein is effective at the beginning of the simulation, *i.e.*$\lambda = 0$, while the glycine C_α hydrogen atom does not interact with the rest of the protein, and *vice versa* at the end of the simulation, *i.e.*$\lambda = 1$. For intermediate values of λ, both the alanine and the glycine side chains participate in non–bonded interactions with the rest of the protein, scaled on the basis of the current value of λ. It should be clearly understood that these side chains never interact with each other. Construction of an appropriate list of excluded atoms, common to the two alternate topologies, is, therefore, necessary.

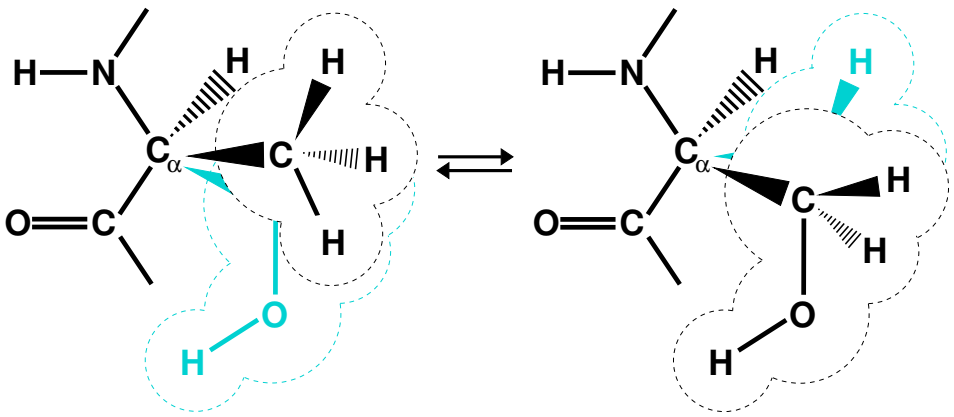

Figure 6: Dual topology description for an alchemical simulation. Case example of the mutation of alanine into serine. The lighter color denotes the non–interacting, alternate state.

It is also worth noting that the free energy calculation does not alter intramolecular potentials, *e.g.*bond stretch, valence angle deformation and torsions, in the course of the simulation. In calculations targeted at the estimation of free energy differences between two states characterized by distinct environments — *e.g.*a ligand, bound to a protein in the first simulation, and solvated in water, in the second — as is the case for most free energy calculations that make use of a thermodynamic cycle, perturbation of intramolecular terms may, by and large, be safely avoided [5].

6.9.2 Implementation of free energy perturbation in NAMD

The procedure implemented in NAMD is particularly adapted for performing free energy calculations that split the λ reaction path into a number of non–physical, intermediate states, or "windows". Separate simulations can be started for each window. Alternatively, the Tcl scripting ability of NAMD can be employed advantageously to perform the complete simulation in a single run. An example making use of such script is supplied at the end of this user guide.

The following keywords can be used to control the alchemical free energy calculations.

- `fep` < Is alchemical FEP to be performed? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Turns on hamiltonian scaling and ensemble averaging for alchemical FEP.

- `lambda` < Coupling parameter value >
  Acceptable Values: positive decimal between 0.0 and 1.0
  Description: The coupling parameter value determining the progress of the perturbation. The non–bonded interactions involving the atoms vanishing in the course of the MD simulation are scaled by (1-`lambda`), while those of the growing atoms are scaled by `lambda`.

- `lambda2` < Coupling parameter comparison value >
  Acceptable Values: positive decimal between 0.0 and 1.0
  Description: The `lambda2` value corresponds to the coupling parameter to be used for sampling in the next window. The free energy difference between `lambda2` and `lambda` is calculated. Through simulations at progressive values of `lambda` and `lambda2` the total free energy difference may be determined.

- `fepEquilSteps` < Number of equilibration steps in a window, before data collection >
  Acceptable Values: positive integer less than `numSteps` or `run`
  Default Value: 0
  Description: In each window `fepEquilSteps` steps of equilibration can be performed before ensemble averaging is initiated. The output also contains the data gathered during equilibration and is meant for analysis of convergence properties of the FEP calculation.

- `fepFile` < `pdb` file with perturbation flags >
  Acceptable Values: filename
  Default Value: coordinates
  Description: `pdb` file to be used for indicating the FEP status for each of the atoms pertaining to the system. If this parameter is not declared specifically, then the `pdb` file specified by `coordinates` is utilized for this information.

- `fepCol` < Column in the `fepFile` that carries the perturbation flag >
  Acceptable Values: X, Y, Z, O or B
  Default Value: B
  Description: Column of the `pdb` file to use for retrieving the FEP status of each atom, *i.e.*a flag that indicates which atom will be perturbed in the course of the simulation. A value of `-1` in the specified column indicates the atom will vanish during the FEP calculation, whereas a value of `1` indicates that the atom will grow.

- `fepOutFreq` < Frequency of FEP energy output in time–steps >
  Acceptable Values: positive integer
  Default Value: 5
  Description: Every `fepOutFreq` number of MD steps, the output file `fepOutFile` is updated by dumping energies that are used for ensemble averaging. This variable could be set to `1` to include all the configurations for ensemble averaging. Yet, it is recommended to update `fepOutFile` energies at longer intervals to avoid large files containing highly correlated data.

- `fepOutFile` < FEP energy output filename >
  Acceptable Values: filename
  Default Value: `outfilename`
  Description: `An output file named fepOutFile, generated by NAMD, contains the FEP energies, dumped every fepOutFreq steps.`

6.9.3 Examples of input files for running FEP alchemical calculations

The first example illustrates the use of TCL scripting for running an alchemical transformation with the FEP feature of NAMD. In this calculation, λ is changed continuously from 0 to 1 by increments of $\delta\lambda = 0.1$.

```
fep             on
fepfile         ion.fep
fepCol          X
fepOutfile      ion.fepout
fepOutFreq      5
fepEquilSteps   5000
```

Turn FEP functionality on.
File containing the information about growing/shrinking atoms described in column `X`.
Output file containing the free energy.
Frequency at which `fepOutFreq` is updated.
Number of equilibration steps per λ–state.

```
set step        0.0
set dstep       0.1
```

Starting value of λ.
Increment of λ, *i.e.*$\delta\lambda$.

```
while {$step <= 1.0} {
  lambda $step
  set step [expr $step + $dstep]
  lambda2 $step
  run  10000
}
```

TCL script to increment λ:
(1) set `lambda` value;
(2) increment λ;
(3) set `lambda2` value;
(4) run 10,000 MD steps.

The user should be reminded that by setting `run 10000`, 10,000 MD steps will be performed, which includes the preliminary `fepEquilSteps` equilibration steps. This means that here, the ensemble average of equation (9) will be computed over 5,000 MD steps.

Alternatively, λ–states may be declared explicitly, avoiding the use of TCL scripting:

```
lambda          0.0
lambda2         0.1
run             10000
```

(1) set `lambda` value;
(2) set `lambda2` value;
(3) run 10,000 MD steps.

This option is generally preferred to set up windows of diminishing widths as $\lambda \rightarrow 0$ or 1 — a way to circumvent end–point singularities caused by appearing atoms that may clash with their surroundings. It may be used in conjunction with a soft–core potential (see relevant section).

6.9.4 Description of FEP simulation output

The `fepOutFile` contains electrostatic and van der Waals energy data calculated for `lambda` and `lambda`, written every `fepOutFreq` steps. The column `dE` is the energy difference of the single configuration, `dE_avg` and `dG` are the instantaneous ensemble average of the energy and the calculated free energy at the time step specified in column 2, respectively. The temperature is specified in the penultimate column. Upon completion of `fepEquilSteps` steps, the calculation of `dE_avg` and `dG` is restarted. The accumulated net free energy change is written at each lambda value and at the end of the simulation. The cumulative average energy `dE_avg` value may be summed using the trapezoidal rule to obtain an approximate thermodynamic integration (TI) estimate for the free energy change during the run.

Whereas the FEP module of NAMD supplies free energy differences determined from equation (8), the wealth of information available in `fepOutFile` may be utilized profitably to explore different routes towards the estimation of ΔA. As commented on previously, TI may constitute one such route. The simple overlap sampling (SOS) represents an interesting alternative, that combines advantageously *forward* and *reverse* transformations to improve convergence and accuracy of the calculation [20]. The linear scaling of the Hamiltonian highlighted in equation (10) obviates the need for explicit simulation of the reverse transformation, because:

$$\mathcal{H}(\mathbf{x}, \mathbf{p}_x; \lambda_i) - \mathcal{H}(\mathbf{x}, \mathbf{p}_x; \lambda_{i+1}) = \frac{\lambda_i - \lambda_{i+1}}{\lambda_{i+2} - \lambda_{i+1}} \; [\mathcal{H}(\mathbf{x}, \mathbf{p}_x; \lambda_{i+2}) - \mathcal{H}(\mathbf{x}, \mathbf{p}_x; \lambda_{i+1})] \qquad (11)$$

The free energy difference between states λ_i and λ_{i+1} may then be expressed as:

$$\begin{aligned}
\exp(-\beta\Delta A_{i\rightarrow i+1}) &= \frac{\left\langle \exp\left\{-\frac{\beta}{2}\left[\mathcal{H}(\mathbf{x},\mathbf{p}_x;\lambda_{i+1})-\mathcal{H}(\mathbf{x},\mathbf{p}_x;\lambda_i)\right]\right\}\right\rangle_i}{\left\langle \exp\left\{-\frac{\beta}{2}\left[\mathcal{H}(\mathbf{x},\mathbf{p}_x;\lambda_i)-\mathcal{H}(\mathbf{x},\mathbf{p}_x;\lambda_{i+1})\right]\right\}\right\rangle_{i+1}} \\
&= \frac{\left\langle \exp\left\{-\frac{\beta}{2}\left[\mathcal{H}(\mathbf{x},\mathbf{p}_x;\lambda_{i+1})-\mathcal{H}(\mathbf{x},\mathbf{p}_x;\lambda_i)\right]\right\}\right\rangle_i}{\left\langle \exp\left\{-\frac{\beta}{2}\,\frac{\lambda_i-\lambda_{i+1}}{\lambda_{i+2}-\lambda_{i+1}}\,\left[\mathcal{H}(\mathbf{x},\mathbf{p}_x;\lambda_{i+2})-\mathcal{H}(\mathbf{x},\mathbf{p}_x;\lambda_{i+1})\right]\right\}\right\rangle_{i+1}}
\end{aligned} \tag{12}$$

6.10 Locally Enhanced Sampling

Locally enhanced sampling (LES) [25, 26, 27] increases sampling and transition rates for a portion of a molecule by the use of multiple non-interacting copies of the enhanced atoms. These enhanced atoms experience an interaction (electrostatics, van der Waals, and covalent) potential that is divided by the number of copies present. In this way the enhanced atoms can occupy the same space, while the multiple instances and reduces barriers increase transition rates.

6.10.1 Structure Generation

To use LES, the structure and coordinate input files must be modified to contain multiple copies of the enhanced atoms. `psfgen` provides the `multiply` command for this purpose. NAMD supports a maximum of 15 copies, which should be sufficient.

Begin by generating the complete molecular structure and guessing coordinates as described in Sec. 4. As the last operation in your script, prior to writing the psf and pdb files, add the `multiply` command, specifying the number of copies desired and listing segments, residues, or atoms to be multiplied. For example, `multiply 4 BPTI:56 BPTI:57` will create four copies of the last two residues of segment BPTI. You must include all atoms to be enhanced in a single `multiply` command in order for the bonded terms in the psf file to be duplicated correctly. Calling `multiply` on connected sets of atoms multiple times will produce unpredictable results, as may running other commands after `multiply`.

The enhanced atoms are duplicated exactly in the structure—they have the same segment, residue, and atom names. They are distinguished only by the value of the B (beta) column in the pdb file, which is 0 for normal atoms and varies from 1 to the number of copies created for enhanced atoms. The enhanced atoms may be easily observed in VMD with the atom selection `beta != 0`.

6.10.2 Simulation

In practice, LES is a simple method used to increase sampling; no special output is generated. The following parameters are used to enable LES:

- `les` < is locally enhanced sampling active? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether or not LES is active.

`lesFactor` < number of LES images to use >
Acceptable Values: positive integer equal to the number of images present
Description: This should be equal to the factor used in `multiply` when creating the structure. The interaction potentials for images is divided by `lesFactor`.

- `lesReduceTemp` < reduce enhanced atom temperature? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Enhanced atoms experience interaction potentials divided by `lesFactor`. This allows them to enter regions that would not normally be thermally accessible. If this is not desired, then the temperature of these atoms may be reduced to correspond with the reduced potential. This option affects velocity initialization, reinititialization, reassignment, and the target temperature for langevin dynamics. Langevin dynamics is recommended with this option, since in a constant energy simulation energy will flow into the enhanced degrees of freedom until they reach thermal equilibrium with the rest of the system. The reduced temperature atoms will have reduced velocities as well, unless `lesReduceMass` is also enabled.

- `lesReduceMass` < reduce enhanced atom mass? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Used with `lesReduceTemp` to restore velocity distribution to enhanced atoms. If used alone, enhanced atoms would move faster than normal atoms, and hence a smaller timestep would be required.

-

- `lesFile` < PDB file containing LES flags >
  Acceptable Values: UNIX filename
  Default Value: `coordinates`
  Description: PDB file to specify the LES image number of each atom. If this parameter is not specified, then the PDB file containing initial coordinates specified by `coordinates` is used.

- `lesCol` < column of PDB file containing LES flags >
  Acceptable Values: `X`, `Y`, `Z`, `O`, or `B`
  Default Value: `B`
  Description: Column of the PDB file to specify the LES image number of each atom. This parameter may specify any of the floating point fields of the PDB file, either X, Y, Z, occupancy, or beta-coupling (temperature-coupling). A value of 0 in this column indicates that the atom is not enhanced. Any other value should be a positive integer less than `lesFactor`.

6.11 Pair Interaction Calculations

NAMD supportes the calculation of interaction energy calculations between two groups of atoms. When enabled, pair interaction information will be calculated and printed in the standard output file on its own line at the same frequency as energy output. The format of the line is `PAIR INTERACTION: STEP:` *step* `VDW_FORCE:` *fx fy fz* `ELECT_FORCE:` *fx fy fz*. The displayed force is the force on atoms in group 1 and is units of kcal/mol/Å.

For trajectory analysis the recommended way to use this set of options is to use the NAMD Tcl scripting interface as described in Sec. 2.2.2 to run for 0 steps, so that NAMD prints the energy without performing any dynamics.

- `pairInteraction` < is pair interaction calculation active? >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: Specifies whether pair interaction calculation is active.

- `pairInteractionFile` < PDB file containing pair interaction flags >
  Acceptable Values: UNIX filename
  Default Value: `coordinates`
  Description: PDB file to specify atoms to use for pair interaction calculations. If this parameter is not specified, then the PDB file containing initial coordinates specified by `coordinates` is used.

- `pairInteractionCol` < column of PDB file containing pair interaction flags >
  Acceptable Values: `X`, `Y`, `Z`, `O`, or `B`
  Default Value: `B`
  Description: Column of the PDB file to specify which atoms to use for pair interaction calculations. This parameter may specify any of the floating point fields of the PDB file, either X, Y, Z, occupancy, or beta-coupling (temperature-coupling).

- `pairInteractionSelf` < compute within-group interactions instead of bewteen groups >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: When active, NAMD will compute bonded and nonbonded interactions only for atoms within group 1.

- `pairInteractionGroup1` < Flag to indicate atoms in group 1? >
  Acceptable Values: integer
  Description:

- `pairInteractionGroup2` < Flag to indicate atoms in group 2? >
  Acceptable Values: integer
  Description: These options are used to indicate which atoms belong to each interaction group. Atoms with a value in the column specified by `pairInteractionCol` equal to `pairInteractionGroup1` will be assigned to group 1; likewise for group 2.

6.12 Pressure Profile Calculations

NAMD supports the calculation of lateral pressure profiles as a function of the z-coordinate in the system. The algorithm is based on that of Lindahl and Edholm (JCP 2000), with modifications to enable Ewald sums based on Sonne et al (JCP 122, 2005).

The simulation space is partitioned into slabs, and half the virial due to the interaction between two particles is assigned to each of the slabs containing the particles. This amounts to employing the Harasima contour, rather than the Irving-Kirkwood contour, as was done in NAMD 2.5. The diagonal components of the pressure tensor for each slab, averaged over

all timesteps since the previous output, are recorded in the NAMD output file. The units of pressure are the same as in the regular NAMD pressure output; i.e., bar.

The total virial contains contributions from up to four components: kinetic energy, bonded interactions, nonbonded interactions, and an Ewald sum. All but the Ewald sums are computed online during a normal simulation run (this is a change from NAMD 2.5, when nonbonded contributions to the Ewald sum were always computed offline). If the simulations are performed using PME, the Ewald contribution should be estimated using a separate, offline calculation based on the saved trajectory files. The nonbonded contribution using a cutoff different from the one used in the simulation may also be computed offline in the same fashion as for Ewald, if desired.

Pressure profile calculations may be performed in either constant volume or constant pressure conditions. If constant pressure is enabled, the slabs thickness will be rescaled along with the unit cell; the dcdUnitCell option will also be switched on so that unit cell information is stored in the trajectory file.

NAMD 2.6 now reports the lateral pressure partitioned by interaction type. Three groups are reported: kinetic + rigid bond restraints (referred to as "internal", bonded, and nonbonded. If Ewald pressure profile calculations are active, the Ewald contribution is reported in the nonbonded section, and no other contributions are reported.

NAMD 2.6 also permits the pressure profile to be partitioned by atom type. Up to 15 atom groups may be assigned, and individual contribution of each group (for the "internal" pressures) and the pairwise contributions of interactions within and between groups (for the nonbonded and bonded pressures) are reported in the output file.

- `pressureProfile` < compute pressure profile >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: When active, NAMD will compute kinetic, bonded and nonbonded (but not reciprocal space) contributions to the pressure profile. Results will be recorded in the NAMD output file in lines with the format `PRESSUREPROFILE: ts Axx Ayy Azz Bxx Byy Bzz ...` , where `ts` is the timestep, followed by the three diagonal components of the pressure tensor in the first slab (the slab with lowest z), then the next lowest slab, and so forth. The output will reflect the pressure profile averaged over all the steps since the last output.

  NAMD also reports kinetic, bonded and nonbonded contributions separately, using the same format as the total pressure, but on lines beginning with `PPROFILEINTERNAL`, `PPROFILEBONDED`, and `PPROFILENONBONDED`.

- `pressureProfileSlabs` < Number of slabs in the spatial partition >
  Acceptable Values: Positive integer
  Default Value: 10
  Description: NAMD divides the entire periodic cell into horizontal slabs of equal thickness; `pressureProfileSlabs` specifies the number of such slabs.

- `pressureProfileFreq` < How often to output pressure profile data >
  Acceptable Values: Positive integer
  Default Value: 1
  Description: Specifies the number of timesteps between output of pressure profile data.

- `pressureProfileEwald` < Enable pressure profile Ewald sums >
  Acceptable Values: `on` or `off`
  Default Value: `off`
  Description: When enabled, only the Ewald contribution to the pressure profile will be computed. For trajectory analysis the recommended way to use this option is to use the NAMD Tcl scripting interface as described in Sec. 2.2.2 to run for 0 steps, so that NAMD prints the pressure profile without performing any dynamics.

  The Ewald sum method is as described in Sonne et al. (JCP 122, 2005). The number of k vectors to use along each periodic cell dimension is specified by the `pressureProfileEwald`n parameters described below.

- `pressureProfileEwaldX` < Ewald grid size along X >
  Acceptable Values: Positive integer
  Default Value: 10
  Description:

- `pressureProfileEwaldY` < Ewald grid size along Y >
  Acceptable Values: Positive integer
  Default Value: 10
  Description:

- `pressureProfileEwaldZ` < Ewald grid size along Z >
  Acceptable Values: Positive integer
  Default Value: 10
  Description:

- `pressureProfileAtomTypes` < Number of atom type partitions >
  Acceptable Values: Positive integer
  Default Value: 1
  Description: If `pressureProfileAtomTypes` is greater than 1, NAMD will calculate the separate contributions of each type of atom to the internal, bonded, nonbonded, and total pressure. In the case of the internal contribution, there will be n pressure profile data sets reported on each `PPROFILEINTERNAL` line, where n is the number of atom types. All the partial pressures for atom type 1 will be followed by those for atom type 2, and so forth. The other three pressure profile reports will contain $n(n+1)/2$ data sets. For example, if there are $n = 3$ atom types, the six data sets arising from the three inter-partition and the three intra-partition interactions will be reported in the following order: 1–1, 1–2, 1–3, 2–2, 2–3, 3–3. The total pressure profile, reported on the `PRESSUREPROFILE` line, will contain the internal contributions in the data sets corresponding to 1–1, 2–2, etc.

- `pressureProfileAtomTypesFile` < Atom type partition assignments >
  Acceptable Values: PDB file
  Default Value: coordinate file
  Description: If `pressureProfileAtomTypes` is greater than 1, NAMD will assign atoms to types based on the corresponding value in `pressureProfileAtomTypesCol`. The type for each atom must be strictly less than `pressureProfileAtomTypes`!

- `pressureProfileAtomTypesCol` < `pressureProfileAtomTypesFile` PDB column >
  Acceptable Values: PDB file

Default Value: B
Description:

Here is an example snippet from a NAMD input that can be used to compute the Ewald component of the pressure profile. It assumes that the coordinates were saved in the dcd file `pp03.dcd`) every 500 timesteps.

```
Pme             on
PmeGridSizeX    64
PmeGridSizeY    64
PmeGridSizeZ    64

exclude         scaled1-4
1-4scaling      1.0

switching on
switchdist      9
cutoff          10
pairlistdist    11

pressureProfile        on
pressureProfileSlabs   30
pressureProfileFreq    100
pressureProfileAtomTypes 6
pressureProfileAtomTypesFile atomtypes.pdb
pressureProfileEwald  on
pressureProfileEwaldX  16
pressureProfileEwaldY  16
pressureProfileEwaldZ  16

set ts 0
firstTimestep $ts

coorfile open dcd pp03.dcd
while { [coorfile read] != -1 } {
  incr ts 500
  firstTimestep $ts
  run 0
}
coorfile close
```

6.13 Replica Exchange Simulations

The `lib/replica/` directory contains Tcl scripts that implement replica exchange for NAMD, using a Tcl server and socket connections to drive a separate NAMD process for every replica used in the simulation. Replica exchanges and energies are recorded in the potenergy.dat, realtemp.dat, and targtemp.dat files written in the output directory. These can be viewed with, e.g., "`xmgrace -nxy`

`....potenergy.dat`" There is also a script to load the output into VMD and color each frame according to target temperature. An example simulation folds a 66-atom model of a deca-alanine helix in about 10 ns.

This implementation is designed to be modified by the user to implement exchanges of parameters other than temperature or via other temperature exchange methods. The scripts should provide a good starting point for any simulation method requiring a number of loosely interacting systems.

`replica_exchange.tcl` is the master Tcl script for replica exchange simulations, it is run in `tclsh` *outside of NAMD* and takes a replica exchange config file as an argument:

```
tclsh ../replica_exchange.tcl fold_alanin.conf
tclsh ../replica_exchange.tcl restart_1.conf
```

`replica_exchange.tcl` uses code in `namd_replica_server.tcl`, a general script for driving NAMD slaves, and `spawn_namd.tcl`, a variety of methods for launching NAMD slaves.

`show_replicas.vmd` is a script for loading replicas into VMD; first source the replica exchange conf file and then this script, then repeat for each restart conf file or for example just do "`vmd -e load_all.vmd`". This script will likely destroy anything else you are doing in VMD at the time, so it is best to start with a fresh VMD. `clone_reps.vmd` provides the `clone_reps` commmand to copy graphical representation from the top molecule to all other molecules.

A replica exchange config file should define the following Tcl variables:

- `num_replicas`, the number of replica simulations to use,
- `min_temp`, the lowest replica target temperature,
- `max_temp`, the highest replica target temperature,
- `steps_per_run`, the number of steps between exchange attempts,
- `num_runs`, the number of runs before stopping (should be divisible by `runs_per_frame` × `frames_per_restart`).
- `runs_per_frame`, the number of runs between trajectory outputs,
- `frames_per_restart`, the number of frames between restart outputs,
- `namd_config_file`, the NAMD config file containing all parameters, needed for the simulation except `seed`, `langevin`, `langevinDamping`, `langevinTemp`, `outputEnergies`, `outputname`, `dcdFreq`, `temperature`, `bincoordinates`, `binvelocities`, or `extendedSystem`, which are provided by `replica_exchange.tcl`,
- `output_root`, the directory/fileroot for output files,
- `psf_file`, the psf file for `show_replicas.vmd`,
- `initial_pdb_file`, the initial coordinate pdb file for `show_replicas.vmd`,
- `fit_pdb_file`, the coodinates that frames are fit to by `show_replicas.vmd` (e.g., a folded structure),
- `server_port`, the port to connect to the replica server on, and

- `spawn_namd_command`, a command from `spawn_namd.tcl` and arguments to launch NAMD jobs.

The `lib/replica/example/` directory contains all files needed to fold a 66-atom model of a deca-alanine helix:

- `alanin_base.namd`, basic config options for NAMD,
- `alanin.params`, parameters,
- `alanin.psf`, structure,
- `unfolded.pdb`, initial coordinates,
- `alanin.pdb`, folded structure for fitting in `show_replicas.vmd`,
- `fold_alanin.conf`, config file for `replica_exchange.tcl` script,
- `restart_1.conf`, config file to continue alanin folding another 10 ns, and
- `load_all.vmd`, load all output into VMD and color by target temperature.

The `fold_alanin.conf` config file contains the following settings:

```
set num_replicas 8
set min_temp 300
set max_temp 600
set steps_per_run 1000
set num_runs 10000
set runs_per_frame 10
set frames_per_restart 10
set namd_config_file "alanin_base.namd"
set output_root "output/fold_alanin" ; # directory must exist
set psf_file "alanin.psf"
set initial_pdb_file "unfolded.pdb"
set fit_pdb_file "alanin.pdb"
set namd_bin_dir /Projects/namd2/bin/current/Linux64
set server_port 3177
set spawn_namd_command \
  [list spawn_namd_ssh "cd [pwd]; [file join $namd_bin_dir namd2] +netpoll" \
  [list beirut belfast] ]
```

7 Translation between NAMD and X-PLOR configuration parameters

NAMD was designed to provide many of the same molecular dynamics functions that X-PLOR provides. As such, there are many similarities between the types of parameters that must be passed to both X-PLOR and NAMD. This section describes relations between similar NAMD and X-PLOR parameters.

- **NAMD Parameter:** `cutoff`
  X-PLOR Parameter: `CTOFNB`
  When full electrostatics are not in use within NAMD, these parameters have exactly the same meaning — the distance at which electrostatic and van der Waals forces are truncated. When full electrostatics are in use within NAMD, the meaning is still very similar. The van der Waals force is still truncated at the specified distance, and the electrostatic force is still computed at every timestep for interactions within the specified distance. However, the NAMD integration uses multiple time stepping to compute electrostatic force interactions beyond this distance every `stepspercycle` timesteps.

- **NAMD Parameter:** `vdwswitchdist`
  X-PLOR Parameter: `CTONNB`
  Distance at which the van der Waals switching function becomes active.

- **NAMD Parameter:** `pairlistdist`
  X-PLOR Parameter: `CUTNb`
  Distance within which interaction pairs will be included in pairlist.

- **NAMD Parameter:** `1-4scaling`
  X-PLOR Parameter: `E14Fac`
  Scaling factor for 1-4 pair electrostatic interactions.

- **NAMD Parameter:** `dielectric`
  X-PLOR Parameter: `EPS`
  Dielectric constant.

- **NAMD Parameter:** `exclude`
  X-PLOR Parameter: `NBXMod`
  Both parameters specify which atom pairs to exclude from non-bonded interactions. The ability to ignore explicit exclusions is *not* present within NAMD, thus only positive values of `NBXMod` have NAMD equivalents. These equivalences are

  - `NBXMod=1` is equivalent to `exclude=none` — no atom pairs excluded,
  - `NBXMod=2` is equivalent to `exclude=1-2` — only 1-2 pairs excluded,
  - `NBXMod=3` is equivalent to `exclude=1-3` — 1-2 and 1-3 pairs excluded,
  - `NBXMod=4` is equivalent to `exclude=1-4` — 1-2, 1-3, and 1-4 pairs excluded,
  - `NBXMod`=5 is equivalent to `exclude=scaled1-4` — 1-2 and 1-3 pairs excluded, 1-4 pairs modified.

- **NAMD Parameter:** `switching`
  X-PLOR Parameter: `SHIFt, VSWItch, and TRUNcation`
  Activating the NAMD option `switching` is equivalent to using the X-PLOR options `SHIFt` and `VSWItch`. Deactivating `switching` is equivalent to using the X-PLOR option `TRUNcation`.

- **NAMD Parameter:** `temperature`
  X-PLOR Parameter: `FIRSttemp`
  Initial temperature for the system.

- **NAMD Parameter:** `rescaleFreq`
  X-PLOR Parameter: `IEQFrq`
  Number of timesteps between velocity rescaling.

- **NAMD Parameter:** `rescaleTemp`
  X-PLOR Parameter: `FINAltemp`
  Temperature to which velocities are rescaled.

- **NAMD Parameter:** `restartname`
  X-PLOR Parameter: `SAVE`
  Filename prefix for the restart files.

- **NAMD Parameter:** `restartfreq`
  X-PLOR Parameter: `ISVFrq`
  Number of timesteps between the generation of restart files.

- **NAMD Parameter:** `DCDfile`
  X-PLOR Parameter: `TRAJectory`
  Filename for the position trajectory file.

- **NAMD Parameter:** `DCDfreq`
  X-PLOR Parameter: `NSAVC`
  Number of timesteps between writing coordinates to the trajectory file.

- **NAMD Parameter:** `velDCDfile`
  X-PLOR Parameter: `VELOcity`
  Filename for the velocity trajectory file.

- **NAMD Parameter:** `velDCDfreq`
  X-PLOR Parameter: `NSAVV`
  Number of timesteps between writing velocities to the trajectory file.

- **NAMD Parameter:** `numsteps`
  X-PLOR Parameter: `NSTEp`
  Number of simulation timesteps to perform.

8 Sample configuration files

This section contains some simple example NAMD configuration files to serve as templates.

This file shows a simple configuration file for alanin. It performs basic dynamics with no output files or special features.

```
# protocol params
numsteps        1000

# initial config
coordinates     alanin.pdb
temperature     300K
seed            12345

# output params
outputname      /tmp/alanin
binaryoutput    no

# integrator params
timestep        1.0

# force field params
structure       alanin.psf
parameters      alanin.params
exclude         scaled1-4
1-4scaling      1.0
switching       on
switchdist      8.0
cutoff          12.0
pairlistdist    13.5
stepspercycle   20
```

This file is again for alanin, but shows a slightly more complicated configuration. The system is periodic, a coordinate trajectory file and a set of restart files are produced.

```
# protocol params
numsteps        1000

# initial config
coordinates     alanin.pdb
temperature     300K
seed            12345

# periodic cell
cellBasisVector1   33.0 0 0
cellBasisVector2   0 32.0 0
cellBasisVector3   0 0 32.5

# output params
outputname      /tmp/alanin
binaryoutput    no
DCDfreq         10
restartfreq     100

# integrator params
timestep        1.0

# force field params
structure       alanin.psf
parameters      alanin.params
exclude         scaled1-4
1-4scaling      1.0
switching       on
switchdist      8.0
cutoff          12.0
pairlistdist    13.5
stepspercycle   20
```

This file shows another simple configuration file for alanin, but this time with full electrostatics using PME and multiple timestepping.

```
# protocol params
numsteps        1000

# initial config
coordinates     alanin.pdb
temperature     300K
seed            12345

# periodic cell
cellBasisVector1   33.0 0 0
cellBasisVector2   0 32.0 0
cellBasisVector3   0 0 32.5

# output params
outputname      /tmp/alanin
binaryoutput    no
DCDfreq         10
restartfreq     100

# integrator params
timestep        1.0
fullElectFrequency  4

# force field params
structure       alanin.psf
parameters      alanin.params
exclude         scaled1-4
1-4scaling      1.0
switching       on
switchdist      8.0
cutoff          12.0
pairlistdist    13.5
stepspercycle   20

# full electrostatics
PME             on
PMEGridSizeX    32
PMEGridSizeY    32
PMEGridSizeZ    32
```

This file demonstrates the analysis of a DCD trajectory file using NAMD. The file `pair.pdb` contains the definition of pair interaction groups; NAMD will compute the interaction energy and force between these groups for each frame in the DCD file. It is assumed that coordinate frames were written every 1000 timesteps. See Sec. 6.11 for more about pair interaction calculations.

```
# initial config
coordinates     alanin.pdb
temperature     0

# output params
outputname      /tmp/alanin-analyze
binaryoutput    no

# integrator params
timestep        1.0

# force field params
structure       alanin.psf
parameters      alanin.params
exclude         scaled1-4
1-4scaling      1.0
switching       on
switchdist      8.0
cutoff          12.0
pairlistdist    13.5
stepspercycle   20

# Atoms in group 1 have a 1 in the B column; group 2 has a 2.
pairInteraction on
pairInteractionFile pair.pdb
pairInteractionCol B
pairInteractionGroup1 1
pairInteractionGroup2 2

# First frame saved was frame 1000.
set ts 1000

coorfile open dcd /tmp/alanin.dcd

# Read all frames until nonzero is returned.
while { ![coorfile read] } {
  # Set firstTimestep so our energy output has the correct TS.
  firstTimestep $ts
  # Compute energies and forces, but don't try to move the atoms.
  run 0
```

```
  incr ts 1000
}
coorfile close
```

9 Running NAMD

NAMD runs on a variety of serial and parallel platforms. While it is trivial to launch a serial program, a parallel program depends on a platform-specific library such as MPI to launch copies of itself on other nodes and to provide access to a high performance network such as Myrinet if one is available.

For typical workstations (Windows, Linux, Mac OS X, or other Unix) with only ethernet networking (100 Megabit or Gigabit), NAMD uses the Charm++ native communications layer and the program charmrun to launch namd2 processes for parallel runs (either exclusively on the local machine with the ++local option or on other hosts as specified by a nodelist file). The namd2 binaries for these platforms can also be run directly (known as standalone mode) for single process runs.

For workstation clusters and other massively parallel machines with special high-performance networking, NAMD uses the system-provided MPI library (with a few exceptions) and standard system tools such as mpirun are used to launch jobs. Since MPI libraries are very often incompatible between versions, you will likely need to recompile NAMD and its underlying Charm++ libraries to use these machines in parallel (the provided non-MPI binaries should still work for serial runs.) The provided charmrun program for these platforms is only a script that attempts to translate charmrun options into mpirun options, but due to the diversity of MPI libraries it often fails to work.

9.1 Mac OS X Users Must Install the IBM XL C/C++ Run-Time Library

The IBM XL C/C++ compiler provides a significant performance boost to NAMD on PowerPC G4 and G5 processors. Unfortunately, the runtime library cannot be statically linked, so you must download it from `http://ftp.software.ibm.com/aix/products/ccpp/vacpp-rte-macos/` and install it based on the the README file in that directory. If the library is not installed, running NAMD will product this error:

```
dyld: ./namd2 can't open library: /opt/ibmcmp/lib/libibmc++.A.dylib
```

9.2 Individual Windows, Linux, Mac OS X, or Other Unix Workstations

Individual workstations use the same version of NAMD as workstation networks, but running NAMD is much easier. If your machine has only one processor you can run the namd2 binary directly:

```
namd2 <configfile>
```

For multiprocessor workstations, Windows and Solaris released binaries are based on SMP versions of Charm++ that can run multiple threads. For best performance use one thread per processor with the +p option:

```
namd2 +p<procs> <configfile>
```

Since the SMP versions of NAMD are relatively new, there may be bugs that are only present when running multiple threads. You may want to try running with charmrun (see below) if you experience crashes.

For other multiprocessor workstations the included charmrun program is needed to run multiple namd2 processes. The ++local option is also required to specify that only the local machine is being used:

```
charmrun namd2 ++local +p<procs> <configfile>
```

You may need to specify the full path to the namd2 binary.

9.3 Linux, Mac OS X, or Other Unix Workstation Networks

The same binaries used for individual workstations as described above can be used with charmrun to run in parallel on a workstation network. The only difference is that you must provide a "nodelist" file listing the machines where namd2 processes should run, for example:

```
group main
host brutus
host romeo
```

The "group main" line defines the default machine list. Hosts brutus and romeo are the two machines on which to run the simulation. Note that charmrun may run on one of those machines, or charmrun may run on a third machine. All machines used for a simulation must be of the same type and have access to the same namd2 binary.

By default, the "rsh" command ("remsh" on HPUX) is used to start namd2 on each node specified in the nodelist file. You can change this via the CONV_RSH environment variable, i.e., to use ssh instead of rsh run "setenv CONV_RSH ssh" or add it to your login or batch script. You must be able to connect to each node via rsh/ssh without typing your password; this can be accomplished via a .rhosts files in your home directory, by an /etc/hosts.equiv file installed by your sysadmin, or by a .ssh/authorized_keys file in your home directory. You should confirm that you can run "ssh hostname pwd" (or "rsh hostname pwd") without typing a password before running NAMD. Contact your local sysadmin if you have difficulty setting this up. If you are unable to use rsh or ssh, then add "setenv CONV_DAEMON" to your script and run charmd (or charmd_faceless, which produces a log file) on every node.

You should now be able to try running NAMD as:

```
charmrun namd2 +p<procs> <configfile>
```

If this fails or just hangs, try adding the ++verbose option to see more details of the startup process. You may need to specify the full path to the namd2 binary. Charmrun will start the number of processes specified by the +p option, cycling through the hosts in the nodelist file as many times as necessary. You may list multiprocessor machines multiple times in the nodelist file, once for each processor.

You may specify the nodelist file with the "++nodelist" option and the group (which defaults to "main") with the "++nodegroup" option. If you do not use "++nodelist" charmrun will first look for "nodelist" in your current directory and then ".nodelist" in your home directory.

Some automounters use a temporary mount directory which is prepended to the path returned by the pwd command. To run on multiple machines you must add a "++pathfix" option to your nodelist file. For example:

```
group main ++pathfix /tmp\_mnt /
host alpha1
host alpha2
```

There are many other options to charmrun and for the nodelist file. These are documented at in the Charm++ Installation and Usage Manual available at http://charm.cs.uiuc.edu/manuals/ and a list of available charmrun options is available by running charmrun without arguments.

If your workstation cluster is controlled by a queueing system you will need build a nodelist file in your job script. For example, if your queueing system provides a HOST_FILE environment variable:

```
set NODES = `cat $HOST_FILE`
set NODELIST = $TMPDIR/namd2.nodelist
echo group main >! $NODELIST
foreach node ( $nodes )
  echo host $node >> $NODELIST
end
@ NUMPROCS = 2 * $#NODES
charmrun namd2 +p$NUMPROCS ++nodelist $NODELIST <configfile>
```

Note that NUMPROCS is twice the number of nodes in this example. This is the case for dual-processor machines. For single-processor machines you would not multiply $#NODES by two.

Note that these example scripts and the setenv command are for the csh or tcsh shells. They must be translated to work with sh or bash.

9.4 Windows Workstation Networks

Windows is the same as other workstation networks described above, except that rsh is not available on this platform. Instead, you must run the provided daemon (charmd.exe) on every node listed in the nodelist file. Using charmd_faceless rather than charmd will eliminate consoles for the daemon and node processes.

9.5 BProc-Based Clusters (Scyld and Clustermatic)

Scyld and Clustermatic replace rsh and other methods of launching jobs via a distributed process space. There is no need for a nodelist file or any special daemons, although special Scyld or Clustermatic versions of charmrun and namd2 are required. In order to allow access to files, the first NAMD process must be on the master node of the cluster. Launch jobs from the master node of the cluster via the command:

```
charmrun namd2 +p<procs> <configfile>
```

For best performance, run a single NAMD job on all available nodes and never run multiple NAMD jobs at the same time. You should probably determine the number of processors via a script, for example on Scyld:

```
@ NUMPROCS = `bpstat -u` + 1
charmrun namd2 +p$NUMPROCS <configfile>
```

You may safely suspend and resume a running NAMD job on these clusters using kill -STOP and kill -CONT on the process group. Queueing systems typically provide this functionality, allowing you to suspend a running job to allow a higher priority job to run immediately.

If you want to run multiple NAMD jobs simultaneously on the same cluster you can use the charmrun options ++startpe and ++endpe to specify the range of nodes to use. The master node (-1) is always included unless the ++skipmaster option is given. The requested number of processes are assigned to nodes round-robin as with other network versions, or the ++ppn option can be used to specify the number of processes per node. To limit the master node to one process use the ++singlemaster option.

9.6 SGI Altix

Be sure that the `MPI_DSM_DISTRIBUTE` environment variable is set, then use the Linux-ia64-MPT version of NAMD along with the system mpirun:

```
mpirun -np <procs> <configfile>
```

9.7 Compaq AlphaServer SC

If your machine as a Quadrics interconnect you should use the Elan version of NAMD, other wise select the normal MPI version. In either case, parallel jobs are run using the "prun" command as follows:

```
prun -n <procs> <configfile>
```

There are additional options. Consult your local documentation.

9.8 IBM POWER Clusters

Run the MPI version of NAMD as you would any POE program. The options and environment variables for poe are various and arcane, so you should consult your local documentation for recommended settings. As an example, to run on Blue Horizon one would specify:

```
poe namd2 <configfile> -nodes <procs/8> -tasks_per_node 8
```

9.9 Origin 2000

For small numbers of processors (1-8) use the non-MPI version of namd2. If your stack size limit is unlimited, which DQS may do, you will need to set it with "limit stacksize 64M" to run on multiple processors. To run on ¡procs¿ processors call the binary directly with the +p option:

```
namd2 +p<procs> <configfile>
```

For better performance on larger numbers of processors we recommend that you use the MPI version of NAMD. To run this version, you must have MPI installed. Furthermore, you must set two environment variables to tell MPI how to allocate certain internal buffers. Put the following commands in your .cshrc or .profile file, or in your job file if you are running under a queuing system:

```
setenv MPI_REQUEST_MAX 10240
setenv MPI_TYPE_MAX 10240
```

Then run NAMD with the following command:

```
mpirun -np <procs> namd2 <configfile>
```

9.10 Memory Usage

NAMD has traditionally used less than 100MB of memory even for systems of 100,000 atoms. With the reintroduction of pairlists in NAMD 2.5, however, memory usage for a 100,000 atom system with a 12A cutoff can approach 300MB, and will grow with the cube of the cutoff. This extra memory is distributed across processors during a parallel run, but a single workstation may run out of physical memory with a large system.

To avoid this, NAMD now provides a pairlistMinProcs config file option that specifies the minimum number of processors that a run must use before pairlists will be enabled (on fewer processors small local pairlists are generated and recycled rather than being saved, the default is "pairlistMinProcs 1"). This is a per-simulation rather than a compile time option because memory usage is molecule-dependent.

9.11 Improving Parallel Scaling

While NAMD is designed to be a scalable program, particularly for simulations of 100,000 atoms or more, at some point adding additional processors to a simulation will provide little or no extra performance. If you are lucky enough to have access to a parallel machine you should measure NAMD's parallel speedup for a variety of processor counts when running your particular simulation. The easiest and most accurate way to do this is to look at the "Benchmark time:" lines that are printed after 20 and 25 cycles (usually less than 500 steps). You can monitor performance during the entire simulation by adding "outputTiming *steps*" to your configuration file, but be careful to look at the "wall time" rather than "CPU time" fields on the "TIMING:" output lines produced. For an external measure of performance, you should run simulations of both 25 and 50 cycles (see the stepspercycle parameter) and base your estimate on the additional time needed for the longer simulation in order to exclude startup costs and allow for initial load balancing.

We provide both standard (UDP) and new TCP based precompiled binaries for Linux clusters. We have observed that the TCP version is better on our dual processor clusters with gigabit ethernet while the basic UDP version is superior on our single processor fast ethernet cluster. When using the UDP version with gigabit you can add the +giga option to adjust several tuning parameters. Additional performance may be gained by building NAMD against an SMP version of Charm++ such as net-linux-smp or net-linux-smp-icc. This will use a communication thread for each process to respond to network activity more rapidly. For dual processor clusters we have found it that running two separate processes per node, each with its own communication thread, is faster than using the charmrun ++ppn option to run multiple worker threads. However, we have observed that when running on a single hyperthreaded processor (i.e., a newer Pentium 4) there is an additional 15% boost from running standalone with two threads (namd2 +p2) beyond running two processors (charmrun namd2 ++local +p2). For a cluster of single processor hyperthreaded machines an SMP version should provide very good scaling running one process per node since the communication thread can run very efficiently on the second virtual processor. We are unable to ship an SMP build for Linux due to portability problems with the Linux pthreads implementation needed by

Charm++. The new NPTL pthreads library in RedHat 9 fixes these problems so an SMP port can become the standard shipping binary version in the future.

On some large machines with very high bandwidth interconnects you may be able to increase performance for PME simulations by adding either "+strategy USE_MESH" or "+strategy USE_GRID" to the command line. These flags instruct the Charm++ communication optimization library to reduce the number of messages sent during PME 3D FFT by combining data into larger messages to be transmitted along each dimension of either a 2D mesh or a 3D grid, respectively. While reducing the number of messages sent per processor from N to 2*sqrt(N) or 3*cbrt(N), the total amount of data transmitted for the FFT is doubled or tripled.

Extremely short cycle lengths (less than 10 steps) will also limit parallel scaling, since the atom migration at the end of each cycle sends many more messages than a normal force evaluation. Increasing pairlistdist from, e.g., cutoff + 1.5 to cutoff + 2.5, while also doubling stepspercycle from 10 to 20, may increase parallel scaling, but it is important to measure. When increasing stepspercycle, also try increasing pairlistspercycle by the same proportion.

NAMD should scale very well when the number of patches (multiply the dimensions of the patch grid) is larger or rougly the same as the number of processors. If this is not the case, it may be possible to improve scaling by adding "twoAwayX yes" to the config file, which roughly doubles the number of patches. (Similar options twoAwayY and twoAwayZ also exist, and may be used in combination, but this greatly increases the number of compute objects. twoAwayX has the unique advantage of also improving the scalability of PME.)

10 NAMD Availability and Installation

NAMD is distributed freely for non-profit use. NAMD 2.6 is based on the Charm++ messaging system and the Converse communication layer (`http://charm.cs.uiuc.edu/`) which have been ported to a wide variety of parallel platforms. This section describes how to obtain and install NAMD 2.6.

10.1 How to obtain NAMD

NAMD may be downloaded from `http://www.ks.uiuc.edu/Research/namd/`. You will be required to provide minimal registration information and agree to a license before receiving access to the software. Both source and binary distributions are available.

10.2 Platforms on which NAMD will currently run

NAMD should be portable to any parallel platform with a modern C++ compiler to which Charm and Converse have been ported. Precompiled NAMD 2.6 binaries are available for the following platforms:

- Windows (NT, etc.) on x86 processors
- Mac OS X (also called Darwin) on PowerPC and Intel processors
- AIX on POWER processors (with and without MPI)
- Linux on x86, x86-64 (AMD64/EMT64) and Itanium (IA64) processors
- Scyld Beowulf on x86 processors
- Clustermatic 4/5 on x86 processors
- Solaris on Sparc processors (with and without MPI)
- Tru64 Unix on Alpha processors (with and without MPI)
- Compaq AlphaServer SC (using the Quadrics Elan library)
- SGI Origin 2000 (with and without MPI)
- SGI Altix (with MPI)

10.3 Compiling NAMD

We provide complete and optimized binaries for all platforms to which NAMD has been ported. It should not be necessary for you to compile NAMD unless you wish to add or modify features or to improve performance by using an MPI library that takes advantage of special networking hardware.

Directions for compiling NAMD are contained in the release notes, which are available from the NAMD web site `http://www.ks.uiuc.edu/Research/namd/` and are included in all distributions.

10.4 Documentation

All available NAMD documentation is available for download without registration via the NAMD web site `http://www.ks.uiuc.edu/Research/namd/`.

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