

README FOR FREE ENERGY BENCHMARK V1.0

Shirts Research Group; May 18, 2011

I. Benchmark Test Set Energies:

The benchmark set contains starting configurations and parameter files for all 100 uncorrelated starting configurations in three formats, corresponding to three different molecular dynamics packages, GROMACS (*.gro, *.top & *.mdp), AMBER (*.inpcrd, *.prmtop, *.in) and DESMOND (*.cms & *.cfg). Additionally, we have calculated the single point energies of the 100 structures using the input files and the corresponding MD package. Coordinates are matched to 0.00001 Angstroms, the highest precision that all of the programs can distinguish.

II. Difficulties in Exact Energy Matching:

Significantly, single point configuration energies calculated with typical run parameters for different MD programs do not match each other. Each simulation package differs in the way long-range energy corrections are implemented for both van der Waals and Coulomb interactions, use different tapering functions. Additionally, the choice of combination rules makes it difficult to compare force field parameters directly without significant manipulation of input files. Even the short range van der Waals and Coulomb interactions can differ as each MD program uses different schemes to perform cutoffs over charge groups straddling the cutoff. We have therefore reported two different single point energies from single point simulations; one with

A. Agreement in combination rule: AMBER can use only use Lorentz–Bertholot combination rules (arithmetic mean for σ_{ij} and geometric mean for ϵ_{ij}), while DESMOND and GROMACS can also use the geometric combination rule (using geometric mean for both for σ_{ij} and ϵ_{ij}). The simulation tests performed here were performed with the geometric combination rule. In order to obtain equivalent energies in AMBER, we tailored σ_i and σ_j such that the combined σ_{ij} using Lorentz–Bertholot rules match the σ_{ij} obtained from geometric combining rules. For both methane solvation and dipole inversion, there are only two particle types in each simulation: σ_m (corresponding to solute) and σ_o (corresponding to water oxygen). We calculate an effective σ_m^E as follows: by geometric combining rules, $(\sigma_{mo})_G = (\sigma_m * \sigma_o)^{1/2}$ and with Lorentz–Bertholot rules $(\sigma_{mo})_{LB} = (\sigma_m^E + \sigma_o)/2$. Setting $(\sigma_{mo})_G = (\sigma_{mo})_{LB}$, we get $\sigma_m^E = 2(\sigma_{mo})_G - \sigma_o$. For both of these cases, there are no solute-solute terms, so the total energy remains the same.

However, for anthracene solvation we have 3 particle types: σ_{CH} (corresponding to aromatic carbon with two aromatic carbon neighbors and one hydrogen neighbor), σ_C (corresponding to aromatic carbon with three aromatic carbon neighbors) and σ_o (corresponding to water oxygen). We have now 3 σ_{ij} terms to match σ_{Co} , σ_{CHO} , σ_{CHC} . Among the three it is possible only to match any two. Since anthracene has a nearly rigid structure, deviations in σ_{CHC} will alter the 1-4 intramolecular interaction by approximately 7 kJ/mol. Aside from slight twisting allowed by improper dihedrals, will remain essentially fixed for all configurations of the system. We therefore choose to match σ_{CHO} , and σ_{Co} , rather than σ_{CHC} by calculating calculate σ_C^E and a σ_{CH}^E .

B. Agreement in Cutoff

All simulation packages use slightly different potential tapering functions, so it is impossible to match simulations between different packages using tapering alone. Even using strict cutoffs, however, there are difficulties. GROMACS uses a group based cutoff, so cutoffs of equal length in DESMOND and AMBER are not equivalent. Because of the implementation of charge group dependent cutoffs with GROMACS, we have used a switching potential with a very small switching distance (0.000001 nm), which approximates to strict cutoff in GROMACS; switching distances any smaller do not further change the energy.

C. Agreement in PME Parameters:

Particle Mesh Ewald implementations are sufficiently different between the codes that cutoffs that are in theory equivalent give energies that may differ by up to 40-50 kJ/mol. However, if longer cutoffs are used, the differences are significantly reduced, to the 0.5-2 kJ/mol level.

III. Best Matches to Parameters used in the Benchmark Set Tests:

Energies were calculated by running single point MD runs with AMBER and DESMOND parameters which best approximate parameters used in our molecular dynamics simulations using GROMACS (Table 1).

Table 1 Single point simulation parameters for MD_sim_parm energies for methane solvation, dipole inversion, anthracene solvation. The second set of parameters for number of grid points is for dipole inversion, which had a larger box.

GROMACS	AMBER	DESMOND
PME (switch 0.88nm, cutoff 0.9nm)	PME (cutoff = 0.9 nm)	PME (taper 0.88nm, cutoff 0.9nm)
Fourier Spacing 0.12nm (nkx 32, nky 32 nkz 32)	(nfft1 32, nfft2 32, nfft3 32) (nfft1 36, nfft2 36, nfft3 36)	(n_k = [32 32 32]) (n_k = [36 36 36])

(nkx 36, nky 36 nkz 36)		
Order of spline 4 Ewald_tolerance 1.0e-08	Order of spline 4 Ew_coeff 0.43	order = [4 4 4] r_spread = 4.0
Vdw (switch 0.8nm, cutoff 0.9nm)	Vdw (cutoff = 0.9 nm)	vdw (taper 0.88nm, cutoff 0.9nm)

IV: Long Cutoff Parameters

As second series of single point energy calculations was performed using simulation parameters that match as closely as possible. Single point energies were calculated with increased cutoffs, smaller Fourier spacing, higher order spline interpolation, the same Fourier space vectors nx, ny, nz, and same cutoff scheme followed in all three packages. The GROMACS van der Waals switching function is used to obtain a strict, non-group based cutoff. PME cutoff is kept slightly larger than that of van der Waals to match rlist as required by GROMACS. PME cutoffs are as long as is possible with the box sizes for all three programs before the simulation failing to run for one of the programs (in this case, AMBER).

Table 2 Single point simulation parameters for high cutoff energies for methane solvation and anthracene solvation:

GROMACS	AMBER	DESMOND
PME (switch 1.19999999nm, cutoff 1.2nm)	PME (cutoff = 1.2 nm)	PME (cutoff 1.2nm)
Fourier Spacing 0.06nm (nkx 54, nky 54 nkz 54)	nfft1 50, nfft2 50, nfft3 50	n_k = [50 50 50]
Order of spline 6 Ewald tol. 10e-08	Order of spline 6 Ew_coeff 0.43	order = [6 6 6] r_spread = 4.0
vdW (switch 1.19999999nm, cutoff 1.2nm)	vdW (cutoff = 1.2 nm)	vdW (cutoff 1.2nm)

Table 3 Single point simulation parameters for high cutoff energies for dipole inversion:

GROMACS	AMBER	DESMOND
PME (cutoff 1.6nm)	PME (cutoff = 1.5 nm)	PME (cutoff 1.5nm)
Fourier Spacing 0.06nm (nkx 60, nky 60 nkz 60)	nfft1 60, nfft2 60, nfft3 60	n_k = [60 60 60]
Order of spline 6 Ewald tol. 10e-08	Order of spline 6 Ew_coeff 0.43	order = [6 6 6] r_spread = 4.0
vdw (switch 1.49999999nm, cutoff 1.5nm)	Vdw (cutoff = 1.5 nm)	Vdw (cutoff 1.5nm)

V. Format of output:

All energies correspond to an unconstrained start with the input coordinate files. These energies are reported in two different files for each set of parameters. One file (final_olypot.txt) contains only potential energies corresponding to each configuration calculated in GROMACS, AMBER, and DESMOND. The second file (final_full.txt) has a breakdown of the potential energy into its components: bond energy, angle energy, dihedral energy, Lennard-Jones short range energy, Lennard-Jones dispersion correction energy beyond the cutoff, total Lennard-Jones energy, 1-4 Lennard Jones interaction energy, Coulomb short range interaction energy, Coulomb interaction energy in reciprocal space, total Coulomb interaction energy and 1-4 Coulomb interaction energy. Some MD packages do not print out all the energy components in their output, or add two or three components together into a single term. Comparisons are therefore not always possible between all the energy components for all packages.

VI. File Organization:

The organization of the distribution is as follows. There are four .tgz files, energy_comparisons.tgz, GROMACS.tgz, AMBER.tgz, DESMOND.tgz, containing the single

point energy evaluation results and files for generating the single point energy evaluations using the three molecular simulation packages. The files are laid out as follows:

energy_comparisons/

 Methane_Solvation/

 final_full_shortcutoff.txt

 final_onlypot_shortcutoff.txt

 final_full_longcutoff.txt

 final_onlypot_longcutoff.txt

 Dipole_Inversion/

 final_full_shortcutoff.txt

 final_onlypot_shortcutoff.txt

 final_full_longcutoff.txt

 final_onlypot_longcutoff.txt

 Anthracene_Inversion/

 final_full_shortcutoff.txt

 final_onlypot_shortcutoff.txt

 final_full_longcutoff.txt

 final_onlypot_longcutoff.txt

GROMACS/

 Methane_Solvation/

 gros/

 ms.mdp

 shortcutoff.mdp

 longcutoff.mdp

 Dipole_Inversion/

 gros/

di.top
shortcutoff.mdp
longcutoff.mdp

Anthracene_Solvation/

gros/
as.top
shortcutoff.mdp
longcutoff.mdp

AMBER/

Methane_Solvation/

crds/
ms.prmtop
shortcutoff_md.in
longcutoff_md.in

Dipole_Inversion/

crds/
di.prmtop
shortcutoff_md.in
longcutoff_md.in

Anthracene_Inversion/

crds/
as.prmtop
shortcutoff_md.in
longcutoff_md.in

DESMOND/

Methane_Solvation/

cmss/

shortcutoff.cfg

longcutoff.cfg

Dipole_Inversion/

cmss/

shortcutoff.cfg

longcutoff.cfg

Anthracene_Inversion/

cmss/

shortcutoff.cfg

longcutoff.cfg