Molecular Dynamics Exercise V: The significance of accurate long-range interactions

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This report compares a total of six different methods to treat the long range electrostatic potential in molecular dynamics simulations. For this all methods were used on three test systems (SPC/E water, A-DNA in solvent and B-DNA in solvent) and their performance was evaluated by comparing the peaks of the resulting radial distribution function to experimental values. All simulations were performed using GROMACS.

1 Task I: SPC/E water simulation

1.1 Introduction and Procedure

As the electrostatic potential only decays as $U \propto \frac{1}{r}$, a full treatment would be computationally unfeasible. To address this issue several approximations have been proposed. In this report the performance of six of the them is evaluated. These are the potential shift method (with $r_{cutoff} = 8\,\text{Å}$(SH8) and $r_{cutoff} = 12\,\text{Å}$(SH12)), the truncation method (with $r_{cutoff} = 8\,\text{Å}$(TR8), $r_{cutoff} = 12\,\text{Å}$(TR12) and $r_{cutoff} = 18\,\text{Å}$(TR18)) and the Particle Mesh Ewald Method (PME).

The truncation method just uses the true Coulomb potential just for particles within $r < r_{cutoff}$ and truncates the potential for longer distances. The potential shift method adds a constant to the potential such that it is zero for distances $r > r_{cutoff}$. Finally, the Particle Mesh Ewald method is an improved version of the Ewald lattice summation using the Fast Fourier Transform to increase computation speed. The Ewald lattice summation enables efficient potential calculation by employing additional charge distributions to obtain a fast decaying potential in real space and a smooth potential in Fourier space [1].

For the simulation 2165 water molecules of the SPC/E were placed in a box of size (4 nm × 4 nm × 4 nm). Then an energy minimization, a thermalization using an NVT and a pressure equilibration with a NPT were conducted. Both used respective Berendsen weak coupling methods and were conducted over 10000 steps of $\Delta t = 0.001$ ps and $\Delta t = 0.002$ ps respectively. Prior to any measurement run, a pre production run of 25000 steps of 0.002 ps with Nose-Hoover Thermostat and Parrinello-Rahman barostat was done. The measurement run used 2,500,000 steps of $\Delta t = 0.002$ ps with the same thermostat and barostat.

1.2 Simulation Results

To assess the quality of the results from the six simulations with different treatment of the long range electrostatic forces, the resulting radial distribution functions will be compared to experimental results. The RDF is basically a histogramm of the interparticle distances between

two species of particles. In this case the distance between the oxygen atoms contained in the water molecules is investigated. From experiments it is known that a sharp peak at $0.2799\,\mathrm{nm}$ should be expected signifying the first solvation layers.[3] Further less strongly developed peaks belonging to further layers should appear for larger r . For example, the experiment found that the second peak should be at $0.4515\,\mathrm{nm}$. The results from the six simulation scan be found below (figure 4, table 1.2).

SPC/E Water	SH8	SH12	TR8	TR12	TR18	PME
1st Peak	0.276	0.276	0.276	0.276	0.276	0.274
2nd Peak	0.560	0.430	0.410	0.420	0.450	0.450
			R [nm]			

Table 1: Positions of first and second maxima of the radial distribution function for SPC/E water model.
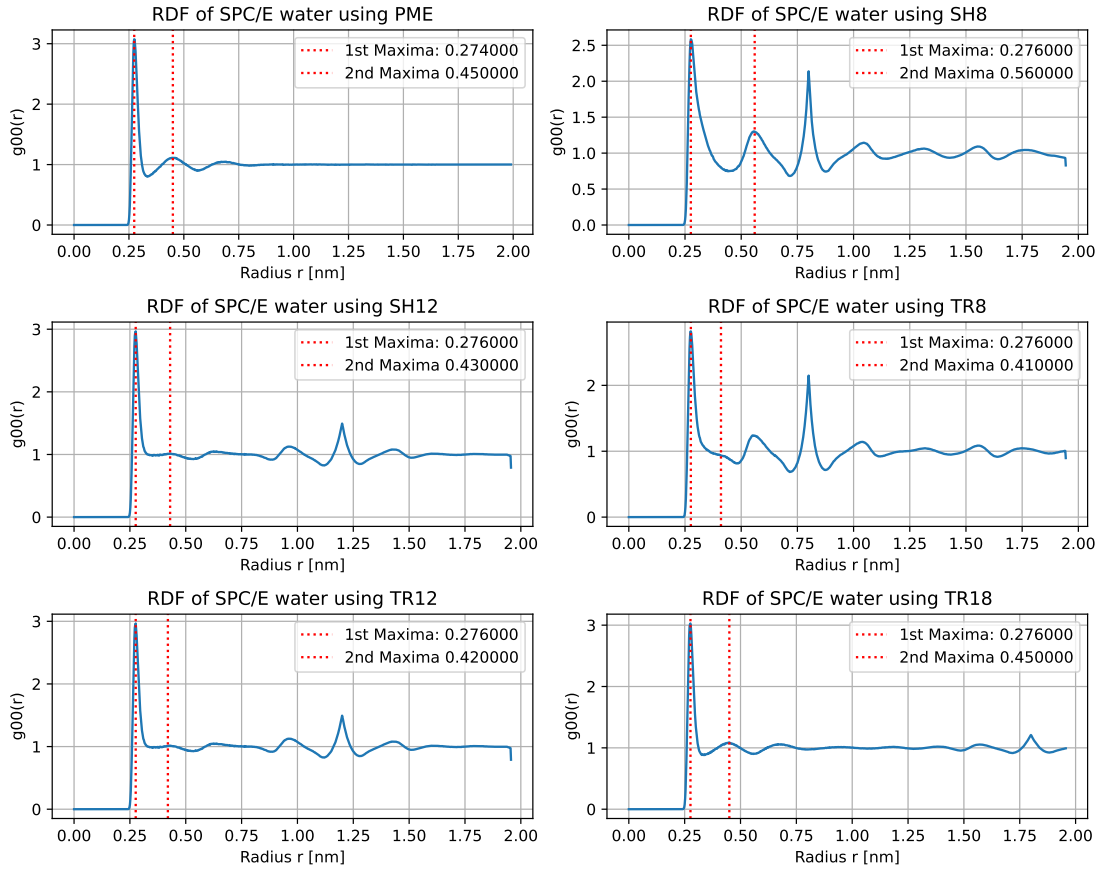

Figure 1: Radial Distribution functions of SPC/E water for different treatments of long range electrostatic forces.

Looking at the plots one finds that the PME method produces a RDF very close to the experimental result. However, the first peak is slighly off in comparison with the other methods, which all yield a distance of $0.276\,\mathrm{nm}$, which is within 2% of the experimental value for the position of the first solvation layer. The expected second maxima only appears for the PME method and the TR18 method. The other methods show only very faint maxima or a larger maxima at larger r values. This is surprising as the second maxima is still be within the respective r_{cutoff} distances. One also observes that all the cutoff methods show an accumulation of atoms at the r_{cutoff} distance. These maxima are artifacts of the methods.

2 Task II: Solvated A-DNA and Solvated B-DNA

2.1 Introduction and Procedure

To further investigate the effects of the long-range potential approximating methods, simulations with more complex biological molecules namely A DNA and B DNA are conducted. For this the respective molecules were placed in a box with dimensions ($5.0\,\text{nm} \times 5.0\,\text{nm} \times 5.0\,\text{nm}$) which was then filled with water molecules of the SPC/E type. Energy minimization, thermal and pressure equilibration was done as described in the previous section. To ensure charge neutrality several ions Na^+ were added to the system. Note that for the SH8 method simulation to run stable, the time step had to be reduced by half.

2.2 Simulation Results

Again a radial distribution function is used to assess the quality of the results. For both A-DNA and B-DNA, the radial distribution of the water oxygen atoms with respect to the neutral phosphate oxygen atoms is investigated. Literature predicts a sharp peak at $0.265\,\text{nm}$ and a smaller peak at about $0.504\,\text{nm}$. After this the radial distribution should remain roughly constant [4].
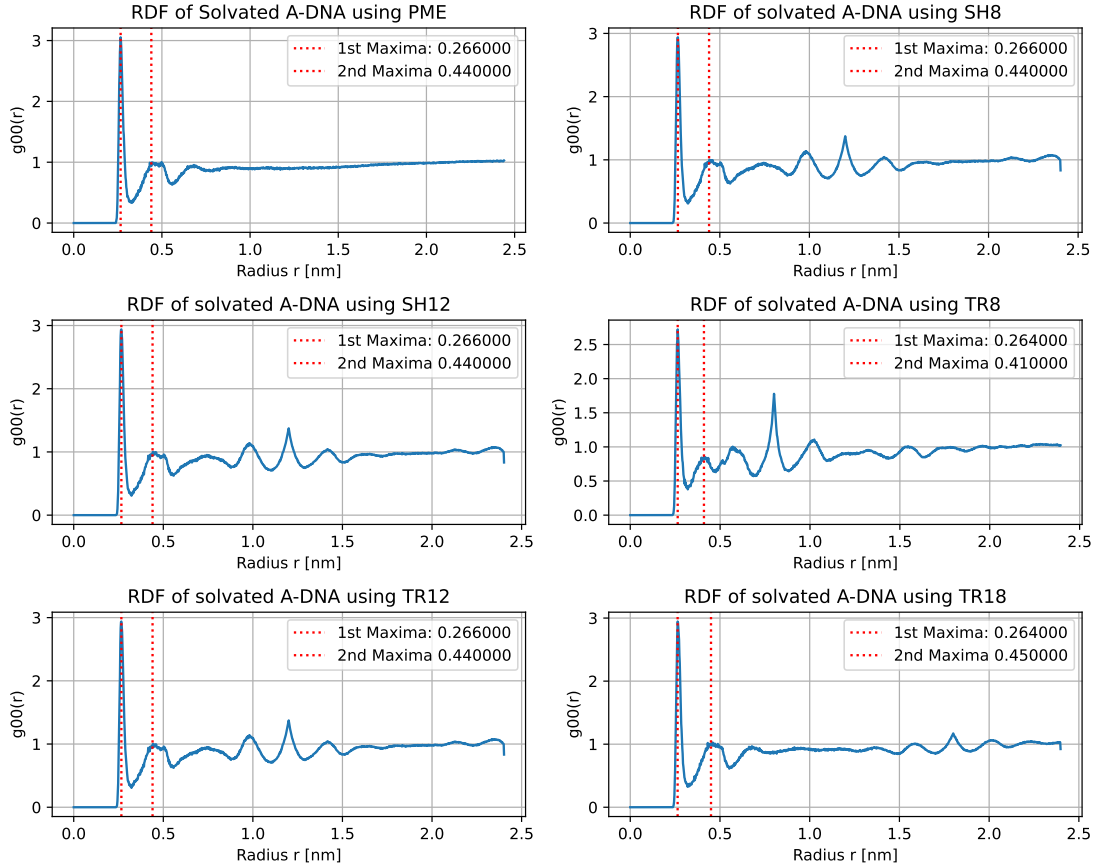

Figure 2: Radial Distribution functions of A-DNA solved in water for different treatments of long range electrostatic forces.

Looking at the plots one finds that the radial distribution function looks almost the same for $r < 0.5\,\text{nm}$. Hence, also the two observed peaks of the function in this region are almost the same for all methods. The difference of the second peak as predicted by literature could be due to the fact that the peak is rather broad. The main differences are in the region

$0.5\,\text{nm} < r < 1.5\,\text{nm}$. Here, according to the literature the function should only have small minimum and then remain constant. This behaviour is only seen in the plots produced by the PEM and the TR18 methods. The other methods, having smaller truncation distances, produce several minima and maxima in this region, which would suggest water solvation layers in this range. Again one notices that a prominent peak is produced right at the cutoff distance. This is also the case for the TR18 method. The radial distribution functions for B-DNA are shown below:
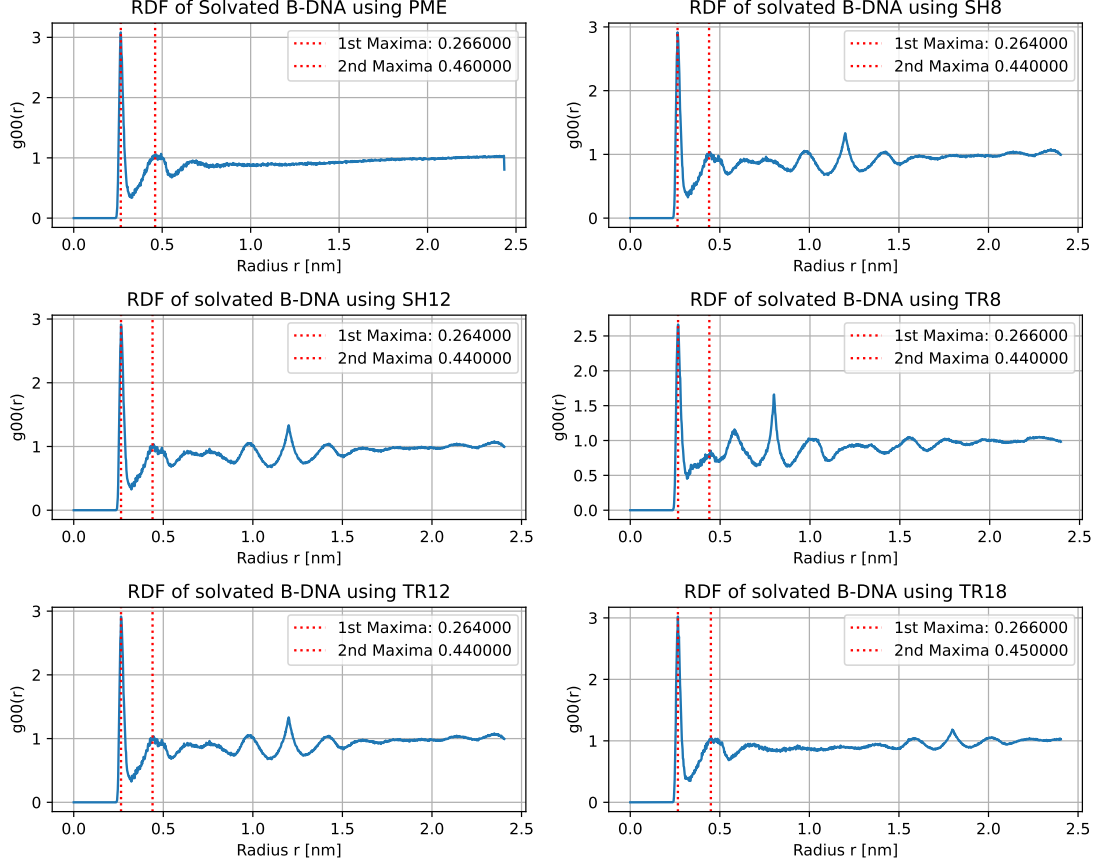

Figure 3: Radial Distribution functions of B-DNA solved in water for different treatments of long range electrostatic forces.

The observations here are identical to the ones form the radial distribution function for the A-DNA. Again PME produces a distribution close to literature, while the cutoff methods produce unphysical distribution peaks in the range $0.5\,\text{nm} < r < 1.5\,\text{nm}$.

Furthermore, the methods should reproduce the fact that B-DNA is slightly more stable than A-DNA which is shown in a lower RMSD value. To test this, all RMSD values with respect to the starting configuration are plotted against simulation time. Furthermore, the time averages are provided (taken after equilibrium value has been reached).
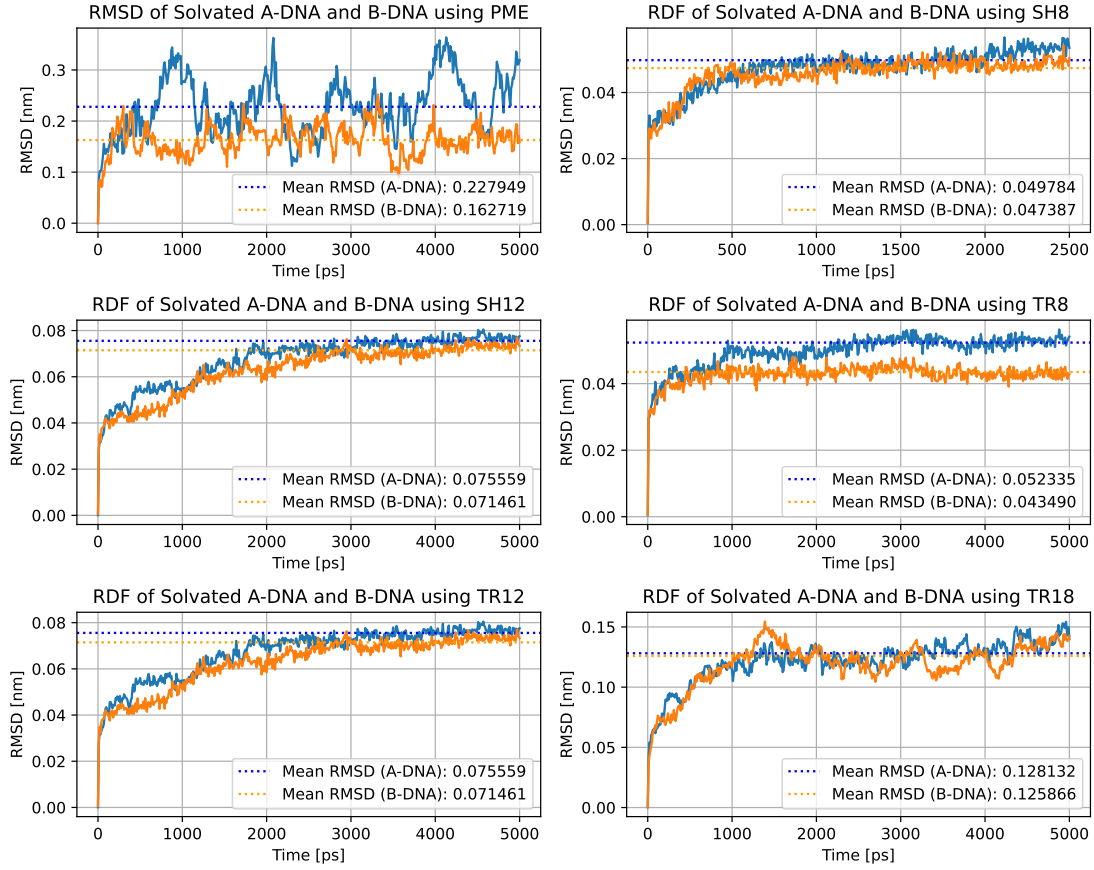
Figure 4: RMSD for A-DNA and B-DNA in water for different treatments of long range electrostatic forces.

Looking at the graphs above one can immediately see that the cutoff methods produce fairly small RMSD values. Comparing the results for TR8, TR12 and TR18, it seems that the value of the RMSD increases with the cutoff radius. Additionally, all methods correctly predict that the RMSD of A-DNA should be larger than the one from B-DNA. Still, only the RMSD average of the PEM method is close to the literature value [5]. The reason for the small RMSD values of the cutoff methods is likely the fact that due to the shortened range of the electrostatic interactions the negatively charged parts of the molecule do not repel each other due to behind behind the cutoff. In this way the force which would usually force the molecules to expand is not felt. From here it also follows why the RMSD of TR18 is larger than of TR12 and TR8: more negative charges on the molecule are seen by each charge and hence can force the molecule to stretch. (According to Wikipedia the distances between the negatively charged phosphate groups are 5.9 Å (A-DNA) and 7.0 Å (B-DNA), which would support this hypothesis [6].)

3   Discussion

Looking at the results presented above the Particle Mesh Ewald Method gives clearly the best results. All methods with a cutoff produce artefacts in the radial density function. Especially at the cutoff range usually an artificially high concentration is created. While the TR18 method produces the best results out of all cutoff methods and produces a good rdf for short to medium range, it still produces an unphysical density of water molecules at $r_{cutoff} = 18$ Å. Furthermore, when considering the required computation times for each method, TR18 requires 3 to 6 times the computation time the PEM method needs. One easily identifies PEM as the most best

method to use as it gives the best results and only requires relatively short computation time (between $r_{cutoff} = 8\,\text{Å}$ and $r_{cutoff} = 12\,\text{Å}$ methods).

System	SH8	SH12	TR8	TR12	TR18	PME
SPC/E Water	24835.479	52682.989	32362.666	52661.818	140247.248	31014.126
A-DNA in solvent	42156.944	140036.047	45626.906	102975.487	262078.542	70083.366
B-DNA in solvent	40752.084	103903.346	46429.297	103874.391	264741.892	59763.313
	Core time [s]					

Table 2: Required Core times for the different methods in seconds.

4   Bibliography

[1] GROMACS Reference Manual https://manual.gromacs.org/documentation/2019-rc1/reference-manual/algorithms/molecular-dynamics.html [accessed 18.05.2023; 18:31]

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[4] Jaiswal, Srivasta, Pandey, Bandyopadhyay; Microscopic picture of water-ethyene glycol interaction near a model DNA by computer simulation; 2018; PLoS ONE 13(11): e0206359

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