2.5 General minimization and dynamics parameters

Each of the variables listed below is input in a namelist statement with the namelist identifier

&cntrl. You can enter the parameters in any order, using keyword identifiers. Variables that are

not given in the namelist input retain their default values. Support for namelist input is included

in almost all current Fortran compilers, and is a standard feature of Fortran 90. A detailed

description of the namelist convention is given in Appendix A.

In general, namelist input consists of an arbitrary number of comment cards, followed by a

record whose first seven characters after a " &" (e.g. " &cntrl ") name a group of variables that

can be set by name. This is followed by statements of the form " maxcyc=500, diel=2.0, ... ",

and is concluded by an " / " token. The first line of input contains a title, which is then followed

by the &cntrl namelist. Note that the first character on each line of a namelist block must be a

blank.

Some of the options and variables are much more important, and commonly modified, than

are others. We have denoted the "common" options by printing them in boldface below. In

general, you can skip reading about the non-bold options on a first pass, and you should change

these from their defaults only if you think you know what you are doing.

2.5.1 General flags describing the calculation

imin

Flag to run minimization

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= 0 (default) Run molecular dynamics without any minimization.

= 1 Perform an energy minimization.

= 5 Read in a trajectory for analysis.

Although sander will write energy information in the output files (using ntpr),

it is often desirable to calculate the energies of a set of structures at a later

point. In particular, one may wish to post-process a set of structures using a

different energy function than was used to generate the structures. A exam-

ple of this is MM-PBSA analysis, where the explicit water is removed and

replaced with a continuum model.

If imin is set to 5, sander will expect to read a trajectory file (the “inptraj”

argument, specified using -y on the command line), and will perform the

functions described in the mdin file (e.g., an energy minimization) for each

of the structures in this file. The final structure from each minimization will

be written out to the normal mdcrd file. If you wish to read in a binary (i.e.,

NetCDF format) trajectory, be sure to set ioutfm to 1 (see below). Note that

this will result in the output trajectory having NetCDF format as well.

For example, when imin = 5 and maxcyc = 1000, sander will minimize each

structure in the trajectory for 1000 steps and write a minimized coordinate set

for each frame to the mdcrd file. If maxcyc = 1, the output file can be used to

extract the energies of each of the coordinate sets in the inptraj file.

Trajectories containing box coordinates can now be post-processed. In order

to read trajectories with box coordinates, ntb should be greater than 0.

IMPORTANT CAVEAT: The input coordinate file used (-c <inpcrd>) should

be the same as the input coordinate file used to generate the original trajectory.

This is because sander sets up parameters for PME from the box coordinates

in the input coordinate file.

nmropt

= 0 (default) No nmr-type analysis will be done.

= 1 NMR restraints and weight changes will be read.

= 2 NMR restraints, weight changes, NOESY volumes, chemical shifts and resid-

ual dipolar restraints will be read.

2.5.2 Nature and format of the input

ntx

Option to read the initial coordinates, velocities and box size from the inpcrd file.

Either 1 or 2 must be used when one is starting from minimized or model-built

coordinates. If an MD restrt file is used as inpcrd, then options 4-7 may be used.

Only options 1 and 5 are in common use.

= 1 (default) Coordinates, but no velocities, will be read; a formatted (ASCII) co-

ordinate file is expected.

= 2 Coordinates, but no velocities, will be read; an unformatted (binary) coordi-

nate file is expected.

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2.5 General minimization and dynamics parameters

= 4 Coordinates and velocities will be read; an unformatted coordinate file is ex-

pected.

= 5 Coordinates and velocities will be read; a formatted (ASCII) coordinate file is

expected. Box information will be read if ntb > 0. The velocity information

will only be used if irest = 1 (see below).

= 6 Coordinates, velocities and box information will be read; an unformatted co-

ordinate file is expected.

irest

Flag to restart a simulation.

= 0 (default) Do not restart the simulation; instead, run as a new simulation. Ve-

locities in the input coordinate file, if any, will be ignored, and the time step

count will be set to 0 (unless overridden by t; see below).

= 1 Restart the simulation, reading coordinates and velocities from a previously

saved restart file. The velocity information is necessary when restarting, so

ntx (see above) must be 4 or higher if irest = 1.

ntrx

Format of the Cartesian coordinates for restraint from the refc file. Note: the pro-

gram expects the refc file to contain coordinates for all the atoms in the system.

The atoms that are to be restrained are specified by a restraintmask entry in the

&cntrl namelist (see below).

= 0 Unformatted (binary)

= 1 (default) Formatted (ASCII)

2.5.3 Nature and format of the output

ntxo

Format of the final coordinates, velocities, and box size (if constant volume or

pressure run) written to file "restrt".

= 0 Unformatted (no longer recommended or allowed: please use formatted restart

files)

= 1 (default) Formatted (ASCII)

ntpr Every ntpr steps, energy information will be printed in human-readable form to

files "mdout" and "mdinfo". "mdinfo" is closed and reopened each time, so it

always contains the most recent energy and temperature. Default 50.

ntave Every ntave steps of dynamics, running averages of average energies and fluctu-

ations over the last ntave steps will be printed out. A value of 0 disables this

printout. Setting ntave to a value 1/2 or 1/4 of nstlim provides a simple way to look

at convergence during the simulation. Default = 0 (disabled).

ntwr Every ntwr steps during dynamics, the “restrt” file will be written, ensuring that

recovery from a crash will not be so painful. No matter what the value of ntwr, a

restrt file will be written at the end of the run, i.e., after nstlim steps (for dynamics)

or maxcyc steps (for minimization). If ntwr < 0, a unique copy of the file, “re-

strt\_<nstep>”, is written every abs(ntwr) steps. This option is useful if for example

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2 Sander basics

one wants to run free energy perturbations from multiple starting points or save a

series of restrt files for minimization. Default = 500.

iwrap If iwrap = 1, the coordinates written to the restart and trajectory files will be

"wrapped" into a primary box. This means that for each molecule, its periodic

image closest to the middle of the "primary box" (with x coordinates between 0

and a, y coordinates between 0 and b, and z coordinates between 0 and c) will be

the one written to the output file. This often makes the resulting structures look bet-

ter visually, but has no effect on the energy or forces. Performing such wrapping,

however, can mess up diffusion and other calculations. If iwrap = 0, no wrapping

will be performed, in which case it is typical to use ptraj as a post-processing pro-

gram to translate molecules back to the primary box. For very long runs, setting

iwrap = 1 may be required to keep the coordinate output from overflowing the tra-

jectory and restart file formats, especially if trajectories are written in ASCII format

instead of NetCDF (see also the ioutfm option). Default = 0.

ntwx Every ntwx steps, the coordinates will be written to the mdcrd file. If ntwx = 0, no

coordinate trajectory file will be written. Default = 0.

ntwv Every ntwv steps, the velocities will be written to the mdvel file. If ntwv = 0, no

velocity trajectory file will be written. If ntwv = -1, velocities will be written to

mdcrd, which then becomes a combined coordinate/velocity trajectory file, at the

interval defined by ntwx. This option is available only for binary NetCDF output

(ioutfm = 1). Most users will have no need for a velocity trajectory file and so can

safely leave ntwv at the default. Default = 0.

ntwe Every ntwe steps, the energies and temperatures will be written to file "mden" in a

compact form. If ntwe = 0, no mden file will be written. Default = 0.

ioutfm The format of coordinate and velocity trajectory files (mdcrd, mdvel and inptraj).

As of Amber 9, the binary format used in previous versions is no longer supported;

binary output is now in NetCDF trajectory format. While not the default option,

binary trajectory files have many advantages: they are smaller, higher precision,

much faster to read and write, and able to accept a wider range of coordinate (or

velocity) values than formatted trajectory files.

= 0 (default) Formatted ASCII trajectory

= 1 Binary NetCDF trajectory

ntwprt The number of atoms to include in trajectory files (mdcrd and mdvel). This flag can be

used to decrease the size of the these files, by including only the first part of the system,

which is usually of greater interest (for instance, one might include only the solute and

not the solvent). If ntwprt = 0, all atoms will be included.

= 0 (default) Include all atoms of the system when writing trajectories.

> 0 Include only atoms 1 to ntwprt when writing trajectories.

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2.5 General minimization and dynamics parameters

idecomp Perform energy decomposition according to a chosen scheme. In former distributions

this option was only really useful in conjunction with mm\_pbsa, where it is turned on

automatically if required. Now, a decomposition of ∂V /∂ λ on a per-residue basis in

thermodynamic integration (TI) simulations is also possible.[13] The options are:

= 0 (default) Do not decompose energies.

= 1 Decompose energies on a per-residue basis; 1-4 EEL + 1-4 VDW are added to inter-

nal (bond, angle, dihedral) energies.

= 2 Decompose energies on a per-residue basis; 1-4 EEL + 1-4 VDW are added to EEL

and VDW.

= 3 Decompose energies on a pairwise per-residue basis; otherwise equivalent to ide-

comp = 1. Not available in TI simulations.

= 4 Decompose energies on a pairwise per-residue basis; otherwise equivalent to ide-

comp = 2. Not available in TI simulations.

If energy decomposition is requested, residues may be chosen by the RRES and/or LRES

card. The RES card is used to select the residues about which information is written out.

See chapters 4.1 or D for more information. Use of idecomp > 0 is incompatible with ntr

> 0 or ibelly > 0.

2.5.4 Frozen or restrained atoms

ibelly Flag for belly type dynamics. If set to 1, a subset of the atoms in the system will

be allowed to move, and the coordinates of the rest will be frozen. The moving

atoms are specified bellymask. This option is not available when igb>0. Note also

that this option does not provide any significant speed advantage, and is maintained

primarily for backwards compatibility with older version of Amber. Most applica-

tions should use the ntr variable instead to restrain parts of the system to stay close

to some initial configuration. Default = 0.

ntr Flag for restraining specified atoms in Cartesian space using a harmonic potential,

if ntr > 0. The restrained atoms are determined by the restraintmask string. The

force constant is given by restraint\_wt. The coordinates are read in "restrt" format

from the "refc" file (see NTRX, above). Default = 0.

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restraint\_wt The weight (in kcal/mol − Å ) for the positional restraints. The restraint is of the

form k(∆x)2 , where k is the value given by this variable, and ∆x is the difference

between one of the Cartesian coordinates of a restrained atom and its reference

position. There is a term like this for each Cartesian coordinate of each restrainted

atom.

restraintmask String that specifies the restrained atoms when ntr=1.

bellymask

String that specifies the moving atoms when ibelly=1.

The syntax for both restraintmask and bellymask is given in Section C. Note that

these mask strings are limited to a maximum of 256 characters.

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2.5.5 Energy minimization

maxcyc The maximum number of cycles of minimization. Default = 1.

ncyc If NTMIN is 1 then the method of minimization will be switched from steepest

descent to conjugate gradient after NCYC cycles. Default 10.

ntmin Flag for the method of minimization.

= 0 Full conjugate gradient minimization. The first 4 cycles are steepest descent at

the start of the run and after every nonbonded pairlist update.

= 1 For NCYC cycles the steepest descent method is used then conjugate gradient

is switched on (default).

= 2 Only the steepest descent method is used.

= 3 The XMIN method is used, see Section 4.12.1.

= 4 The LMOD method is used, see Section 4.12.2.

dx0 The initial step length. If the initial step length is too big then will give a huge

energy; however the minimizer is smart enough to adjust itself. Default 0.01.

drms The convergence criterion for the energy gradient: minimization will halt when

the root-mean-square of the Cartesian elements of the gradient is less than DRMS.

Default 1.0E-4 kcal/mole-Å

2.5.6 Molecular dynamics

nstlim Number of MD-steps to be performed. Default 1.

nscm Flag for the removal of translational and rotational center-of-mass (COM) motion

at regular intervals (default is 1000). For non-periodic simulations, after every

NSCM steps, translational and rotational motion will be removed. For periodic

systems, just the translational center-of-mass motion will be removed. This flag is

ignored for belly simulations.

For Langevin dynamics, the position of the center-of-mass of the molecule is re-

set to zero every NSCM steps, but the velocities are not affected. Hence there

is no change to either the translation or rotational components of the momenta.

(Doing anything else would destroy the way in which temperature is regulated in

a Langevin dynamics system.) The only reason to even reset the coordinates is to

prevent the molecule from diffusing so far away from the origin that its coordinates

overflow the format used in restart or trajectory files.

t The time at the start (psec) this is for your own reference and is not critical. Start

time is taken from the coordinate input file if IREST=1. Default 0.0.

dt The time step (psec). Recommended MAXIMUM is .002 if SHAKE is used, or

.001 if it isn’t. Note that for temperatures above 300K, the step size should be

reduced since greater temperatures mean increased velocities and longer distance

traveled between each force evaluation, which can lead to anomalously high ener-

gies and system blowup. Default 0.001.

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2.5 General minimization and dynamics parameters

nrespa

This variable allows the user to evaluate slowly-varying terms in the force field

less frequently. For PME, "slowly-varying" (now) means the reciprocal sum. For

generalized Born runs, the "slowly-varying" forces are those involving derivatives

with respect to the effective radii, and pair interactions whose distances are greater

than the "inner" cutoff, currently hard-wired at 8 Å. If NRESPA>1 these slowly-

varying forces are evaluated every nrespa steps. The forces are adjusted appropri-

ately, leading to an impulse at that step. If nrespa\*dt is less than or equal to 4 fs

the energy conservation is not seriously compromised. However if nrespa\*dt > 4

fs the simulation becomes less stable. Note that energies and related quantities are

only accessible every nrespa steps, since the values at other times are meaningless.

2.5.7 Temperature regulation

ntt

Switch for temperature scaling. Note that setting ntt=0 corresponds to the micro-

canonical (NVE) ensemble (which should approach the canonical one for large

numbers of degrees of freedom). Some aspects of the "weak-coupling ensemble"

(ntt=1) have been examined, and roughly interpolate between the microcanonical

and canonical ensembles.[14, 15]The ntt=2 and 3 options correspond to the canon-

ical (constant T) ensemble.

= 0 Constant total energy classical dynamics (assuming that ntb<2, as should

probably always be the case when ntt=0).

= 1 Constant temperature, using the weak-coupling algorithm.[16] A single scal-

ing factor is used for all atoms. Note that this algorithm just ensures that the

total kinetic energy is appropriate for the desired temperature; it does nothing

to ensure that the temperature is even over all parts of the molecule. Atomic

collisions will tend to ensure an even temperature distribution, but this is not

guaranteed, and there are many subtle problems that can arise with weak tem-

perature coupling.[17] Using ntt=1 is especially dangerous for generalized

Born simulations, where there are no collisions with solvent to aid in ther-

malization.) Other temperature coupling options (especially ntt=3) should be

used instead.

= 2 Andersen temperature coupling scheme,[18] in which imaginary "collisions"

randomize the velocities to a distribution corresponding to temp0 every vrand

steps. Note that in between these "massive collisions", the dynamics is New-

tonian. Hence, time correlation functions (etc.) can be computed in these

sections, and the results averaged over an initial canonical distribution. Note

also that too high a collision rate (too small a value of vrand) will slow down

the speed at which the molecules explore configuration space, whereas too

low a rate means that the canonical distribution of energies will be sampled

slowly. A discussion of this rate is given by Andersen.[19]

= 3 Use Langevin dynamics with the collision frequency γ given by gamma\_ln,

discussed below. Note that when γ has its default value of zero, this is the

same as setting ntt = 0. Since Langevin simulations are highly susceptible to

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"synchronization" artifacts,[20, 21] you should explicitly set the ig variable

(described below) to a different value at each restart of a given simulation.

temp0 Reference temperature at which the system is to be kept, if ntt > 0. Note that for

temperatures above 300K, the step size should be reduced since increased distance

traveled between evaluations can lead to SHAKE and other problems. Default 300.

temp0les This is the target temperature for all LES particles (see Chapter 6). If temp0les<0,

a single temperature bath is used for all atoms, otherwise separate thermostats

are used for LES and non-LES particles. Default is -1, corresponding to a sin-

gle (weak-coupling) temperature bath.

tempi Initial temperature. For the initial dynamics run, (NTX .lt. 3) the velocities are

assigned from a Maxwellian distribution at TEMPI K. If TEMPI = 0.0, the veloci-

ties will be calculated from the forces instead. TEMPI has no effect if NTX .gt. 3.

Default 0.0.

ig The seed for the pseudo-random number generator. The MD starting velocity is

dependent on the random number generator seed if NTX .lt. 3 .and. TEMPI .ne.

0.0. The value of this seed also affects the set of pseudo-random values used for

Langevin dynamics or Andersen coupling, and hence should be set to a different

value on each restart if ntt = 2 or 3. Default 71277. If ig=-1, the random seed will

be based on the current date and time, and hence will be different for every run.

It is recommended that, unless you specifically desire reproducibility, that you set

ig=-1 for all runs involving ntt=2 or 3.

tautp Time constant, in ps, for heat bath coupling for the system, if ntt = 1. Default is 1.0.

Generally, values for TAUTP should be in the range of 0.5-5.0 ps, with a smaller

value providing tighter coupling to the heat bath and, thus, faster heating and a

less natural trajectory. Smaller values of TAUTP result in smaller fluctuations in

kinetic energy, but larger fluctuations in the total energy. Values much larger than

the length of the simulation result in a return to constant energy conditions.

gamma\_ln The collision frequency γ, in ps−1 , when ntt = 3. A simple Leapfrog integrator is

used to propagate the dynamics, with the kinetic energy adjusted to be correct for

the harmonic oscillator case.[22, 23] Note that it is not necessary that γ approxi-

mate the physical collision frequency, which is about 50 ps−1 for liquid water. In

fact, it is often advantageous, in terms of sampling or stability of integration, to use

much smaller values, around 2 to 5 ps−1 .[23, 24] Default is 0.

vrand If vrand>0 and ntt=2, the velocities will be randomized to temperature TEMP0

every vrand steps.

vlimit If not equal to 0.0, then any component of the velocity that is greater than abs(VLIMIT)

will be reduced to VLIMIT (preserving the sign). This can be used to avoid occa-

sional instabilities in molecular dynamics runs. VLIMIT should generally be set to

a value like 20 (the default), which is well above the most probable velocity in a

Maxwell-Boltzmann distribution at room temperature. A warning message will be

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2.5 General minimization and dynamics parameters

printed whenever the velocities are modified. Runs that have more than a few such

warnings should be carefully examined.

2.5.8 Pressure regulation

In "constant pressure" dynamics, the volume of the unit cell is adjusted (by small amounts

on each step) to make the computed pressure approach the target pressure, pres0. Equilibration

with ntp > 0 is generally necessary to adjust the density of the system to appropriate values.

Note that fluctuations in the instantaneous pressure on each step will appear to be large (several

hundred bar), but the average value over many steps should be close to the target pressure.

Pressure regulation only applies when Constant Pressure periodic boundary conditions are used

(ntb = 2). Pressure coupling algorithms used in Amber are of the "weak-coupling" variety,

analogous to temperature coupling.[16] Please note: in general you will need to equilibrate

the temperature to something like the final temperature using constant volume (ntp=0) before

switching on constant pressure simulations to adjust the system to the correct density. If you

fail to do this, the program will try to adjust the density too quickly, and bad things (such as

SHAKE failures) are likely to happen.

ntp

Flag for constant pressure dynamics. This option should be set to 1 or 2 when

Constant Pressure periodic boundary conditions are used (NTB = 2).

= 0 No pressure scaling (Default)

= 1 md with isotropic position scaling

= 2 md with anisotropic (x-,y-,z-) pressure scaling: this should only be used with

orthogonal boxes (i.e. with all angles set to 90 o ). Anisotropic scaling is

primarily intended for non-isotropic systems, such as membrane simulations,

where the surface tensions are different in different directions; it is generally

not appropriate for solutes dissolved in water.

= 3 md with semiisotropic pressure scaling: this is only available with constant

surface tension (csurften > 0) and orthogonal boxes. This links the pressure

coupling in the two directions tangential to the interface.

pres0 Reference pressure (in units of bars, where 1 bar ≈ 0.987 atm) at which the system

is maintained ( when NTP > 0). Default 1.0.

comp compressibility of the system when NTP > 0. The units are in 1.0 × 10-6 bar-1 ; a

value of 44.6 (default) is appropriate for water.

taup Pressure relaxation time (in ps), when NTP > 0. The recommended value is be-

tween 1.0 and 5.0 psec. Default value is 1.0, but larger values may sometimes be

necessary (if your trajectories seem unstable).

2.5.8.1 Surface tension regulation

Constant surface tension is used in statistical ensembles for simulating liquid interfaces. This

is primarily intended for lipid membrane simulations with two or more interfaces. Constant

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surface tension is only available for simulations with anisotropic pressure or semiisotropic scal-

ing. This algorithm is an extension to the Berendsen pressure scaling algorithm that adjusts the

tangential pressure evaluation in order to maintain a “constant” surface tension [25]. Since the

surface tension is a function of the pressure tensor, fluctuations of the surface tension will be

large.

In order to use constant surface tension, periodic boundary conditions (ntb = 2), anisotropic

or semiisotropic pressure scaling (ntp = 2 or ntp =3), and an orthogonal box must be used.

csurften

Flag for constant surface tension dynamics.

= 0 No constant surface tension (default)

= 1 Constant surface tension with interfaces in the yz plane

= 2 Constant surface tension with interfaces in the xz plane

= 3 Constant surface tension with interfaces in the xy plane

gamma\_ten Surface tension value in units of dyne/cm. Default value is 0.0 dyne/cm.

ninterface Number of interfaces in the periodic box. There must be at least two interfaces in

the periodic box. Two interfaces is appropriate for a lipid bilayer system and is the

default value.

2.5.9 SHAKE bond length constraints

ntc

Flag for SHAKE to perform bond length constraints.[26] (See also NTF in the Po-

tential function section. In particular, typically NTF = NTC.) The SHAKE option

should be used for most MD calculations. The size of the MD timestep is deter-

mined by the fastest motions in the system. SHAKE removes the bond stretching

freedom, which is the fastest motion, and consequently allows a larger timestep to

be used. For water models, a special "three-point" algorithm is used.[27] Conse-

quently, to employ TIP3P set NTF = NTC = 2.

Since SHAKE is an algorithm based on dynamics, the minimizer is not aware of

what SHAKE is doing; for this reason, minimizations generally should be carried

out without SHAKE. One exception is short minimizations whose purpose is to

remove bad contacts before dynamics can begin.

For parallel versions of sander only intramolecular atoms can be constrained. Thus,

such atoms must be in the same chain of the originating PDB file.

= 1 SHAKE is not performed (default)

= 2 bonds involving hydrogen are constrained

= 3 all bonds are constrained (not available for parallel or qmmm runs in sander)

tol Relative geometrical tolerance for coordinate resetting in shake. Recommended

maximum: <0.00005 Angstrom Default 0.00001.

jfastw Fast water definition flag. By default, the system is searched for water residues,

and special routines are used to SHAKE these systems.[27]

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2.5 General minimization and dynamics parameters

= 0 Normal operation. Waters are identified by the default names (given below),

unless they are redefined, as described below.

= 4 Do not use the fast SHAKE routines for waters.

The following variables allow redefinition of the default residue and atom names

used by the program to determine which residues are waters.

WATNAM The residue name the program expects for water. Default ’WAT ’.

OWTNM The atom name the program expects for the oxygen of water. Default ’O

’.

HWTNM1 The atom name the program expects for the 1st H of water. Default ’H1

’.

HWTNM2 The atom name the program expects for the 2nd H of water. Default

’H2 ’.

noshakemask String that specifies atoms that are not to be shaken (assuming that ntc>1). Any

bond that would otherwise be shaken by virtue of the ntc flag, but which involves an

atom flagged here, will \*not\* be shaken. The syntax for this string is given in Chap.

13.5. Default is an empty string, which matches nothing. A typical use would be

to remove SHAKE constraints from all or part of a solute, while still shaking rigid

water models like TIPnP or SPC/E. Another use would be to turn off SHAKE

constraints for the parts of the system that are being changed with thermodynamic

integration, or which are the EVB or quantum regions of the system.

If this option is invoked, then all parts of the potential must be evaluated, that is,

ntf must be one. The code enforces this by setting ntf to 1 when a noshakemask

string is present in the input.

If you want the noshakemask to apply to all or part of the water molecules, you must

also set jfastw=4, to turn off the special code for water SHAKE. (If you are not

shaking waters, you presumably also want to issue the "set default FlexibleWater

on" command in LEaP; see that chapter for more information.)

2.5.10 Water cap

ivcap

Flag to control cap option. The "cap" refers to a spherical portion of water centered

on a point in the solute and restrained by a soft half-harmonic potential. For the

best physical realism, this option should be combined with igb=10, in order to

include the reaction field of waters that are beyond the cap radius.

= 0 Cap will be in effect if it is in the prmtop file (default).

= 1 With this option, a cap can be excised from a larger box of water. For this,

cutcap (i.e., the radius of the cap), xcap, ycap, and zcap (i.e., the location

of the center of the cap) need to be specified in the &cntrl namelist. Note

that the cap parameters must be chosen such that the whole solute is covered

by solvent. Solvent molecules (and counterions) located outside the cap are

ignored. Although this option also works for minimization and dynamics

calculations in general, it is intended to post-process snapshots in the realm

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of MM-PBSA to get a linear-response approximation of the solvation free

energy, output as ’Protein-solvent interactions’.

= 2 Cap will be inactivated, even if parameters are present in the prmtop file.

= 5 With this option, a shell of water around a solute can be excised from a larger

box of water. For this, cutcap (i.e., the thickness of the shell) needs to be

specified in the &cntrl namelist. Solvent molecules (and counterions) located

outside the cap are ignored. This option only works for a single-step mini-

mization. It is intended to post-process snapshots in the realm of MM-PBSA

to get a linear-response approximation of the solvation free energy, output as

’Protein-solvent interactions’.

fcap The force constant for the cap restraint potential.

cutcap Radius of the cap, if ivcap=1 is used.

xcap,ycap,zcap Location of the cap center, if ivcap=1 is used.

2.5.11 NMR refinement options

(Users to should consult the section NMR refinement to see the context of how the following

parameters would be used.)

iscale Number of additional variables to optimize beyond the 3N structural parameters.

(Default = 0). At present, this is only used with residual dipolar coupling and CSA

or pseudo-CSA restraints.

noeskp The NOESY volumes will only be evaluated if mod(nstep, noeskp) = 0; otherwise

the last computed values for intensities and derivatives will be used. (default = 1,

i.e. evaluate volumes at every step)

ipnlty This parameter determines the the functional form of the penalty function for

NOESY volume and chemical shift restraints.

= 1 the program will minimize the sum of the absolute values of the errors; this is

akin to minimizing the crystallographic R-factor (default).

= 2 the program will optimize the sum of the squares of the errors.

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= 3 For NOESY intensities, the penalty will be of the form awt[Ic

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−Io ]2 . Chem-

ical shift penalties will be as for ipnlty=1.

mxsub Maximum number of submolecules that will be used. This is used to determine

how much space to allocate for the NOESY calculations. Default 1.

scalm "Mass" for the additional scaling parameters. Right now they are restricted to all

have the same value. The larger this value, the slower these extra variables will

respond to their environment. Default 100 amu.

pencut In the summaries of the constraint deviations, entries will only be made if the

penalty for that term is greater than PENCUT. Default 0.1.

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tausw

For noesy volume calculations (NMROPT = 2), intensities with mixing times less

that TAUSW (in seconds) will be computed using perturbation theory, whereas

those greater than TAUSW will use a more exact theory. See the theory section (be-

low) for details. To always use the "exact" intensities and derivatives, set TAUSW

= 0.0; to always use perturbation theory, set TAUSW to a value larger than the

largest mixing time in the input. Default is TAUSW of 0.1 second, which should

work pretty well for most systems.

2.5.12 EMAP constraints

EMAP constraints are used to perform targeted conformational search(TCS). EMAP uses

maps to define conformation targets and induce simulation systems to the target conforma-

tions. The constraint map can be either obtained from electron microscopy experiements or

from know protein structures, or from initial simulation coordinates. EMAP can be used to do

rigid docking of molecules into maps and to do flexible fitting to obtain conformations defined

by experimental maps. EMAP can also be used to mantain internal conformations of protein

domains when studying large scale conformational change. Users should consult the section

6.13 to see how to define EMAP constraints.

iemap

Turn on EMAP constrained simulation when iemap>0. (Default = 0). EMAP

constraint information need be input from emap namelists in the input file.

2.6 Potential function parameters

The parameters in this section generally control what sort of force field (or potential function)

is used for the simulation.

2.6.1 Generic parameters

ntf

Force evaluation. Note: If SHAKE is used (see NTC), it is not necessary to calcu-

late forces for the constrained bonds.

= 1 complete interaction is calculated (default)

= 2 bond interactions involving H-atoms omitted (use with NTC=2)

= 3 all the bond interactions are omitted (use with NTC=3)

= 4 angle involving H-atoms and all bonds are omitted

= 5 all bond and angle interactions are omitted

= 6 dihedrals involving H-atoms and all bonds and all angle interactions are omit-

ted

= 7 all bond, angle and dihedral interactions are omitted

= 8 all bond, angle, dihedral and non-bonded interactions are omitted

ntb

This variable controls whether or not periodic boundaries are imposed on the sys-

tem during the calculation of non-bonded interactions. Bonds spanning periodic

boundaries are not yet supported. There is no longer any need to set this variable,

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since it can be determined from igb and ntp parameters. The “proper” default for

ntb is chosen (ntb=0 when igb > 0, ntb=2 when ntp > 0, and ntb=1 otherwise).

This behavior can be overridden by supplying an explicit value, although this is

discouraged to prevent errors. The allowed values for NTB are

= 0 no periodicity is applied and PME is off (default when igb > 0)

= 1 constant volume (default when igb and ntp are both 0)

= 2 constant pressure (default when ntp > 0)

If NTB .NE. 0, there must be a periodic boundary in the topology file. Constant

pressure is not used in minimization (IMIN=1, above).

For a periodic system, constant pressure is the only way to equilibrate density if the

starting state is not correct. For example, the solvent packing scheme used in LEaP

can result in a net void when solvent molecules are subtracted which can aggregate

into "vacuum bubbles" in a constant volume run. Another potential problem are

small gaps at the edges of the box. The upshot is that almost every system needs

to be equilibrated at constant pressure (ntb=2, ntp>0) to get to a proper density.

But be sure to equilibrate first (at constant volume) to something close to the final

temperature, before turning on constant pressure.

dielc Dielectric multiplicative constant for the electrostatic interactions. Default is 1.0.

Please note this is NOT related to dielectric constants for generalized Born or

Poisson-Boltzmann calculations. It should only be used for quasi-vacuum simu-

lations, e.g. where one wants ε = 4r; in this case you would also set the eedmeth

variable as well.

cut This is used to specify the nonbonded cutoff, in Angstroms. For PME, the cutoff is

used to limit direct space sum, and 8.0 is usually a good value. When igb>0, the

cutoff is used to truncate nonbonded pairs (on an atom-by-atom basis); here a larger

value than the default is generally required. A separate parameter (RGBMAX)

controls the maximum distance between atom pairs that will be considered in car-

rying out the pairwise summation involved in calculating the effective Born radii,

see the generalized Born section below.

When igb > 0, the default is 9999.0 (effectively infinite)

When igb==0, the default is 8.0.

nsnb Determines the frequency of nonbonded list updates when igb=0 and nbflag=0;

see the description of nbflag for more information. Default is 25.

ipol When set to 1, use a polarizable force field. See Section 2.6.5 for more information.

Default is 0.

ifqnt Flag for QM/MM run; if set to 1, you must also include a &qmmm namelist. See

Section 6.4 for details on this option. Default is 0.

igb Flag for using the generalized Born or Poisson-Boltzmann implicit solvent models.

See Section 3.1 for information about using this option. Default is 0.

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2.6 Potential function parameters

irism Flag for 3D-reference interaction site model (RISM) molecular solvation method.

See Section3.3for information about this option. Default is 0.

ievb If set to 1, use the empirical valence bond method to compute energies and forces.

See Section 6.3 for information about this option. Default is 0.

iamoeba Flag for using the amoeba polarizable potentials of Ren and Ponder.[28, 29] When

this option is set to 1, you need to prepare an amoeba namelist with additional

parameters. Also, the prmtop file is built in a special way. See Section 3.5 for more

information about this option. Default is 0.

2.6.2 Particle Mesh Ewald

The Particle Mesh Ewald (PME) method is always "on", unless ntb = 0. PME is a fast

implementation of the Ewald summation method for calculating the full electrostatic energy

of a unit cell (periodic box) in a macroscopic lattice of repeating images. The PME method

is fast since the reciprocal space Ewald sums are B-spline interpolated on a grid and since the

convolutions necessary to evaluate the sums are calculated via fast Fourier transforms. Note

that the accuracy of the PME is related to the density of the charge grid (NFFT1, NFFT2, and

NFFT3), the spline interpolation order (ORDER), and the direct sum tolerance (DSUM\_TOL);

see the descriptions below for more information.

The particle mesh Ewald (PME) method was implemented originally in Amber 3a by Tom

Darden, and has been developed in subsequent versions of Amber by many people, in particular

by Tom Darden, Celeste Sagui, Tom Cheatham and Mike Crowley.[30–33] Generalizations of

this method to systems with polarizable dipoles and electrostatic multipoles is described in

Refs. [34, 35].

The &ewald namelist is read immediately after the &cntrl namelist. We have tried hard to

make the defaults for these parameters appropriate for solvated simulations. Please take care

in changing any values from their defaults. The &ewald namelist has the following variables:

nfft1, nfft2, nfft3 These give the size of the charge grid (upon which the reciprocal sums are

interpolated) in each dimension. Higher values lead to higher accuracy (when the

DSUM\_TOL is also lowered) but considerably slow the calculation. Generally

it has been found that reasonable results are obtained when NFFT1, NFFT2 and

NFFT3 are approximately equal to A, B and C, respectively, leading to a grid

spacing (A/NFFT1, etc.) of 1.0 Å. Significant performance enhancement in the

calculation of the fast Fourier transform is obtained by having each of the integer

NFFT1, NFFT2 and NFFT3 values be a product of powers of 2, 3, and/or 5. If the

values are not given, the program will chose values to meet these criteria.

order The order of the B-spline interpolation. The higher the order, the better the accu-

racy (unless the charge grid is too coarse). The minimum order is 3. An order of 4

(the default) implies a cubic spline approximation which is a good standard value.

Note that the cost of the PME goes as roughly the order to the third power.

verbose Standard use is to have VERBOSE = 0. Setting VERBOSE to higher values (up to

a maximum of 3) leads to voluminous output of information about the PME run.

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ew\_type Standard use is to have EW\_TYPE = 0 which turns on the particle mesh ewald

(PME) method. When EW\_TYPE = 1, instead of the approximate, interpolated

PME, a regular Ewald calculation is run. The number of reciprocal vectors used

depends upon RSUM\_TOL, or can be set by the user. The exact Ewald summation

is present mainly to serve as an accuracy check allowing users to determine if

the PME grid spacing, order and direct sum tolerance lead to acceptable results.

Although the cost of the exact Ewald method formally increases with system size

at a much higher rate than the PME, it may be faster for small numbers of atoms

(< 500). For larger, macromolecular systems, with > 500 atoms, the PME method

is significantly faster.

dsum\_tol This relates to the width of the direct sum part of the Ewald sum, requiring that

the value of the direct sum at the Lennard-Jones cutoff value (specified in CUT

as during standard dynamics) be less than DSUM\_TOL. In practice it has been

found that the relative error in the Ewald forces (RMS) due to cutting off the direct

sum at CUT is between 10.0 and 50.0 times DSUM\_TOL. Standard values for

DSUM\_TOL are in the range of 10−6 to 10−5 , leading to estimated RMS deviation

force errors of 0.00001 to 0.0005. Default is 10−5 .

rsum\_tol This serves as a way to generate the number of reciprocal vectors used in an

Ewald sum. Typically the relative RMS reciprocal sum error is about 5-10 times

RSUM\_TOL. Default is 5 x 10−5 .

mlimit(1,2,3) This allows the user to explicitly set the number of reciprocal vectors used in a

regular Ewald run. Note that the sum goes from -MLIMIT(2) to MLIMIT(2) and

-MLIMIT(3) to MLIMIT(3) with symmetry being used in first dimension. Note

also the sum is truncated outside an automatically chosen sphere.

−1

ew\_coeff Ewald coefficient, in Å . Default is determined by dsum\_tol and cutoff. If it is

explicitly inputed then that value is used, and dsum\_tol is computed from ew\_coeff

and cutoff.

nbflag If nbflag = 0, construct the direct sum nonbonded list in the "old" way, i.e. update

the list every nsnb steps. If nbflag = 1 (the default when imin = 0 or ntb > 0),

nsnb is ignored, and the list is updated whenever any atom has moved more than

1/2 skinnb since the last list update.

skinnb Width of the nonbonded "skin". The direct sum nonbonded list is extended to cut

+ skinnb, and the van der Waals and direct electrostatic interactions are truncated

at cut. Default is 2.0 Å. Use of this parameter is required for energy conservation,

and recommended for all PME runs.

nbtell If nbtell = 1, a message is printed when any atom has moved far enough to trigger a

list update. Use only for debugging or analysis. Default of 0 inhibits the message.

netfrc The basic "smooth" PME implementation used here does not necessarily conserve

momentum. If netfrc = 1, (the default) the total force on the system is artificially

removed at every step. This parameter is set to 0 if minimization is requested,

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which implies that the gradient is an accurate derivative of the energy. You should

only change this parameter if you really know what you are doing.

vdwmeth Determines the method used for van der Waals interactions beyond those included

in the direct sum. A value of 0 includes no correction; the default value of 1 uses a

continuum model correction for energy and pressure.

eedmeth Determines how the switch function for the direct sum Coulomb interaction is eval-

uated. The default value of 1 uses a cubic spline. A value of 2 implies a linear

table lookup. A value of three implies use of an "exact" subroutine call. When

eedmeth=4, no switch is used (i.e. the bare Coulomb potential is evaluated in the

direct sum, cut off sharply at CUT). When eedmeth=5, there is no switch, and a

distance-dependent dielectric is used (i.e. the distance dependence is 1/r2 rather

than 1/r). The last two options are intended for non-periodic calculations, where

no reciprocal term is computed.

eedtbdns Density of spline or linear lookup table, if eedmeth is 1 or 2. Default is 500 points

per unit.

column\_fft 1 or 0 flag to turn on or off, respectively, column-mode fft for parallel runs. The

default mode is slab mode which is efficient for low processor counts. The column

method can be faster for larger processor counts since there can be more columns

than slabs and the communications pattern is less congested. This flag has no effect

on non-parallel runs. Users should test the efficiency of the method in comparison

to the default method before performing long calculations. Default is 0 (off)